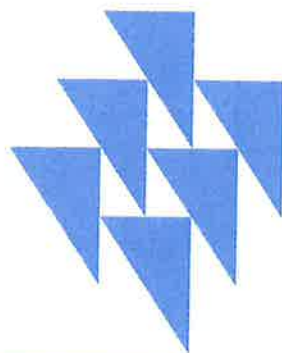Raine Hermans

INTERNATIONAL MEGA-TRENDS AND GROWTH PROSPECTS OF THE FINNISH BIOTECHNOLOGY INDUSTRY

Essays on New Economic Geography,
Market Structure of the Pharmaceutical
Industry, Sources of Financing, Intellectual
Capital and Industry Projections

Raine Hermans

International Mega-Trends and Growth Prospects of the Finnish Biotechnology Industry

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Essays on New Economic Geography,
Market Structure of the Pharmaceutical Industry,
Sources of Financing, Intellectual Capital
and Industry Projections

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INTERNATIONAL MEGA-TRENDS AND GROWTH PROSPECTS OF THE FINNISH BIOTECHNOLOGY INDUSTRY – *Essays on New Economic Geography, Market Structure of the Pharmaceutical Industry, Sources of Financing, Intellectual Capital and Industry Projections.*[1] Helsinki: ETLA, Elinkeinoelämän Tutkimuslaitos, The Research Institute of the Finnish Economy, 2004, 172 p. (A, ISSN 0356-7435; No. 40). ISBN 951-628-410-8.

ABSTRACT: The aim of this dissertation is to predict the economic growth impacts of the Finnish biotechnology industry on the Finnish economy and analyze the international and industry-specific factors behind these predictions. The New Economic Geography of the European regions suggests that spatial agglomeration of economic activities will be strengthened internationally if European integration deepens. Sparsely populated geographic peripheries, such as Finland, might have difficulties in creating a critical mass of factors of production. For example, the Finnish pharmaceutical industry has enjoyed high regulatory protection and it has achieved similar price markups during the 70s-90s as its counterpart in the US. After changes in regulatory systems and problems in drug development within large pharmaceutical companies strong pressure for lower markups arose. This drives large pharmaceutical companies to outsource their R&D activities to small biotechnology companies. The large companies are also interested in taking over the most prominent and maturing biotechnology companies. The takeovers offer one pathway of exit to the investors of start-up companies.

According to the analysis of small and medium-sized Finnish biotechnology industry, it seems that most promising biotechnology companies have a well-balanced combination of intellectual capital. According to the analysis of intellectual capital, there are many promising branches in addition to drug development activities, such as applications related to biomaterials, diagnostics, food and feed, industrial enzymes, agriculture and forestry. Despite expectations of rapid growth, it will take decades rather than years for the biotechnology industry to catch up with the

three pillars of the Finnish industry: pulp and paper, metal products and engineering, and the electronics industries. To fulfill the expectations, there is a need for the creation of a critical mass of factors of production and comparative advantage by building collaboration and financing networks between the biotechnology industry and traditional industries, such as forest industry, electronics industry and pharmaceutical industry. Most of the current Finnish biotechnology companies are related to health care activities. The health care sector has reached a major crossroads owing to the aging of the population and advances made in medical science. On the one hand, the aging of the population and the medical possibilities to diagnose and treat more illnesses than before increase the cost pressures on health care. On the other hand, biotechnology applications are expected to spawn cost savings over the long run by, for example, making time-consuming diagnostic methods more efficient and facilitating targeted therapy. As a policy implication for companies, public sector and academia, this dissertation concludes how the Finnish biotechnology industry could offer solutions to the cost crisis in health care while at the same time spurring development of an internationally competitive industrial cluster.

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(in Finnish; Translation in Celebration)

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Valmistelimme siirtymistäni ETLAn ennusteryhmästä Etlatietoon yritys- ja toimialatutkimuksen pariin vuoden 2001 aikana yhdessä Pekka Ylä-Anttilan ja Petri Rouvisen kanssa. Petri ja Pekka näkivät tuohon aikaan, että bioteollisuus on tutkimisen arvoinen toimiala. Olin osallistunut aiemmin Petrin vetämään projektiin, jossa tarkasteltiin Suomen kemianteollisuuden kansainvälistä kilpailukykyä. Tuossa yhteydessä tuli esiin bioteknisten sovellusten mahdollinen merkitys arvonlisäyksen aikaansaajana. Tein Petrin kanssa useita Suomen bioteollisuutta koskevia tutkimushakemuksia. Petrin eräänä ajatuksena oli liittää bioteollisuuden kehitys porterilaiseen klusteritarkasteluun. Väitöskirjan jälkeisessä tutkimuksessa on tarkoitus analysoida Suomen bioteknisen tutkimuksen osaamisperustojen ja markkinapotentiaalin välistä yhteyttä myös porterilaisesta näkökulmasta.

Vuoden 2002 alusta siirryin ETLAn omistamaan Etlatieto Oy:hyn ja samalla Pekka Ylä-Anttilan johtamaan yritys- ja toimialatutkimusryhmään. Ennusteryhmässä olin pohtinut jonkin verran Nokian vaikutuksia Suomen kansantalouteen ja oli luontevaa aloittaa tutkimus Nokian roolista Suomen innovaatiojärjestelmässä yhdessä Jyrki Ali-Yrkön kanssa. Jyrki ja Pekka jakoivat avoimesti tietojaan ja käsityksiään Suomen innovaatiojärjestelmästä. Tällä on ollut myöhemmin tärkeä sija bioteollisuuden tutkimuksessa, onhan innovaatiojärjestelmä tiedeperustaisen bioteollisuuden keskeinen voimavara.

Tein yhteistyötä VTT:stä ETLAan siirtyneen Terttu Luukkosen kanssa bioteollisuutta koskevien rahoitushakemusten loppuun viemisessä. Etlatieto sai rahoitusta tutkimushankkeeseen "Bioteollisuus osana kansallista innovaatiojärjestelmää" kauppa- ja teollisuusministeriön ja Tekesin Pro-ACT-tutkimusohjelmasta ja myöhemmin NeoBio-tutkimusohjelmasta. Aloin suunnitella Tertun kanssa bioteknikkayrityksille suunnattua kyselyä. Kiitän Terttua yhteistyöstä.

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Raine Hermans

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INTERNATIONAL MEGA-TRENDS AND GROWTH PROSPECTS OF THE FINNISH BIOTECHNOLOGY INDUSTRY:
An Introductory and Concluding Essay[2]

Abstract

The aim of this dissertation is to predict the economic growth impacts of the Finnish biotechnology industry on the Finnish economy and analyze the international and industry-specific factors behind these predictions. The New Economic Geography of the European regions suggests that spatial agglomeration of economic activities will be strengthened internationally if European integration deepens. Sparsely populated geographic peripheries, such as Finland, might have difficulties in creating a critical mass of factors of production. For example, the Finnish pharmaceutical industry has enjoyed high regulatory protection and it has achieved similar price markups during the 70s-90s as its counterpart in the US. After changes in regulatory systems and problems in drug development within large pharmaceutical companies strong pressure for lower markups arose. This drives large pharmaceutical companies to outsource their R&D activities to small biotechnology companies. The large companies are also interested in taking over the most prominent and maturing biotechnology companies. The takeovers offer one pathway of exit to the investors of start-up companies.

According to the analysis of small and medium-sized Finnish biotechnology industry, it seems that most promising biotechnology companies have a well-balanced combination of intellectual capital. According to the analysis of intellectual capital, there are many promising branches in addition to drug development activities, such as applications related to biomaterials, diagnostics, food and feed, industrial enzymes, agriculture and forestry. Despite expectations of rapid growth, it will take decades rather than years for the biotechnology industry to catch up with the three pillars of the Finnish industry: pulp and paper, metal products and

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engineering, and the electronics industries. To fulfill the expectations, there is a need for the creation of a critical mass of factors of production and comparative advantage by building collaboration and financing networks between the biotechnology industry and traditional industries, such as forest industry, electronics industry and pharmaceutical industry. Most of the current Finnish biotechnology companies are related to health care activities. The health care sector has reached a major crossroads owing to the aging of the population and advances made in medical science. On the one hand, the aging of the population and the medical possibilities to diagnose and treat more illnesses than before increase the cost pressures on health care. On the other hand, biotechnology applications are expected to spawn cost savings over the long run by, for example, making time-consuming diagnostic methods more efficient and facilitating targeted therapy. As a policy implication for companies, public sector and academia, this dissertation concludes how the Finnish biotechnology industry could offer solutions to the cost crisis in health care while at the same time spurring development of an internationally competitive industrial cluster.

Key Words: spatial agglomeration, price-cost margins, capital structure, intangible assets, input-output analysis.

1.1 Introduction

1.1.1 Background and Objectives

The topic of the present doctoral dissertation is the economic growth prospects of the Finnish biotechnology industry. The dissertation is based on five partly overlapping studies on the topic (Essay 1, Hermans, 2003b; Essay 2, Hermans – Linnosmaa, 2003; Essay 3, Hermans, 2003a, 2004; Essay 4, Hermans – Kauranen, 2003 and Essay 5, Hermans – Kulvik, 2004a). Each research study is included in the dissertation as a separate essay. Essays 1 and 2 deal with economic mega-trends behind the Finnish biotechnology industry and the rest of the essays analyze the present and anticipated states of the Finnish biotechnology industry.

The objective of the introductory essay of the doctoral dissertation is to present an overview of and conclusions on the five essays. The introductory essay analyzes Finland's biotechnology industry from the viewpoints of international and regional integration (Essay 1), the market structure of the pharmaceutical industry (Essay 2), capital and ownership structures of bio-pharmaceutical companies (Essay 3), as well as companies' intangible assets and growth expectations (Essay 4) and discusses the results of a forecasting model based on the companies' growth expectations and the probability of their success (Essay 5).

At the beginning of the introductory essay an overview of the innovation policy of Finland from the perspective of the biotechnology industry is given. The biotechnology industry plays a special role in Finnish growth and innovation policy. This special role has shaped the questions addressed in these five studies and the way in which the research was carried out.

Because biotechnology has played a significant role in Finnish innovation policy, certain conclusions are drawn regarding each of the five studies both from the viewpoint of firms' strategies as well as business and innovation policy. The last essay discusses the potential of the biotechnology industry to grow into one of Finland's main manufacturing industries or growth clusters, comparing it to the forest, machinery and electronic industries.[3]

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[3] See also Hermans and Ylä-Anttila (2004), which deals with the same topic.

1.1.2 Definitions

The biotechnology industry does not exist as an individual branch in any official statistical classification. A single definition has preliminarily been agreed upon at an OECD ad hoc meeting held in 2002.[4] According to the definition, biotechnology is: *"The application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services."* In addition, a list-based definition specifies biotechnology processes in more detail.[5] Companies can develop biotechnology processes or they can apply biotechnology processes in their production. The former can be called biotechnology research companies and the latter biotechnology using firms. An individual company can be classified as belonging simultaneously to both categories. In this case the company can be called as an integrated firm.[6]

The present dissertation employs with the biotechnology related data drawn from the ETLA survey.[7] The ETLA survey was conducted in the beginning of the year 2002 and it covers 84 companies.[8] There were approximately 120 biotechnology companies in Finland in the end of the year 2001. Thus, the coverage of the data seems sufficient. The problem of how to define biotechnology companies was solved by choosing the firms in the database of the Finnish Bioindustries Federation to represent the population of Finnish biotechnology companies.

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[4] The third OECD ad hoc meeting on biotechnology statistics was held in Espoo, Finland 13-15 May 2002.

[5] The following five categories were agreed on at the OECD ad hoc meeting. The list is indicative (not exhaustive):

   a) DNA (the coding): genomics, pharmaco-genetics, gene probes, DNA sequencing/synthesis/amplification, genetic engineering.

   b) Proteins and molecules (the functional blocks): protein/peptide, sequencing/synthesis, lipid/protein engineering, proteomics, hormones, and growth factors, cell receptors/signalling/pheromonics.

   c) Cell/tissue culture, tissue engineering, hybridization, cellular fusion, vaccine/immune stimulants, embryo manipulation.

   d) Process biotechnologies: bioreactors, fermentation, bioprocessing, bioleaching, bio-pulping, bio-bleaching, biodesulphurization, bioremediation and biofiltration.

   e) Sub-cellular organisms: gene therapy, viral vectors.

[6] See Nilsson (2001).

[7] ETLA stands for The Research Institute of the Finnish Economy.

[8] The first descriptive analysis of ETLA biotechnology survey was presented by Hermans and Luukkonen (2002).
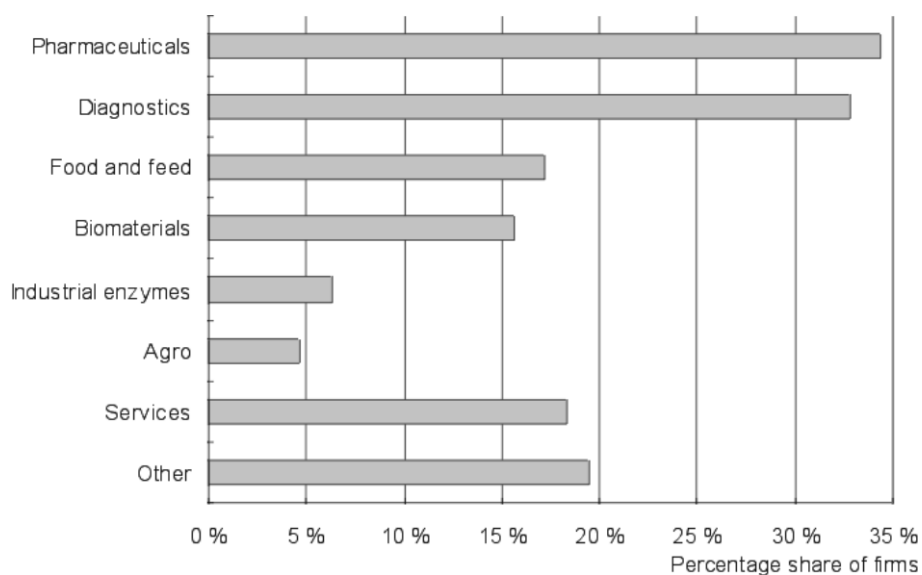
Figure 1. **Activities of the biotechnology companies in ETLA survey by branches.**

The Finnish Bioindustries Federation classified its member companies into 7 categories. In the ETLA survey an individual company could classify itself simultaneously in several categories. Figure 1 depicts in which categories the biotechnology companies consider themselves to be. Most of the companies are involved in the businesses of pharmaceuticals and diagnostics.

1.2 Current Situation

The following discussion on the current situation of the Finnish innovation system is partially based on Hermans and Ylä-Anttila (2004). The structural change that occurred in the Finnish economy in the 1990s was relatively swift from an international perspective as well as relative to Finland's own economic history. The transformation toward a competence-driven economy has continued for several decades already, but it accelerated considerably in the 1990s and strengthened the structural change. Technology policy played an important role even though most of the development was company driven (Ylä-Anttila – Lemola, 2003). Economic integration and the opening of the economy to international competition spawned a competence-driven phase of growth. The innovation intensive sectors benefited more than other sectors from the new markets. Productivity and capital efficiency increased considerably.

The roots of the Finland's current innovation policy date back to the 1970s and 1980s, when the decisions to increase science and technological investment were made.[9] Then and partly already in the 1960s the basic pillars of research policy were built and the first programs for applied research were started. The goal was to lift the technological level of Finnish industries and to reduce the dependence on raw material driven production and exports. The one-sided structure of exports was regarded as a problem – the intermittent problems with deep imbalances in the economy were due largely to strong cyclical fluctuations in the export industry.

Still at the end of the 1970s Finland's research and development (R&D) expenditures relative to gross domestic product (GDP) was one of the lowest in the industrialized countries. The 1980s was a decade for systematic and goal-oriented technology policy. One of the key vehicles for implementing this policy was the National Technology Agency of Finland, Tekes, established in 1983. Regional science parks and technological centers were established to support the dissemination of research findings and utilization of regionally generated information. The R&D expenditures grew in real terms at a rate of about 10 percent per annum, which was one of the fastest in the OECD countries.

The main tools for implementing technology policy were technology programs, which fostered the implementation of a strategic innovation policy, thus making use of the small country's scarce resources. According to this policy, heavy investments were made in information and communication technology (ICT) in several technology programs that were initiated already before the founding of Tekes. The huge success of Nokia and the ICT cluster that emerged around it was a sign of the successful policy choice, even though the policy naturally accounted for only part of the success (Rouvinen – Ylä-Anttila, 2003).

The 1990s can be called a decade of the national innovation system in terms of innovation or science and technology policy. Innovation activities started to be seen more and more as a key product of dialogue and interaction between different actors – companies, research institutes, financiers of innovative activities and other policy makers.

Changes in technology and business policy and innovation policy inevitably have an impact also on the biotechnology sector. The impacts are clearly apparent in at least two respects.

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[9] For more on the background and development of science and technology policy, see Lemola (2002), Georghiou et al. (2003) and Ylä-Anttila – Lemola (2003).
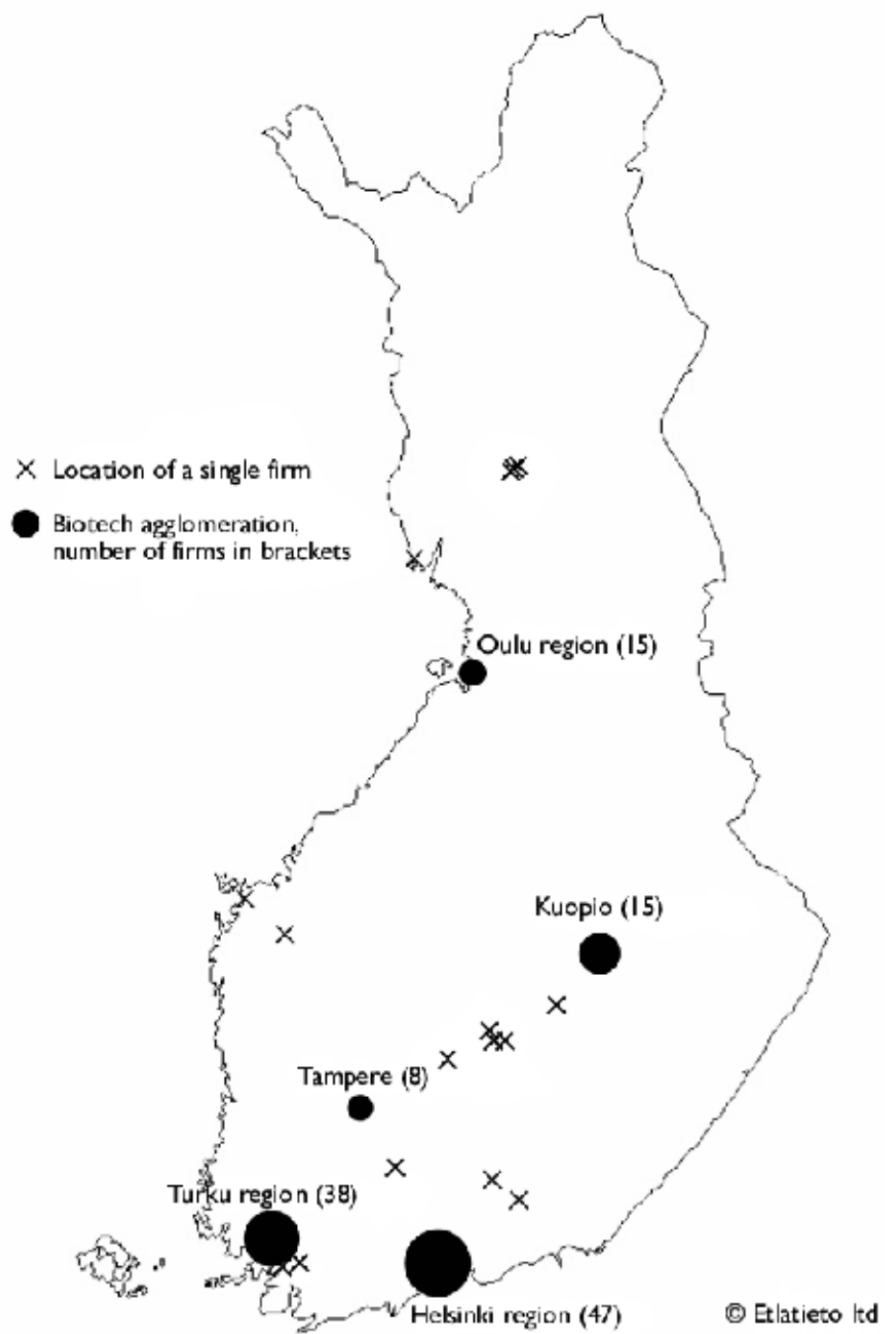
Figure 2. **Location of the Finnish biotechnology companies in 2003.**

First, since it was possible to use policy to foster the success of the ICT sector, it was deemed possible to do the same thing in the biotechnology sector. The R&D investments of the companies in the ICT sector – mainly Nokia – rose sharply in the 1990s and the early 2000s (Ali-Yrkkö and Hermans, 2004). As regards research activities Finland has specialized more in the ICT sector than any other country in the world. Public investment was especially important in the 1980s and 1990s during the recession. By the end of the decade research activity become more company-oriented, even though the ICT sector's share of public research funds is still substantial. Public investment in the ICT sector had spawned a considerable increase in private investment: the ICT sector seems to be an example of a successful strategy of innovation policy, so it could be worthwhile to search for another sector with new potential, biotechnology.

Second, the founding of regional competence centers has had a positive impact on the biotechnology sector and on investment in companies in this sector. Most of the companies in this sector are located in five of the science and technology parks located around Finland (see Figure 2). From the standpoint of the biotechnology and bioresearch, the situation is problematic: it is difficult to find a sufficient critical mass. Furthermore, Kafatos et al. (2002) pointed out that there is little cooperation between the regional biotechnology centers in Finland.

The differences between the biotechnology and ICT sectors from the standpoint of the functioning of the innovation system and technology policy are significant, as Luukkonen and Palmberg (2004) demonstrate. Biotechnology is not closely affiliated with existing sectors that are currently strong in Finland – the sector has no strong manufacturers or growth engines. The Finnish biotechnology sector has concentrated – as in several other countries – on biopharmaceuticals. The significance of the pharmaceutical sector in Finland's industrial structure has nevertheless been relatively small compared to many other countries. There is relatively little biotechnology research and manufacturing activity related to the large traditional processing industries, such as the forest and chemical industry.

The research and manufacturing activity related to biomedicine – or biotechnology in general – has been chosen as a focal point of business and technology policy in almost all developed countries. Competition in the sector is thus keen and demands high investments. The risks related to the public financing of innovation policy and biotechnology are great.

Table 1.   Biotechnology industry in Finnish enterprise sector.

	Million euros			Biotechnology industry's share (%) of enterprise sector	
	Bio-technology industry SMEs	Total bio-technology industry* (incl. multi-sector firms)	Total enterprise sector	SMEs	Total bio-technology industry* (incl. multi-sector firms)
Number of companies	110	130	225,000	0.05 %	0.06 %
Sales revenues	200	1,400	272,000	0.1 %	0.5 %
Value added	90	500	88,000	0.1 %	0.6 %
Employees	2,000	14,000	1,319,000	0.2 %	1.1 %
Exports	120	600	54,000	0.2 %	1.1 %
R&D expenditures	162	300	3,300	4.9 %	9.1 %

Table is based on data for 2001 (ETLA, Statistics Finland)

* Sales revenues and exports of multi-sector companies are estimated for biotechnology production and employment and for employment as a whole.

Sales revenues, value added, exports and R&D expenditures are based on figures provided by enterprises regarding extent of biotechnology activities.

Finland's biotechnology sector is currently quite small. In 2001 the value added by the entire biotechnology sector was about EUR 500 million (table 1). This figure includes an estimate for biotechnology-related production of large multi-sector enterprises. The total value added of small and medium-sized biotechnology enterprises was less than EUR 100 million in 2001.

The situation of the biotechnology industry is illustrated by the fact that the R&D expenditures of the small and medium-sized enterprises (SMEs) are considerably higher (approximately 40%) than their value added. The research investments have for the time being generated very little production. The research investments of SMEs are funded primarily by the government. Since the public financing of the biotechnology sector's research has been about EUR 400 million since the beginning of the 1990s (Figure 3), the average financing per SME has been EUR 3-4 million. This sum includes both direct funding to the SMEs and also funding to universities and research institutions that companies can utilize indirectly.

Mill. euros in 2002 prices
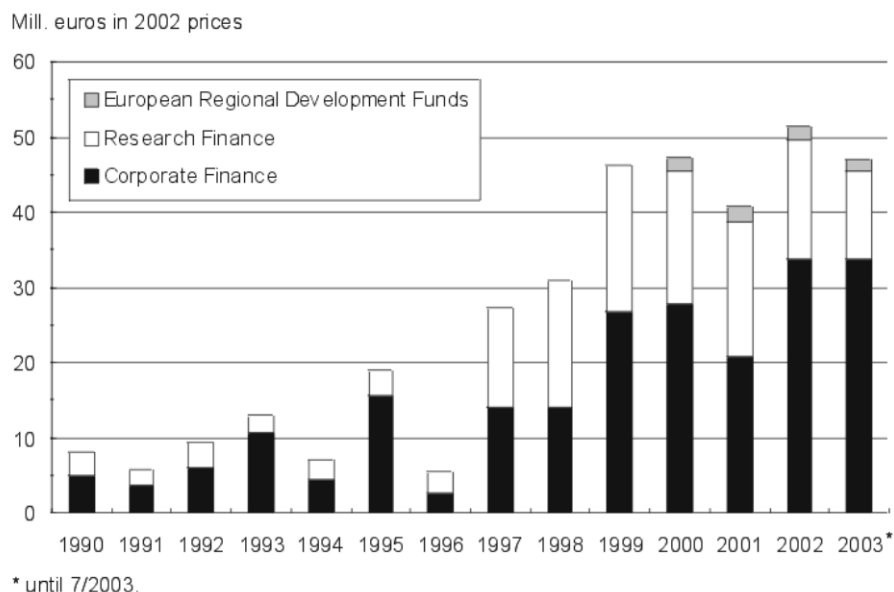
Figure 3. **Biotechnology-related funding from Tekes, The National Technology Agency of Finland, the years 1990-2003.**

Even though public financing has not been comparatively high, relative to the size of the economy and the number of active enterprises it has been of significant magnitude.

1.3 Growth Prospects of Biotechnology Sector

1.3.1 Economic Integration and Regional Competitive Advantages

The biotechnology industry cannot be treated as a sector of its own isolated from the mega-trends affecting international economic developments. Essay 1 investigates the effects of economic integration on the regional location of production in line with the body of the international trade literature known as the new economic geography theory.[10]

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[10] The earlier version of Essay 1 was printed as ETLA's Discussion Paper Series no. 883 (Hermans, 2003b). A preliminary version of the essay was presented in Eco-Mod Conference on Policy Modeling, held 4-6 July 2002 in Brussels.

The main idea of this study is to compare the differences between countries' internal regional structures, on the one hand, and international regional structures, on the other hand. Economic integration can be assumed to be deeper within countries than internationally. For decades there has been free trade within countries and ordinarily clear cultural unity between different regions within the same country. This situation can be considered an extreme economic integration. At the same time, there are certain trade barriers between countries including tariffs or quotas as well as cultural differences and geographic location. Economic integration in recent years has nevertheless deepened in Europe and globally.

One of the main findings of Essay 1 is that economic activity is inclined to become concentrated on regions where the innovation intensity is higher than in other regions. On the other hand, this kind of conclusion could not be made in the international context. However, if the integration between separate economies occurs in the same nature as it has occurred in the internal economic context, then by investigating the countries' internal regional structures we can predict and evaluate the trends in the international economy.

Based on the findings of Essay 1, it can be predicted that at the international level economic activities will become concentrated in regions where there is a high intensity of investment in innovative activity. This scenario brings challenges also for Finland, which is located geographically on the periphery of Europe.

The new economic geography framework enables us to make policy recommendations of a general nature. Fostering a high intensity of innovative activity, for instance, is a key way of attracting direct investment and keeping jobs in the region. In order to deepen the policy recommendations it is fruitful to look at the theoretical framework of Ricardo as well as Heckscher, Ohlin and Samuelson (HOS), which are based on comparative advantage. According to the HOS framework, free trade leads to regional specialization of production in goods requiring resources (knowledge, capital, natural resources) that are relatively abundant in the region. Also Nelson (1990) emphasizes the significance of comparative advantages generated by natural resources and intellectual capital facilitating the functioning of the national innovation system. Taking advantage of the principle of comparative advantage at the international level is deemed to increase the welfare of all the countries participating in free trade.

1.3.2 Market Structure of the Pharmaceutical Industry in Finland and the US

The pharmaceutical industry is one of the main sectors that has been able to take advantage of biotechnology in its product development. It is thus important to evaluate the market structure of the pharmaceutical industry in order to be able to conceptualize the "playing field" where also most of the Finnish biotechnology companies operate.

Essay 2 compares the price cost margins of the pharmaceutical industry prevailing in Finland and the United States in 1975-1999.[11] The study is based on the same theoretical framework as Linnosmaa, Hermans and Hallinen (2004). The effects of research and development costs have been added to the model.

The development of drugs is heavily regulated by the public sector in both Finland and the United States via the procedures for getting new drugs approved. The pharmaceutical market in Finland has been marked by extensive price regulation while price setting in the US has been free (Rinta 2001). Most of the pharmaceutical industry's products in both countries have ended up meeting domestic demand during the period under investigation. It could be imagined that the domination of markets by domestic manufacturers and differences in price controls would mean that the price-cost margins of the Finnish pharmaceutical industry would remain at a lower level than in the US. In other words we can assume that Finnish companies have less price setting power than US companies.

A main finding of Essay 2 was that no difference between Finland and the United States in the average price-cost margins of the pharmaceutical industry could be found during the period under investigation. This result is surprising given the fundamental difference in price controls in the respective two countries.

On the one hand, this phenomenon may stem from the dual nature of the pharmaceutical markets in both countries. Drugs protected by patents or brand name products can be priced at a higher level in the United States in line with monopolistic principles. In Finland, on the other

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[11] The earlier version of Essay 2 was printed in ETLA's Discussion Paper Series, no. 883 (Hermans and Linnosmaa, 2003). Preliminary versions of the essay were presented in the 24th Nordic Health Economists' Study Group Meeting, 15-16 August 2003, Bergen, Norway, and in the 4th World Congress, International Health Economics Association, 15-18 June 2003, San Francisco, USA.

hand, patent-protected products have been subject to price controls. In the United States after patent protection expires there are huge markets for generic drugs and competition is fierce, which pushes down the level of prices.

In Finland, competition with respect to generic products has not been as keen owing to the relatively small market potential and the tendency of domestic manufacturers to turn their products into brand names. The above-described differences between the market structures of these two countries and the segmentation of markets between patent-protected and generic products may lead to the same average overall price-cost margins in the pharmaceutical industry.

It is also possible that the Finnish price control system has not worked in the way desired, but rather the pharmaceutical companies have been able to negotiate a relatively high price level for their drugs. Deeper analysis of the market structure and regulatory schemes is necessary so that we can shed light on the reasons behind the similarities in the market power of the pharmaceutical industry.

The historical development of the drug industry, its competitive situation and price setting behavior are of great significance for the biotechnology industry. Owing to the considerable costs and risks associated with drug development, large pharmaceutical manufacturers have begun to outsource the initial stages of its research and development activities, for example to external biotechnology companies.

1.3.3 Capital Structure of the Finnish Bio-Pharmaceutical Industry

The length of time needed for product development is very long in the pharmaceutical industry. The time from the initial product innovation to launch of the final product on the market can take as long as 10-15 years. The product life cycle is considerably longer than in most other manufacturing sectors. For example, innovations in the software industry are on the store shelves within two years on average. Drug development thus entails considerable risks for the financiers of the R&D work. The profit expectations regarding drugs that are able to break through successfully onto the global market are also high. Nevertheless only a small fraction of the development projects become commercially successful.

Drug development is heavily regulated in the industrialized countries. The drugs have to go through pre-clinical tests on animals and clinical

tests on people, a process that ordinarily takes several years. The tests are designed to assess the suitability of the drug molecules for humans as well as the desired effects on a certain sickness or alleviation of symptoms. Depending on the type of medication, the number of people to be tested may climb into the hundreds or even thousands. Especially the third stage of clinical tests costs vast sums of money.

The international marketing of pharmaceuticals is very expensive and even large-scale marketing efforts cannot guarantee a product breakthrough. Many new drugs are marketed directly to the physicians who write the prescriptions. On the other hand, the advertising of prescription medication is to a growing extent also directed toward the final consumers.

As a consequence of the uncertain and expensive product development and marketing process, the development and investment company 3i estimates that turning one blockbuster drug into a commercial success costs on an average about USD 500-800 million. In Finland, SMEs as a whole in the bio-pharmaceutical sector have received financing of about EUR 225 million for their activities. We can therefore easily conclude that Finnish companies will not try to export drugs to the global markets by themselves, but rather they will do it in cooperation with larger partners such as international pharmaceutical manufacturers.

As the innovative activity of large international pharmaceutical companies is unable to produce enough new commercially successful products, large pharmaceutical companies have decided to outsource their R&D activities and risks to small biotechnology companies. Large pharmaceutical companies can help bring the most promising innovations of small biotechnology companies to the market. In practice, the large companies can buy licenses, all of the rights or a majority or minority stake in the companies that undertook the development work.

According to Essay 3, the transfer of prolonged promising projects to another pharmaceutical company reflects upon the ownership structure of Finnish bio-pharmaceutical companies.[12] The older companies generating sales revenues have a different ownership structure than the younger ones. The owners of the older companies are mostly other companies. The ownership of the younger companies, on the other hand, is rather

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[12] The earlier version of Essay 3 was printed in ETLA's Discussion Paper Series, no. 888 (Hermans, 2004). A Finnish version of the essay was published in Dosis, Pharmaceutical Journal, vol. 19, no. 3 (Hermans, 2003a).

evenly distributed among the persons actively engaged in the company, Sitra[13] and private capital venture firms.

1.3.4 Intangible Assets and Growth Expectations of Biotechnology Companies

The present value of a company is based on the expectations of its future returns. The historical accounting data for the biotechnology industry does not enable us to form expectations based on previous revenue and profitability figures. When making investments, external investors should have indicators at hand that help them project future earnings in light of the company's current situation. Without these kinds of measures, the earning expectations with respect to the potential investment target may be distorted.

According to the literature related to knowledge management, intangible assets and intellectual capital inherently reflect a company's potential to create value and future earning expectations. Essay 4 investigates whether the growth expectations of Finnish small and medium-sized biotechnology companies are attributable to their intangible assets.[14] The objective of Essay 4 is to empirically verify impacts of intellectual capital on the anticipated future sales of companies.

In the study the value of a company's intangible assets is quantified and defined by modeling the intellectual capital and value creation of companies from the viewpoint of knowledge management. The model is able to explain about 70% of the biotechnology companies' anticipated sales in 2006. Technically, the model's ability to explain 70% of the variance of the anticipated future sales controls for the risk of randomness of these anticipations disclosed by the biotechnology companies. This means that a large portion of the companies' growth expectations is based on the value stemming from intangible assets. This approach also

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[13]   The Finnish National Fund for Research and Development (Sitra) is a public foundation under the supervision of the Finnish Parliament.

[14]   The earlier version of Essay 4 was printed in ETLA's Discussion Paper Series, no. 856 (Hermans and Kauranen, 2003). It was submitted to R&D Management and it is still under review process. Preliminary versions of the essay were presented in "Innovations and Entrepreneurship in Biotech/ Pharmaceuticals and IT/ Telecom", School of Technology Management & Economics, Chalmers University of Technology, May 19-20, 2003, Gothenburg, Sweden and in the Workshop "The Economics and Business of Bio-Sciences & Biotechnologies: What can be learnt from the Nordic countries and the UK?" September 25-27, 2002, Gothenburg, Sweden.

offers a means for making economic projections based on the companies' growth expectations.

It seems that a well-balanced combination of human capital, structural capital, and relational capital implies value creation potential and high- anticipated future sales. This notion calls for a well-prepared strategy even for the early stages of the company in order to attract capital inflows. Despite of the fact that many companies which are involved in drug development have high growth anticipations, there are many other promising, albeit occasionally under-resourced, branches within the biotechnology industry. These include applications related to biomaterials, diagnostics, food and feed, industrial enzymes, agriculture and forestry.

1.3.5 Impact of Biotechnology Industry Growth on Finnish Economy in Near Future

Essay 5 compiles an economic growth forecast where the probability distribution is formed from the companies' sales growth forecast and their current sales revenues.[15] The model also incorporates the bankruptcy risk. The modeling technique is based on the sectoral input-output method utilizing the purchase and sales volumes announced by companies in the respective sectors.

According to the forecast model based on the data from the year 2001 the biotechnology cluster is able to produce EUR 850-1200 million worth of value added with a probability of 90 % in the year 2006. In the year 2001 the entire biotechnology sector's value added was about EUR 500 million, meaning that annual growth of the entire cluster would be approx. 10-18 percent. Despite this, the value added will remain relatively low because the biotechnology companies use a high amount of funds for purchasing services and goods from outside the firm. According to the forecasting model, by 2006 the biotechnology cluster's contribution to annual GDP growth will be about 0.05-0.09 percentage points.

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[15] The earlier version of Essay 5 was printed in ETLA's Discussion Paper Series, no. 894 (Hermans and Kulvik, 2004a). It was then submitted to The International Journal of Biotechnology and it is still under review process. Preliminary versions of the essay were presented in the conference of BioTech Society, 29-30 September 2003, Espoo, Finland, and in the 4th Triple Helix Conference, Track 10: Technology Foresight in the Triple Helix, 6-9 November 2002, Copenhagen, Denmark.
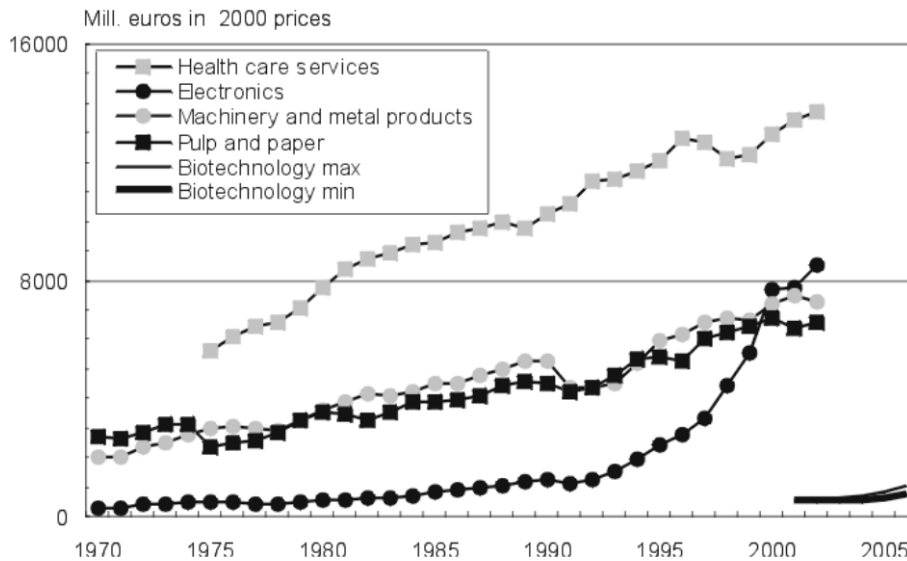
Figure 4. **Production by sector 1970-2002, in year 2000 prices (Hermans and Kulvik 2004b).**

Industrial history shows us that if a region or a country has no previous industrial traditions in a certain sector successful businesses and new growth emerge slowly or only seldom. Finland has pinned high hopes on biotechnology as a source of new research-intensive growth. Almost all industrialized countries have the same goal, and many of them already have long traditions in this sector. The biotechnology sector has a short history in Finland. The biotechnology sector's volume of production measured by value added is about EUR 500 million. In order to put the growth possibilities of the biotechnology sector in perspective, we can ask when Finland's currently strong sectors – the forest, machinery and electronics industries – were in the same situation (Figure 4).

In the year 2000 prices, the value of forest industry production was half a billion euros in the early 1950s. The electronics industry reached that level in the mid-1970s. If the biotechnology sector achieved the same growth as that of the electronics industry fueled by Nokia, it would be reach the position of the "fourth pillar" of industry in about 30 years. If the life cycle of the biotechnology industry as an independent sector is like that of the forest industry, it would take 50 years. If a long run growth rate of production of the biotechnology sector is sustained at the same level as in the forecast period 2001-2006, it would take 15-30 years to reach the same production level as electronics or pulp and paper industry have today.

The health care sector's domestic service production is at relatively high level compared even with highly export-oriented industries (Figure 4). The massive health care sector has reached a major crossroads owing to the aging of the population and advances made in medical science. On the one hand, the aging of the population and the medical possibilities to diagnose and treat more illnesses than before increase the cost pressures on health care. On the other hand, biotechnology applications are expected to spawn cost savings over the long run by, for example, making time-consuming diagnostic methods more efficient and facilitating targeted therapy. It is investigated below some policy implications how the Finnish biotechnology industry could offer solutions to the cost crisis in health care while at the same time spurring development of an internationally competitive industrial cluster.

1.4   Conclusions

1.4.1   Policy Implications

A small country cannot do everything itself. From the standpoint of innovation intensity, the safeguarding of sufficient critical mass is of profound importance if the emergence of a biotechnology industry is deemed worthy in Finland. In order to foster the success of biopharmaceutical companies, a business concept ranging "from services to development of own drugs" must be developed, which will spawn profitable business activities also in the pharmaceutical sector. The protection of intangible rights and exploitation of business expertise right from the onset of the research projects will help biotechnology companies receive financing and launch successful business activities. The growth of the biotechnology companies can be facilitated by directing resources to niches where Finland has comparative advantages and where the commercial applications have substantial market potential in the future.

The following list comprehends 5 implications broadly derived from the essays of the thesis.

> **Essay 1. Market structure and regional concentration**: In order to reach a critical mass, small companies seek to concentrate their activities in the vicinity of other companies in the same sector. In the future it is expected that the activities of companies will become more concentrated on innovation-intensive regions also across international borders.

Implication 1: Sufficient innovation intensiveness and critical mass must be safeguarded and defined in the individual biotechnology competence segments in the future if Finland wants to have an economy based on knowledge, not e.g. wage cost advantages.

Essay 2. The price-cost structure in the pharmaceutical industry seems to be the same in a small economy with price controls as in a large economy without price controls. In order to bolster profitability the pharmaceutical industry, companies outsource their research and development because of the considerable risk associated with these activities.

Implication 2: In the near future it is possible to operate profitably as a small entrepreneur in certain niches in the pharmaceutical sector. Some large Finnish pharmaceutical company could strengthen its position in global markets by collaborating with small and technologically advanced Finnish biotechnology companies. The kind of collaboration could offer synergy in the combination of most modern technology of small biotechnology companies and resources and logistics of a large pharmaceutical company.

Essay 3. The investigation of financial sources and business strategy of biopharmaceutical companies confirmed that the main sources of financing for young companies are the persons working at the company, private venture capitalists and the public sector. The growth expectations of young companies are pointed far into the future. The older biopharmaceutical companies owned by other firms have already been able to generate revenues, which is indicative of the pharmaceutical industry's new strategy of outsourcing R&D activities.

Implication 3: The equity financing of biopharmaceutical companies in the start-up phase is based on the premise that the investors think they can exit at a later stage. In the current situation in the international financial markets the most common way to exit is via an acquisition or other type of restructuring. The company is an attractive target for acquisition and its value will simultaneously grow when the company has begun to produce considerable amounts of revenues or its product development has proceeded far enough. This calls for dynamic corporate strategies, in which positive cash flows can be generated even at the start-up phase of the company in order to finance the later development phases of the company's products.

Essay 4. The analysis of intangible assets and growth potential of Finnish small and medium-sized biotechnology companies concludes that when a company's intellectual capital (human capital,

structural capital and relational capital) are balanced and soundly managed, the company's present value is relatively high. Then potential investors or buyers of the company are able to make a strategically justified estimate of the company's future earnings expectations and the present value. Financing paves the way for the company to turn its innovations into commercial products.

Implication 4: The management of biotechnology companies' intangible assets and competencies is an important measure of future earnings expectations and therefore the company's present value. Thus the integration of business expertise right from the start as a part of the technological development occurring in the network of biopharmaceutical companies helps determine whether the company's business strategy is based on development of the market potential of products, not just technological competencies.

Essay 5. The growth forecast for the biotechnology industry presents the SMEs in the biotechnology industry as a sector of its own. Growth impacts of the biotechnology industry extend to many sectors, foremost the chemical industry, which includes also the pharmaceutical sector.

Implication 5: The biotechnology industry as a distinct sector will not become one of the main pillars of the Finnish economy for at least a decade, even if the growth is swift. It is likely that the Finnish economy's new engine of growth will emerge from a combination of already existing new and old sectors. In this case, biotechnology may play a significant role of its own. To fulfill the anticipations, there is a need for the creation of a critical mass of factors of production and comparative advantage by building collaboration and financing networks between the biotechnology industry and traditional industries, such as the forest industry, electronics industry and pharmaceutical industry.

Health care cost crisis and growth potential of biotechnology industry

As seen above biotechnology is often linked with drug development and various types of health care applications such as diagnostics and biomaterials (Figure 1). Almost 60 percent of the small and medium-sized biotechnology companies indicate that they operate in the pharmaceutical industry or have ties with clients in the pharmaceutical industry. Fields linked indirectly with health care include functional foodstuffs, enzymes and assorted research services. However, the Finnish pharmaceutical industry and other health care-related industry is nevertheless relatively small on a global scale.

Inaccurate diagnoses or a lack of appropriate treatment leads to a wasteful use of personnel resources and medication. In other words, if the illness is not known or it cannot be treated, the patient has to undergo time-consuming procedures and the treatment may have to be changed numerous times. The patient may have to be institutionalized due to inefficient treatment. If more efficient ways can be found to make diagnoses and treat patients that would otherwise need long-term care, relatively expensive methods can generate cost savings by shortening the duration of treatment times (see case study; Hermans and Kulvik 2004b).

Case study: Use of biotechnology and related fields in treating strokes: more efficient treatment and decrease in total cost of treatment (Kaste, 2004)

A stroke is the most common type of disruption of blood circulation to the brain. Its treatment takes many days of acute treatment, which has led to an increase in treatment costs. In 1999 about 6 percent of total health care expenses were related to treatment of strokes. The acute treatment of patients suffering from brain circulation disorders takes an average of about 2.5 years, which in Helsinki costs about 100,000 euros (Kaste, Fogelholm and Rissanen 1998; Finne-Soveri 2003). Fogelholm, Rissanen ja Nenonen (2002) estimate that the aging of the population means that the need for acute treatment will double by the year 2030.

The neurological polyclinic of the Helsinki University Central Hospital (HYKS) has started to treat stroke patients with so-called thrombolysis, where a doctor tries to remove a blood clot by dissolving it. Thrombolysis uses alteplasis medication, which is recombinant DNA, produced with the help of hamsters' ovarian cells. Despite the favorable results obtained by the thrombolysis, it has two drawbacks. First, the medication is relatively expensive: one dose costs over 1000 euros. Second, the thrombolysis must be started quickly, about 3-4 hours, after a stroke.

In 2002 about 8 percent of the stroke patients coming to the HYKS neurological clinic received the solvent treatment with good results. About 60 percent of the patients receiving thrombolysis recovered. The total cost savings with respect to the recovered patients was about 84,000 euros per patient, which represents over 80 percent of the non-recovering patients' total costs (Lindsberg, Roine ja Kaste 2000; Finne-Soveri 2003). *"The timely and efficient treatment of stroke victims is the cheapest alternative for society in economic terms, but for the patient it is like winning the lottery."* (Kaste, 2004.)

Targeted therapy is based on a deep understanding of the interaction of organs even on a genetic level, so that treatment of illnesses can be given on a patient group-specific basis or even on a patient-specific basis. Targeted therapy requires development of diagnostic methods and equipment together with targeted medicines or dosages. In order for targeted therapy to become economically feasible, the actors from different fields will have to engage in intensive cooperation and offer comprehensive services and product concepts to customer groups and interest groups.

Instead of individual drugs, the comprehensive service and product concept caters to different patient groups by offering customized diagnostic methods, variations of medication, other new treatment methods as well as related equipment and software.

In addition to the training of end users, the financiers of health care can be offered calculation models of the cost savings vis-à-vis ordinary procedures without targeted therapy. The comprehensive product concept based on these kinds of product mixes and related services offers a means for cooperation between biotechnology companies and global distributors with complementary expertise so that the benefits gained by the customer are maximized in terms of the effectiveness and cost efficiency of the treatment. At the same time the knowledge base of small biotechnology companies will become more diversified as cooperation with firms in closely related sectors spawns new operative procedures and innovations.

In Finland there are several types of diseases significant from a public health care perspective, the treatment of which have considerable macroeconomic effects. The macroeconomic effects can entail other costs than those stemming directly from health care. For example, worker absenteeism and premature pensions affect the productivity of various industries.

Illnesses significant from a public health care perspective have steered the allocation of domestic research resources, which has spawned internationally significant areas of expertise in medical science and related fields. The research knowledge and demand for its commercial applications arising from these kinds of public health care needs enable the domestic market to be used as a commercial test market. Finnish end users of health care products represent the top experts in their fields, which promotes the product development of biotechnology companies and development of service concepts as well as prepares companies products and services to compete on international markets.

1.4.2   Topics for Further Research

Further research is needed to evaluate which potential niches the bio-technology sector should seek to fill when developing products with commercial potential. When seeking to identify these niches, it is important to keep in mind that the competence base must be sufficiently large to generate the critical mass necessary for spawning products and services with sufficiently large market potential. We can look at the pre-conditions for turning research into commercial products from the standpoint of the competence base underlying this critical mass: knowledge-intensive entrepreneurship, financing possibilities and international market potential

1) by distinguishing the main incentives and barriers regarding entrepreneurship in a research segment with a deep competence base. In addition, by investigating the distribution of biotechnology companies that have already emerged, we can seek to find niches that have a considerable competence base but also a "commercialization gap".

2) by analyzing the preferences of financiers investing in biotechnology companies, which is then compared with the distribution of the competence base of biotechnology research.

3) by analyzing and comparing the international market potential to Finland's competence base.

This type of further research would be beneficial for planners of general technology policies and actors in various sub-sectors of the biotechnology industry. Technology policy experts can benefit from the research results when gauging use of alternative types of aid in light of the principle of comparative advantage based on international trade analysis. In Finland substantial amounts of state aid are directed to the biotechnology sector. The private and public investment activity is rather modest by international standards. Resources should thus be allocated prudently.

Biotechnology research can be applied in many diverse areas. There is a danger that when making financing decisions the authorities are unable to "see the forest for the trees". Therefore, start-ups that base their activities on isolated top-notch research fields may end up without financing. A reason can be the lack of a viable business plan even if the segment has considerable market potential.

Further research should offer such new information about the biotechnology sector that would assist public and private financiers in better understanding the biotechnology sector and its companies. A proper understanding is necessary for making sound decision when scarce resources are steered toward promising fields of application.

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ESSAY 1.
New Economic Geography of Market Potential – Innovation Intensity and Labor Structure in EU Regions[16]

Abstract

In the present study, we ask how economic integration affects the location of economic activities and the spatial distribution of market potential in Europe. The theoretical framework is based on the new economic geography approach in the trade analysis literature. Empirical analysis transforms data into a synthetic free trade area (SFTA) that is constructed by standardizing the values of each variable to a comparable level in each country. Then SFTA is compared with the real trade area (RTA). The comparison offers insights into how "extreme" integration within countries (SFTA) has affected the location of economic activities and how this integration differs from the spatial structures among countries (RTA).

The empirical results suggest that regional innovation intensity has affected the spatial market potential within countries but not among the same countries. This has important implications for the discussion about regional development during the economic integration process. The results imply that if international integration gets forms similar to those that "extreme" integration has had within countries, lower international trade barriers will lead to geographic concentration in the region with high innovation intensity. The conclusions of the results change in some respects when we use different data subgroups. Innovation intensity does not seem to be a relevant driver in all the subgroups formed. However, the labor share of agriculture remains a pow-

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erful predictor of geographical concentration in all the subsets and models.

1.1 Introduction

The economic and political integration process has been recently deepening globally. European countries in particular have integrated relatively rapidly and the plans for the expansion of the EU have been widely discussed. There has been much discussion on how the deepening integration affects the regional distribution of economic activities. Theoretical developments in trade analysis, in particular, have advanced rapidly in recent years. Krugman (1991a, 1991b) set the basis for the new economic geography by applying the monopolistic competition framework *á la* Dixit and Stiglitz (1977). Krugman and Venables (1995) and Venables (1996) extended the framework to the use of intermediaries in manufacturing. Puga (1999) solved the model analytically. Fujita, Krugman, and Venables (1999) concluded the theoretical contributions of the time. Ottaviano (2001) endogenized capital inputs in the models. Martin and Rogers (1995), Baldwin et al. (2003) considered the role of regional policy in the framework. However, there are few empirical studies published in the field (e.g. Hanson, 1998; Davis and Weinstein, 1999; Redding and Venables, 2000; Midelfart-Knarvik et al., 2000).

The present study aims to analyze how economic integration affects the location of economic activities and the spatial distribution of market potential in Europe. The theoretical framework behind the empirical analysis in this paper employs an approach called new economic geography, which takes into consideration the interrelation between market structure and the spatial structure of economic activities. The independent variables for the analysis are chosen in accordance with the theory.

The empirical section presents a regression analysis of the inner areas of 12 EU countries. The inner area of each country is assumed to have integrated extensively. In contrast, there have been relatively high trade barriers on the international level between these countries. An analytical tool, called the Synthetic Free Trade Area (SFTA) is constructed in order to compare the spatial structures both within the countries and between them. The SFTA is constructed first by standardizing all the variables within single countries. Second, all the data is pooled together to form a SFTA aggregate, which is, in turn, used in regression analysis.

International economic structures are compared with the internal spatial economic structures of traditional states. International trade is here assumed to have higher trade barriers and higher trade costs than intrastate trade. Therefore, we can compare SFTA and the actual data of the Real Trade Area (RTA) in order to obtain more information about spa-

tial agglomerations in highly integrated regions (within countries) and among less integrated regions (among countries).

In other words, if the form of economic integration between countries is similar to that of intra-state areas, then economic integration might have a similar impact on the international structure of spatial market potential as individual countries have had on intra-state trade. In order to make such an analysis possible, the actual area, including 187 regions, and the corresponding synthetic area of the same size are presented on the NUTS2 level. Changes of cross-sectional regression coefficients are investigated over time. The SFTA analysis is also benchmarked by using a more conventional panel data analysis.

The remainder of the study is as follows. Chapter 2 presents the theoretical model that describes how the market structure affects the location of economic activities. Empirical methodology and variable construction appears in Chapter 3. Chapter 4 discusses the empirical results and the last section concludes the study.

1.2   The Theoretical Model

The theoretical model used in this study is based on the monopolistic competition model by Dixit and Stiglitz (1977). The spatial framework relies mainly on Krugman (1991a, 1991b).

1.2.1   Consumption Structure

Let us assume that there are two production sectors in two economies. Sector A produces identical goods under perfect competition and constant returns to scale (CRS). This sector is referred to as a local agricultural sector. Sector M produces differentiated goods under monopolistic competition and increasing returns to scale (IRS). It is often referred to as a manufacturing sector. [17] The theoretical presentation focuses here on the latter sector.

Consumer preferences can be presented as a Cobb-Douglas function between the two sectors.

(1) $U = C_M^{\pi} C_A^{(1-\pi)}, 0 < \pi < 1$.

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[17]   For example, Krugman, 1991a; Krugman, 1991b; Krugman and Venables, 1995.

The consumption aggregate C_M of sector M is the share π (percent) of the total consumption and the consumption of product C_A of sector A is then the share $1-\pi$ (percent). Manufactures are consumed as the constant elasticity to substitution (CES) aggregate function implies:

$$(2) \qquad C_M = \left[\sum_i c_i^{\frac{\sigma-1}{\sigma}} \right]^{\frac{\sigma}{\sigma-1}}, \sigma > 1, \ i = 1,...,N \ .$$

The term c_i in equation above is a single manufacturing good. The number of goods (N) produced in the sector is large, although all the possible varieties are not produced. The elasticity of substitution is simply σ (sigma), according to the CES preferences of the consumer:

$$(3) \qquad \frac{d(c_j/c_k)}{c_j/c_k} \cdot \frac{d(p_k/p_j)}{p_k/p_j} = \sigma, \ j \neq k \ .$$

Consumer preferences are presented by a constant elasticity to scale (CES) function within industrial sector goods. The terms j and k denote differentiated product variations. This preference type implies the symmetrical but imperfect substitutability of the goods. The larger the value of sigma, the more substitutable the goods are with each other, and vice versa.

1.2.2 Production Structure

Increasing returns to scale are introduced in the model through fixed (sunk) costs. Sunk costs are denoted as α. Marginal costs are denoted as β. The production volume of a single manufacturing firm is measured by x_{Mi}. The production function is of the linear form:

$$(4) \qquad L_{Mi} = \alpha + \beta x_{Mi} \, ,$$

where L_{Mi} is the labor used to produce x_{Mi} goods output. Sunk costs can be regarded as costs caused by research and development (R&D) activities or marketing and advertising activities which are related to consumer preferences. And *vice versa*, the consumer preferences are directly related to the scale economies of the production process. When new firms are allowed to enter the market, then no firm can capture abnormal profits in the long run. This implies the following link between the cost structure of a firm and the consumer preferences:

$$(5) \qquad p_i = \frac{\sigma}{\sigma - 1} \beta w$$

The term *w* denotes the wage level. The interpretation of σ is related to elasticity of substitution and consumer preferences (see eq. 2 and 3). The price of a single product is a mark-up over marginal costs. The mark-up is related to the elasticity of substitution. Accordingly, the average unit costs of the production must also be covered when the production process contains not only marginal costs, but also sunk costs.

We can solve the quantity of goods produced by a manufacturer with the help of a price equation (eq. 5) and by using a zero-profit assumption. The assumption is related to the long-run definition: market entry is free in the long run and, therefore, the profit margin drops. The production quantity is then:

$$(6) \qquad x_i = \frac{\alpha(\sigma - 1)}{\beta}$$

The higher the sunk costs, the more a single firm produces. On the other hand, the consumer preferences limit the sunk cost effect.

We can also count the number of firms in a market:

$$(7) \qquad n = \frac{L_M}{\alpha + \beta x_i} = \frac{L_M}{\alpha \sigma}$$

The smaller the number of firms, the higher the sunk costs. The market structure is then affected considerably by sunk costs (for instance R&D activities) and also by consumer preferences. These simplifications play an important part when we determine how the market structure is related to the firms' decisions about the location of their activities.

1.2.3 Two-region Model

The present study follows Krugman (1991a, 1991b) to construct the two-region model. The only essential modification made concerns the numeric simulation presentations. In addition, some corrections are made to partial derivations in the end of the analysis. This model describes a situation where manufacturing has agglomerated in the other region, whereas the agricultural workers are evenly distributed between both regions. The trade barriers, or trade costs, between the two regions

are presented by Samuelsonian iceberg costs. The simplest example of trade barriers is transport costs due to the distance between the regions. According to the iceberg costs part of the goods exported to another region "melts away" during the transportation.

In the present study, the wage level of the agriculture sector is chosen to be unity. We also assume that the total production of both regions, and the amount of total labor, equals unity. There is π (percent) of workers employed in the manufacturing activities. The term π is at the same time the proportional share of manufacturing labor out of the total labor and manufacturing production out of total production. Because region 1 (labelled with the subscript one) is a core region, its gross regional product, and income, (Y) is:

$$(8) \qquad Y_1 = \frac{1+\pi}{2}.$$

The regional income of the peripheral area, region 2, is presented in equation 9:

$$(9) \qquad Y_2 = \frac{1-\pi}{2}.$$

We form the ratio of regional incomes between regions 1 and 2:

$$(10) \qquad \frac{Y_1}{Y_2} = \frac{1+\pi}{1-\pi}.$$

When all the manufacturing goods are produced in region 1, the sales (V) of a single manufacturing firm in region 1 is:

$$(11) \qquad V_1 = \frac{\pi}{n}.$$

The wage levels (w) can vary between the regions.

$$(12) \qquad \frac{w_2}{w_1} = \left(\frac{P_2}{P_1}\right)^\pi = \left(\frac{1}{\tau}\right)^\pi$$

The competitive wage level must equal the price index (P) ratio between the regions weighted by the manufacturing labor share. This in turn depends on trade costs (τ) between the regions. The larger the

trade costs between the core and periphery, the higher the wage level offered in the periphery must be when labor is mobile between the regions as assumed. The imported manufacturing goods are more expensive in the periphery than in the core region due to the trade costs between the regions. This implies also a higher price level and demand for higher wages in order to achieve the same utility level in both regions.

The sales of a potential entrant manufacturer in the periphery are shown in equation 13.

$$(13) \qquad V_2 = \frac{\pi}{n} \left[\ (\frac{w_2}{w_1 \tau})^{-(\sigma-1)} Y_1 + (\frac{w_2 \tau}{w_1})^{-(\sigma-1)} Y_2 \ \right]$$

$$= \frac{\pi}{n} \left[\ \frac{1+\pi}{2} (\frac{w_2}{w_1 \tau})^{-(\sigma-1)} + \frac{1-\pi}{2} (\frac{w_2 \tau}{w_1})^{-(\sigma-1)} \ \right].$$

From equations 11 and 13 we get the manufacturer's sales ratio between the regions:

$$(14) \qquad \frac{V_2}{V_1} = \frac{1}{2} \tau^{\pi(\sigma-1)} \left[(1+\pi)\tau^{\sigma-1} + (1-\pi)\tau^{-(\sigma-1)} \right].$$

The sales ratio exceeds the wage ratio:

$$(15) \qquad \frac{V_2}{V_1} > \frac{w_2}{w_1} = \frac{1}{\tau^{\pi}}.$$

The outcome can be derived from the zero-profit assumption. The sunk costs must be covered by operating incomes and the sales must exceed the wage ratio.

1.2.4   Theoretical Results

A keystone of the theoretical analysis is based on equation 16. We get the market potential of a region by multiplying both sides of equation 14 by the result of the wage ratio in equation 15.

$$(16) \qquad \upsilon = \frac{1}{2} \tau^{\pi\sigma} \left[(1+\pi)\tau^{\sigma-1} + (1-\pi)\tau^{-(\sigma-1)} \right].$$

Equation 16 presents the market potential index. When the market potential index is lower than 1, it is not profitable to set up a firm in the peripheral region. When the value is greater than 1, it is profitable to start manufacturing also in the periphery. The market potential index emphasizes three drivers, which affect the firms' choices about where to locate their production activities according the model. These three drivers are 1) trade costs, 2) the labor share of manufacturing, and 3) the increasing returns to scale in manufacturing. Note that the increasing returns to scale are related to the sunk costs as well as consumer preferences in this model.

We take partial derivatives from equation 16 in order to analyze how the central parameters affect the location decisions of firms, and, therefore, the spatial agglomeration of economic activities.

First, we check how the market potential index is affected when the labor share of manufacturing alters, other things being equal:

$$(17) \qquad \frac{\partial \upsilon}{\partial \pi} = \upsilon\sigma(\ln\tau) + \frac{1}{2}\tau^{\sigma\pi}\left[\tau^{\sigma-1} - \tau^{-(\sigma-1)}\right].$$

The result of equation 17 is simulated also numerically in Figure 1.
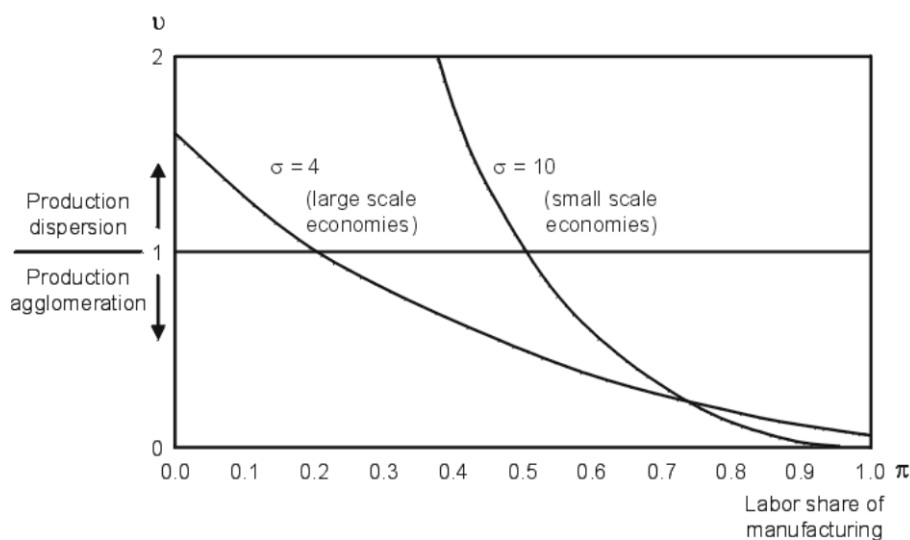
Figure 1.   Determining the location of production activities by changes in labor share of manufacturing.

The labor share of the sector experiencing scale economies (here: manufacturing) has a straightforward impact on the spatial agglomeration. If the labor share is relatively low, it is profitable to start production also in the periphery. And if the labor share is relatively high, staying in the core region is the profitable choice. Sunk costs implying increasing returns to scale in manufacturing affect, in a parallel manner, the profitable location choices. Enhancing scale economies lowers the dispersion boundary of spatial agglomeration.

In equation 18 we analyze how interregional trade costs affect the location decisions of the firms:

$$(18) \qquad \frac{\partial \upsilon}{\partial \tau} = \frac{\pi \sigma \upsilon}{\tau} + \frac{\tau^{\pi \sigma}(\sigma - 1)\left[(1 + \pi)\tau^{\sigma - 1} - (1 - \pi)\tau^{-(\sigma - 1)}\right]}{2\tau}$$

Figure 2 presents a numeric solution for the partial derivative. The change in trade costs (or trade barriers) affects the profitability of the location of the manufacturing firm. When the trade costs diminish, the spatial agglomeration becomes the profitable way to organize the business. However, if the scale economies are relatively low (e.g. for small R&D activities), the geographical concentration occurs only when the trade costs are very low.
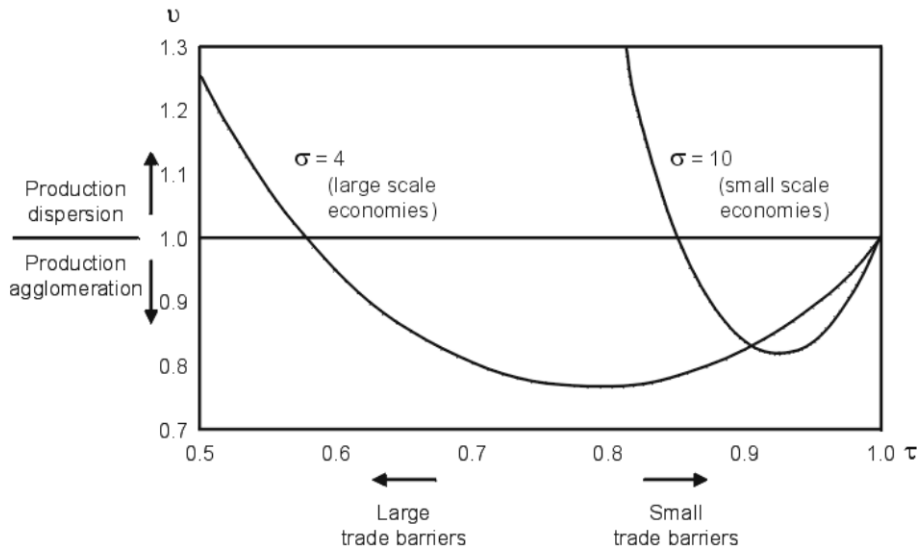
Figure 2. Determining the location of production activities by changes in trade barriers [costs].

Lastly, we control for the changes in the scale economies of the model. The effect has been captured in the two previous figures:

$$(19) \qquad \frac{\partial \upsilon}{\partial \sigma} = \ln(\tau)\left\langle \pi \upsilon + \frac{1}{2}\tau^{\pi\sigma}\left[(1+\pi)\tau^{\sigma-1} - (1-\pi)\tau^{-(\sigma-1)}\right]\right\rangle$$

$$= \ln(\tau)(\frac{\tau}{\sigma})(\frac{\partial \upsilon}{\partial \tau}) \, .$$

The partial derivative of equation 19 states that high scale economies imply high spatial agglomeration. The trade costs work in the same direction as presented above in Figure 2.

The theoretical results contribute to the empirical investigation of the economic reasoning behind the location of economic activities. The results of the model can be generalized from equations 16-19 and presented as a function of the labor share of agriculture, increasing returns to scale and trade costs:

$$(20) \qquad \text{Market potential} = a\left(\overset{-}{\text{labor share of agriculture}}, \overset{+}{\text{sunk costs}}, \overset{(-)+}{\text{trade costs}}\right).$$

The market potential index, ν in equation 16, is denoted as market potential below and in equation 20. There are three main independent variables derived from the model. First, the market potential is affected by labor share of agriculture, $1-\pi$, which is a reciprocal variable of the labor share of manufacturing, π, presented in the model above. Second, in the model, high sunk costs imply increasing returns to scale in production and corresponding changes in consumer preferences, $\sigma/(\sigma-1)$. The relation between increasing returns to scale and sunk costs ensues from the condition for the optimal price setting in equation 5. Accordingly, the firms set a sufficient mark-up over marginal costs in order to cover also sunk costs. Third, there are trade costs, τ, which affect to the market potential.

1.3   Empirical Analysis

1.3.1   Background

The present study examines the regional distribution of the market potential, or "density" of economic activities, the market structure and the labor structure of an economy in accordance with the model by Krugman (1991a). The effect of trade barriers is taken into account in a novel way. We compare the spatial structure of the intra-country trade costs with the international spatial structure of the trade costs, which are conventionally assumed to be greater internationally than within the countries. A close example of statistical regression analysis is Hanson's (1998) analysis of the distribution of regional demand shocks in the United States. Hanson estimates the effect of the distance between the regions on the demand for labor and on changes in the wage level in different regions.

The regional market potential[18] is specified on the NUTS2 level of European regions.[19] The data is described with the help of statistical and geographical information.[20] In the present study, an object of interest is whether there appear to be geographic agglomeration advantages on the level of NUTS2 regions and how the existence of such regional agglomeration advantages can be explained.

According to Hanson (1998) the question concerning the reasons for the formation of spatial agglomeration was theoretically undefined earlier, but Krugman (1991b) derived the causal relation of the market structure and spatial agglomerations theoretically. Hanson here takes advantage of the concept of market potential. The market potential of a

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[18] Literature of Economic geography (initially Harris, 1954; Hanson, 1998, 9) presents

$$MP_j = \sum_{k \in K} Y_k f(d_{jk}),$$

market potential as follows: in which MP_j depicts the market potential of region j, Y_k the production level of region k and d_{jk} the distance between the regions j and k. Function f( ) is a monotonically decreasing function, which presents how geographic distance affects the transport or trade costs. Here we simplify the definition of market potential to the form GDP / km² and transport / trade costs are analysed by Real Trade Area and Synthetic Free Trade Area analysis.

[19] NUTS is an abbreviation for the nomenclature of Territorial Units for Statistics. According to the NUTS classification, Eurostat has sought to form a division of member countries for the collection of coherent statistical data from the regions of the EU. Cultural differences have also been taken into account, due to which the differences between the sizes of some regions are notable. (European Commission 1994, 172).

[20] For example, Bivand (1998) specifies the methods of spatial-economic research.

region is determined by its size and relative location. With the help of the market potential estimates obtained from the regional data of the United States, Hanson simulates how strongly a demand shock that has occurred in one region affects the wage levels of other regions. Hanson uses numerical geographical information and computer-assisted maps to demonstrate the results.

The mobility of the labor force was emphasized in the theoretical model presented earlier. Hanson's hypothesis is that a high wage level explains the density of economic activities, that is, the market potential. Hermans (2000) uses innovation intensity as an instrument variable to explain the income level. The result of the 2SLS cross-section model is that the wage level significantly affects both the international and the intranational distribution of economic activities. In the present study, innovation intensity is used directly as a theory-based depiction of increasing returns to scale in production.

1.3.2   Assumptions

In the statistical analysis we assume that the trade between the inner regions of a country has been free with relatively low barriers for decades. The concept of a synthetic free trade area is constructed so that we could analyze spatial structures within countries. The real situation, where proportionately high trade barriers between the countries have appeared, is compared with the synthetic free trade area. Although the trade barriers between the countries have recently become lower, for example, between European countries, it can still be thought that there have been more trade barriers between countries than within a separate country. One reason is that the trade barriers were caused by the exchange of currency and cultural and linguistic differences. Naturally, there are still trade barriers within the countries but, by and large, it is reasonable to suppose that within the countries trade barriers have historically been relatively lower than between the countries.[21]

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[21] For example Davis and Weinstein (1999) conclude in their empirical research that the advantages of spatial agglomeration are significant between the regions within the country but not internationally. They maintain this is the case because within the countries the transport costs and other trade barriers are lower than on the international level and that the mobility of factors of production between the inner regions of the countries is greater than internationally.

The central assumptions of the analysis concerning the synthetic free trade area can be divided into two main parts: the nature of trade within the countries and between them. When both inputs and final products are looked at, the assumption concerning free trade within the countries and international trade barriers can be characterized with the help of the following example. In the supply of inputs, in this case the labor force, it is evident that in Finland the supply and mobility of the labor force can be relatively flexible, for example, between eastern and southern Finland in comparison with, for example, the situation between Estonia and southern Finland. There have been regulations that restrict the labor mobility between the countries. Although internationalization is nowadays rapid, evidently in past decades the international markets can nevertheless be said to have been open to free trade in Europe concerning both inputs and final products if compared to markets within countries. On the basis of this assumption an effort is made to demonstrate how economic activity has been organized spatially within the countries in "extreme integration" over a long period in comparison with way economic activities have been agglomerated internationally. International development has been affected by trade barriers that are greater than under "extreme integration".

Economic integration into the international economy has strengthened and widened remarkably, for example, concerning Austria, Finland, and Sweden in the 1990s. These countries joined the EU in 1995. Due to the stage-by-stage nature of integration, available time series are short-term and with their help the possible long-term effects of integration cannot be found. However, by forming a synthetic free trade area, the spatial structure within the countries can be aggregated and compared with the real trade area.

Another central assumption concerns the significance of different sectors (agriculture, industries, and services) in an economy as an independent variable. The different sectors are operationalized as an estimation of the share of agricultural labor out of the total employed labor. On the international level, the labor share of agriculture largely describes the stage of the economic development (e.g. Camm *et al.* 1986). On the other hand, within the countries the share of agricultural labor out of the total employed labor is probably frequently bound to the surface area of the land, since the soil is used as an input in agriculture.

The second independent variable is the increasing returns to scale (IRS) in production processes. High sunk costs imply high increasing returns to scale in the model, *ceteris paribus*. We assume that a signifi-

cant part of sunk costs are related to R&D activities. Consequently, IRS is denoted as innovation intensity measured by the region's patent applications per GDP. The theoretical model suggests that the greater the IRS, the greater is also the spatial agglomeration of market potential. The third theoretically relevant variable, trade costs (or trade barriers), is investigated by comparing the results of RTA and SFTA analysis.

1.3.3 Data

The data employed in this study comes from Eurostat's New Chronos Regio database. The database covers a great deal of different regional information. Unfortunately, the Regio database includes a serious problem of time series deficiencies. The selected data comprises NUTS2 regions in 12 countries. The whole set of observations covers the years 1996-1999.

The 12 countries in the study include 187 regions in the following countries: Austria, Belgium, Finland, France, Germany, Greece, Italy, the Netherlands, Portugal, Spain, Sweden, and the United Kingdom. The countries are selected according to the data available in the period covering 1996-1999. The subgroup of 8 countries is used in analyzing the longer period 1989-1999 containing 128 regions. The 4-country subgroup of Austria, Finland, Sweden, and the United Kingdom contains 59 regions and covers the years 1996-1999.

Figure 3 depicts the distribution of economic activities among European regions in 1999. The activities are measured by GDP per km^2. The distribution is not equal over the regions, but the densest agglomeration is located within the area reaching from Northern Italy to South-East England. The areas located on the geographic peripheries are mainly economically less active than those located near the geographic gravity centers of the EU.

The overseas regions of France have been omitted from the data due to the lack of time series. Furthermore, these regions do not seem to have significant relevance for the economic integration process within Europe. The regions located in the former East Germany have been omitted from the analysis partially also due to the lack of time series. In addition, the East German regions have been developed under a non-market-oriented environment during recent decades. Hence, the development of economic structures varies from the rest of the data.
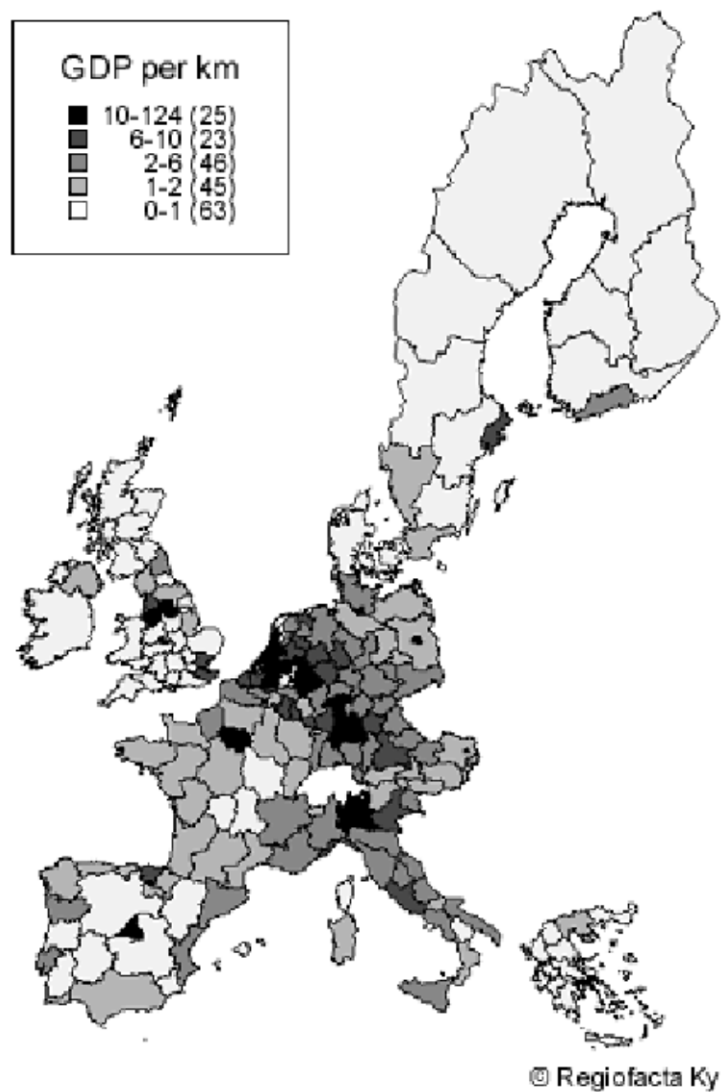
**Figure 3.   Geographic distribution of market potential (GDP per km²
in Millions of Euros) in European NUTS2[22] regions.**

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[22] Eurostat utilizes the NUTS classification in producing and combining European statistics. The abbreviation stands for Nomenclature of Territorial Units for Statistics.

1.3.4 Variable Construction

In the theory described above the spatial agglomeration of market potential is regarded as a convenient dependent variable for empirical analysis. We measure spatial agglomeration of market potential as annual Gross Domestic Product (GDP)[23] per region's surface area in square kilometers. The independent variables in the models are the labor share of agriculture (LSA) and increasing returns to scale (IRS). The trade costs, or trade barriers, are investigated in comparing the two sets of models. Due to the different scales of regions, we construct a Metropolitan dummy variable. It is zero for the regions that are classified alike at both NUTS1 and NUTS2 levels. Each variable is logarithmized before other transformations.

Labor structure (LSA) is formed as the share of agricultural labor out of the total labor employed in the region. The labor share of manufacturing in the model is converted reciprocally into the labor share of agriculture. The theoretical model above contains only two sectors, manufacturing and agriculture. However, some service activities have also tended to agglomerate spatially. Thus, we measure the labor share of agriculture $(1-\pi$ in the model) instead of the manufacturing share. It is arguable that agriculture is a proper measure for the empirical analysis because agriculture uses land intensively as an input in its production.

Increasing returns to scale in production activities are linked with the firms' cost structure in the model. There is an absence of sunk cost figures available in our data. In the present study, the number of patent applications is regarded as the outcome of R&D activities and sunk costs. Accordingly, the increasing returns to scale in the model are measured by innovation intensity, that is, patent application per capita.

The trade costs in the previous model are investigated empirically in comparison with two models. We form the Real Trade Area (RTA) and Synthetic Free Trade Area (SFTA) in order to analyze the effects of the different levels of trade costs, or trade barriers. All the annual values are standardized by reducing the annual mean of the same variable in the entire data. Then each outcome is divided by the respective standard errors. In this manner we form the RTA, which describes actual data but is strictly comparable with the following SFTA transformation.

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[23] GDP is purchasing power parity stabilized in each country.

The Synthetic Free Trade Area (SFTA) is constructed by standardizing each variable separately in each country according to Hermans (2000). The standardization is then done by reducing the country-specific means and dividing them by country-specific standard errors. Then we pool the data and analyze one entity (SFTA). SFTA describes a synthetic area, in which the spatial structures have been developed under "extreme" economic integration, in intra-country conditions.

Table 1. Definition of variables.

Theoretical model	Basic variable for empirical analysis	Real trade area (RTA)	Synthetic free trade area (SFTA)
Agglomeration of market potential index (dependent variable)	Regional market potential *GDP per km²* (log)	*GDP / km²* of a region subtracted by its average of entire data and then divided by standard deviation of entire data	*GDP / km²* of a region subtracted by its average in a country and then divided by standard deviation in a country
Labor share of non-agriculture	*Labor share of agriculture*	*Labor share of agriculture* of a region subtracted by its average of entire data and then divided by standard deviation of entire data	*Labor share of agriculture* of a region subtracted by its average in a country and then divided by standard deviation in a country
Increasing returns to scale	Innovation intensity measured as *patent applications per population*	*Patent applications per population* of a region subtracted by its average of entire data and then divided by standard deviation of entire data	*Patent applications per population* of a region subtracted by its average in a country and then divided by standard deviation in a country
Trade barriers	Benchmarking the results of RTA and SFTA models		

Table 1 concludes the construction methods and definitions of variables included in the empirical analysis below.

1.4　Empirical Results

The statistical analysis is divided into two parts. First, the data is analyzed by a regression model based on the evolution of the cross-sectional regressors of RTA and SFTA. Secondly, the conventional panel data analysis is used as a benchmark for the first phase results.

1.4.1　Results of Synthetic Free Trade Area (SFTA) Analysis

We employ OLS as a basic regression method. Each year's parameters are estimated separately as cross sections. The RTA describes drivers affecting the spatial agglomeration of economic activities among the countries and the SFTA within the countries. Table 2 presents the results of the 12-country model.

The results of the 12-country model emphasize the difference between the agglomeration forces in the RTA and SFTA. Spatial agglomeration in the RTA is affected solely by the labor share of agriculture. This implies that the high international distribution of economic activities cannot be explained by the IRS effect, or innovation intensity. According to the theory, this might be due to high international trade barriers.

Instead, the SFTA model seems to imply that IRS affects relatively strongly the agglomeration of market potential (table 3). In 1996-1999, the IRS effect is significant. Because there are some changes in the level of significance, this may imply a collinearity problem. However, the SFTA model implies that the IRS effect, or innovation intensity, is parallel with the spatial distribution of market potential over the entire period investigated here.

Table 2. Regression analysis (OLS) of 12 countries[24] 1996-1999.

	Dependent variable: Agglomeration of market potential (GDP per km²), 12 countries				
	Real Trade Area				
Year	Descriptives	Constant	Labor structure effect, LSA (labor share of agriculture)	Increasing returns to scale effect, IRS (patents per capita)	Metropolitan area (NUTS1)
1996	R² = 0.658 F=106.512*** N = 170	**-.037** **(.044)**	**-.704*** (.057)	**0.004** (0.050)	**1.043*** (0.260)
1997	R² = 0.617 F=89.245*** N = 170	**-.040** **(.047)**	**-.696*** (.062)	**-.005** (.053)	**.871** (.285)
1998	R² = .649 F=107.869*** N = 179	**-.045** **(.045)**	**-.723*** (.057)	**-.010** (.051)	**1.045*** (.274)
1999	R² = .607 F=76.081*** N = 152	**-.035** **(.054)**	**-.718*** (.070)	**.035** (.056)	**1.025*** (.287)

Standard errors are in parentheses.
The asterisk labels (*) stand for: * 5 percent risk level, ** 1 percent risk level, *** 0.1 percent risk level.

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[24] The 12 countries include the same countries as the 8-country analysis, but Austria, Finland, and Sweden are also included. The countries are selected according to the data available in the period covering 1996-1999.

Table 3.   **Regression analysis (OLS) of 12 countries[25] 1996-1999.**

			Dependent variable: Agglomeration of market potential (GDP per km²), 12 countries		
	Synthetic Free Trade Area				
Year	Descriptives	Constant	Labor structure effect, LSA (labor share of agriculture)	Increasing returns to scale effect, IRS (patents per capita)	Metropolitan area (NUTS1)
1996	R^2 = .708 F=134.160*** N = 170	-.032 (.040)	-.700*** (.046)	.094* (.043)	.932*** (.233)
1997	R^2 = .687 F=121.592*** N = 170	-.017 (.041)	-.689*** (.047)	.091* (.044)	.833*** (.245)
1998	R^2 = 0.714 F=145.314*** N = 179	-.054 (.040)	-.693*** (0.045)	0.154*** (0.042)	1.095*** (0.235)
1999	R^2 = .703 F=116.687*** N = 152	-.043 (.045)	-.700*** (.052)	.124** (.046)	.930*** (.239)

Standard errors are in parentheses. The asterisk labels (*) stand for: * 5 percent risk level,   ** 1 percent risk level,   *** 0.1 percent risk level.

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[25]   The 12 countries include the same countries as the 8-country analysis, but Austria, Finland, Sweden and the UK are also added. The countries are selected according to the data available in the period covering 1995-1999.

When we compare the annual values of regression coefficients between the RTA and SFTA, it seems evident that economic integration has evolving under lower trade barriers within countries (SFTA) than between them (RTA). The labor share of agriculture explains the variance of spatial agglomeration in all the cases at the 0.1 percent risk level. The IRS effect deviates from zero at least at the 5 percent risk level in all the years in the SFTA but not even once in the RTA. Accordingly, this implies different spatial structures among the countries and within them. If international economic integration acquires similar forms to those of intra-national "extreme" economic integration[26], the innovation intensity can be expected to be a driving force in the relocation of economic activities. However, it is noticeable that the selected country sets have some effects on the qualitative implications.

Tables A1 and A2 in the Appendix present the results of the 8-country analysis during 1989-1999. The model is adjusted by removing the four countries with the shortest time series. Thus, the data ranges from 1989 to 1999. The labor share is still a significant predictor of spatial market potential. As in the 12-country model, the IRS effect, innovation intensity, is not a significant predictor of spatial agglomerations in the RTA. In contrast with the 12-country model, the IRS effect does not significantly expound spatial distribution of market potential in the SFTA even at the 5 percent risk level, excluding 1998. Therefore, the difference described above in the spatial structures within the countries and internationally is no longer as significant as it is with tighter risk level requirements. According to the theory, the smaller difference between the RTA and SFTA could be explained by the fact that the integration among the countries is already quite advanced. On the other hand, it seems to be a difficult question: how to select the most plausible set of countries for the analysis. We can try to use as long as possible time series with a limited number of countries, or the highest number of countries with a limited time series. In other words, there is a trade-off between the maximum number of years and the number of countries chosen for the analysis.

Finally, the set of four countries, Austria, Finland, Sweden, and the United Kingdom, omitted in the 8-country analysis, are also analyzed separately (see Tables A3 and A4 in the Appendix). The results provide parallel support to the first model with 12 countries. Though the labor

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[26] Intra-national development in Europe can be mostly emphasized by free trade, relatively low transport costs, and low cultural barriers during the past decades. Such an economic environment describes the "extreme" integration which has formed the economic structures within countries such as they are.

share of agriculture is still the significant force of the distribution of market potential. The IRS effect is also significant in every year in the SFTA, but not in the RTA. This implies that trade barriers are lower in intra-national trade than internationally. It may tell something about specific features of Finland and Sweden, which have large sparsely populated regions. These countries have high innovation intensity but a relatively low level of market potential in general. However, market potential has agglomerated in some regions within these countries.

Figures 4 and 5 present the information on cross-sectional regression coefficients. The evolution in the RTA seems to be similar in every subset of the data (Figure 4). The labor share of agriculture significantly limits the spatial agglomeration of economic activities and simultaneously the IRS effect does not expound the spatial market potential. As mentioned above, none of the RTA models offered confirmation for the significance of the IRS effect (innovation intensity).
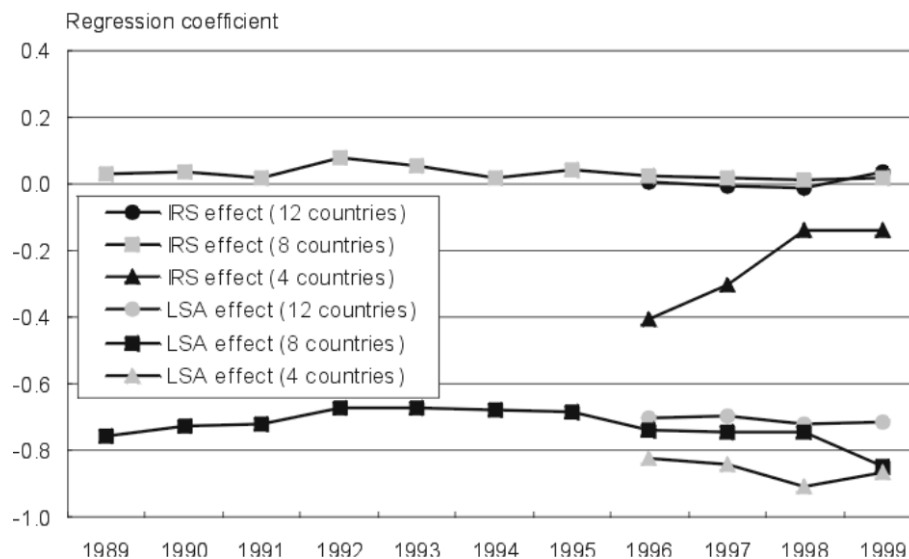
Figure 4.   Real Trade Area (RTA). Innovation intensity and the labor share of agriculture explaining the regional agglomeration of economic activities among the countries.

Figure 5 presents the evolution of the SFTA regression parameters. The labor share of agriculture does affect the distribution of economic activities in a consistent way in different data sets (the lower part of the figure). Apart from the RTA scheme, the IRS effect seems to affect spatial market potential more consistently in the 4- and 12-country models than the entire 8-country model.
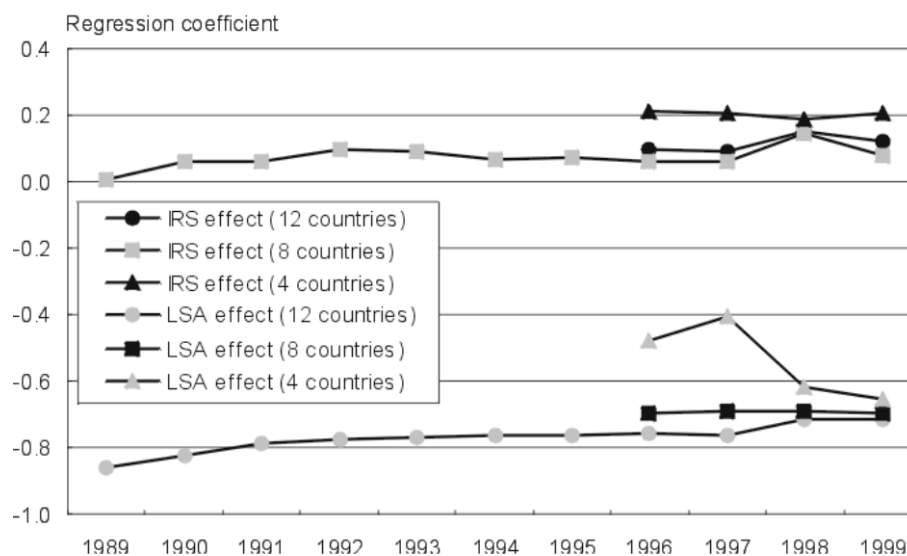
Figure 5. Synthetic Free Trade Area (SFTA). Innovation intensity and the labor share of agriculture explaining the regional agglomeration of economic activities within the countries.

1.4.2 Results of Panel Data Analysis

We also benchmark the results of the RTA and SFTA analyses by using the more conventional panel data analysis.[27] Panel data is analyzed in two ways. First, the data is investigated using fixed effect models in within-countries and between-countries frameworks. Secondly, we introduce dummies for each country and each year in the entire panel data. The results are presented in Table 4.

In the fixed effect (within-countries) model, both the labor share of agriculture and IRS effect are significant drivers affecting the market potential. Furthermore, the IRS effect is not a significant driver of spatial agglomerations in the between-countries model. The dummy model implies that both of the basic regressors are significant and that market potential levels are systematically higher in most of the countries than in Sweden, which is selected to be the base. Sweden and Finland score the lowest average market potential. At the same time, there are no significant agglomeration variations over the years in the model.

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[27] Panel data contains the data of the 8 countries covering the period of 1989-1999.

Table 4.   Results from regression analysis of the panel data.

Dependent variable: Agglomeration of market potential (GDP per km²)			
Variable	**Fixed effect**	**Between countries**[28]	**OLS with dummies**
Constant	-1.940*** (.078)	-4.528 (2.273)	-4.152*** (.127)
Metropolitan area (NUTS1)	1.269*** (.090)		1.268*** (.090)
Labor structure effect, LSA (labor share of agriculture)	-.981*** (.020)	-1.443* (.563)	-.980*** (.020)
Increasing returns to scale effect, IRS (patent appl. per GDP)	.031* (.013)	-.296 (.239)	.030* (.013)
Belgium			2.202*** (.101)
Germany			2.279*** (.094)
Greece			2.530*** (.121)
Spain			1.971*** (.105)
France			1.782*** (.097)
Italy			2.649*** (.010)
The Netherlands			2.920*** (.010)
Austria			2.020*** (.118)
Portugal			2.347*** (.133)
Finland			.259 (.155)
The United Kingdom			1.833*** (.099)
Year 1999			0.056 (0.067)
Year 1998			0.056 (0.064)
Year 1997			0.086 (0.064)
Year 1996			0.051 (0.064)
Year 1995			0.028 (0.066)
Year 1994			0.074 (0.068)
Year 1993			0.040 (0.068)
Year 1992			0.068 (0.068)
Year 1991			0.070 (0.069)
Year 1990			0.077 (0.070)
Number of observations	1509	1509	1509
F	1419.06	3.83	325.83
R² (overall)	0.6755	0.5616	0.8405

Standard errors are in parentheses. The asterisk labels (*) stand for: * 5 percent risk level, ** 1 percent risk level, *** 0.1 percent risk level.

* 5 percent risk level, ** 1 percent risk level, *** 0.1 percent risk level.

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[28]   When the model also contains the metropolitan area dummy variable, as a regressor, the regression coefficients of the constant, metropolitan area, labor structure effect, and sunk cost effect are (standard errors in parentheses): -4.015 (2.279), -8.731 (7.625), -1.166 (0.604), and -.311 (.235), respectively. None of them deviates significantly from zero at the 5 percent risk level.

The results are consistent with the RTA and SFTA comparison at the 5 percent risk level. The IRS effect seems to be parallel with the spatial market potential within the countries but not between them. And as mentioned above, if international integration is as deep as the intra-country has been, we can expect that the IRS effect will become an important driver of the relocation of economic activities.

1.5   Conclusions

In the present study, the research question was: How does economic integration affect the location of economic activities? First, we constructed a theoretical model of the new economic geography from the international trade literature. Secondly, we tested the theoretical model empirically using data covering 187 NUTS2 level regions in 12 European countries. The data was divided into three subsets according to the information availability over time. Data on 8 of the countries covered the years 1989-1999 while data on the other 4 countries was available for the years 1996-1999. All the countries were also pooled together in 1996-1999.

The theoretical model raised three main drivers affecting the geographical concentration of market potential. The dependent variable, market potential, was measured as GDP per km^2. The first driver, the labor structure effect was measured by the labor share in non-agricultural working activities in the theoretical model. In the empirical analysis, it was converted into its opposite, the labor share of agriculture. The second driver, increasing returns to scale in production, theoretically related to sunk costs, was measured as innovation intensity (patent applications per capita in a region). The third driver, trade costs or trade barriers were investigated by a comparison between Real Trade Area (RTA) and Synthetic Free Trade Area (SFTA). The RTA and SFTA framework was constructed so as to get strictly comparable coefficients over time. A dummy variable, metropolitan area, controlled for the dichotomous effect of five regions defined simultaneously as NUTS1 and NUTS2 regions. Lastly, the results, obtained from the SFTA and RTA analyses, were also benchmarked by conventional panel data analysis.

The economic integration was assumed to be very deep within countries. In other words, trade barriers were assumed to be low between the regions within the same country. This was expected to imply different spatial structures in RTA and SFTA contexts.

An important result of the comparison between SFTA and actual data was that market potential has agglomerated in different ways within the countries on the one hand and internationally on the other: the market structure had strongly affected the location of economic activities within the countries, but not positively internationally among the countries during the period 1996-1999 in the entire data of 12 countries.

The results of both the RTA-SFTA analysis and the panel data analysis seem to have some consistent aspects. As expected, the labor share of agriculture was the strongest driver affecting the geographical concentration of market potential in both the RTA and SFTA models. However, the IRS effect seemed to be related to spatial agglomerations of market potential only in the within-country context. An exception to this was the 8-country set in which the IRS effect was significant only at the end of the time series. This is to say, generally speaking that business activities have not been located internationally according to the level of the IRS effect or innovation potential of regions. This implies that economic integration has not been as deep internationally as it has been within the countries.

The model was adjusted by removing the four countries with the shortest time series. Thus, the data ranged from 1989 to 1999. Then the statistical model employed involved the problem of varying results depending on the group of countries investigated. The increasing returns to scale (IRS) effect (sunk cost effect / innovation intensity) no longer predicted the agglomeration of economic activities as significantly as in the 12-country case either in SFTA or in RTA. However, the four countries removed were also analyzed separately. Then the IRS effect was significant in any period in SFTA in the four-country model. Finally, we used the entire time series (1989-1999) panel data and benchmark the above results by a conventional panel data analysis. The benchmark supported the results obtained from the entire 12-country and 4-country models. The IRS effect steered the location of economic activities within the countries, but not between them.

In the present study, we scrutinized the regional structures emerging within and among the countries. Although the regional time series available were relatively short, the assumption of "extreme" integration within countries guided us in understanding the long-run development. The current spatial structures have been developed over many decades. Hence, the short time series capture only the outcome of the long-run development. The small variation of the coefficients over time supports the statement: Regional effects of economic integration did not seem to change during the period investigated. The only exception was the 8-country subset in which we observed this phenomenon only at the end of the time series.

Innovation intensity seems to be an important target for further research. Industrial sectors and their market structures could be analyzed in a regional context. The industry-specific empirical framework could offer new insights for the discussion on regional development especially in the industries with high innovation intensity.

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Appendix 1. Regression analysis of 8 countries.

Table A1.   **Regression analysis (OLS) of 8 countries 1989-1999.**

	Dependent variable: Agglomeration of market potential (GDP per km²), 8 countries			
	Real Trade Area			
Year	**Descriptives** **Constant**	**Labor structure effect, LSA (labor share of agriculture)**	**Increasing returns to scale effect, IRS (patents per capita)**	**Metro-politan area (NUTS1)**
1989	R² = .751 F=109.436*** **.014** N = 113 (.042)	-.758*** (.059)	.029 (.039)	.351 (.364)
1990	R² = .771 F=112.525*** **.115**** N = 104 (.043)	-.727*** (.057)	.039 (.041)	.857** (.280)
1991	R² = .760 F=114.758*** **.011** N = 113 (.042)	-.721*** (.057)	.016 (.042)	.850** (.287)
1992	R² = .761 F=120.766*** **.001** N = 118 (.042)	-.670*** (.055)	.078 (.042)	1.055*** (.285)
1993	R² = .762 F=123.043*** **-.017** N = 119 (.039)	-.675*** (.052)	.052 (.038)	.939*** (.269)
1994	R² = .761 F=122.992*** **.003** N = 120 (.038)	-.681*** (.053)	0.017 (.039)	.095*** (.268)
1995	R² = .750 F=115.735*** **-.004** N = 120 (.041)	-.686*** (.057)	.043 (.043)	.850** (.295)
1996	R² = .766 F=131.899*** **.098*** N = 125 (.040)	-.741*** (.058)	.027 (.042)	1.225*** (.272)
1997	R² = .731 F=108.061*** **.111*** N = 123 (.043)	-.743*** (.064)	.017 (.045)	1.075*** (.298)
1998	R² = .719 F=100.577*** **.127**** N = 122 (.043)	-.745*** (.065)	.012 (.045)	1.261*** (.347)
1999	R² = .746 F=87.267*** **.234**** N = 93 (.047)	-.846*** (.078)	.016 (.044)	.670* (.303)

Standard errors are in parentheses. The asterisk labels (*) stand for: * 5 percent risk level, ** 1 percent risk level, *** 0.1 percent risk level.

Table A2.   Regression analysis (OLS) of 8 countries 1989-1999.

	Dependent variable: Agglomeration of market potential (GDP per km²), 8 countries				
	Synthetic Free Trade Area				
Year	**Descriptives**	**Constant**	**Labor structure effect, LSA (labor share of agriculture)**	**Increasing returns to scale effect, IRS (patents per capita)**	**Metropolitan area (NUTS1)**
1989	R² = .765 F=118.264*** N = 113	.016 (.047)	-.859*** (.054)	.009 (.053)	.535 (.383)
1990	R² = .771 F=112.392*** N = 104	.007 (.049)	-.826*** (.054)	.058 (.053)	.952** (.310)
1991	R² = .746 F=106.607*** N = 113	-.001 (.049)	-.789*** (.055)	.061 (.055)	.936** (.330)
1992	R² = .740 F=107.899*** N = 118	-.013 (.048)	-.775*** (.053)	.097 (.053)	1.051** (.325)
1993	R² = .747 F=112.888*** N = 119	-.005 (.047)	-.767*** (.052)	.092 (.051)	1.023** (.321)
1994	R² = .743 F=111.901*** N = 120	.004 (.046)	-.764*** (.052)	.069 (.051)	.096** (.318)
1995	R² = .721 F=100.008*** N = 120	-.018 (.050)	-.762*** (.056)	.074 (.054)	1.065** (.339)
1996	R² = .724 F=106.017*** N = 125	-.029 (.047)	-.759*** (.053)	.060 (.051)	1.214*** (.325)
1997	R² = .729 F=106.747*** N = 123	-.015 (.047)	-.766*** (.053)	.062 (.052)	1.066** (.332)
1998	R² = .695 F=89.444*** N = 122	-.033 (.049)	-.714*** (.054)	.143** (.053)	1.320** (.053)
1999	R² = .662 F=58.181*** N = 93	-.031 (.061)	-.713*** (.069)	.079 (.063)	.970* (.382)

Standard errors are in parentheses. The asterisk labels (*) stand for: * 5 percent risk level, ** 1 percent risk level, *** 0.1 percent risk level.

Appendix 2. Regression analysis of 4 countries.

Table A3.   Regression analysis (OLS) of 4 countries 1996-1999.

	Dependent variable: Agglomeration of market potential (GDP per km²), 4 countries				
	Real Trade Area				
Year	**Descriptives**	**Constant**	**Labor structure effect, LSA (labor share of agriculture)**	**Increasing returns to scale effect, IRS (patents per population)**	**Metro-politan area (NUTS1)**
1996	R² = 0.654 F=25.791*** N = 45	**-.354*** **(.137)**	**-.825*** (.117)	**-.405** (.308)	**.723** (.482)
1997	R² = 0.637 F=25.177*** N = 47	**-.416**** **(.131)**	**-.841*** (.121)	**-.302** (.268)	**.449** (.510)
1998	R² = .732 F=48.224*** N = 57	**-.470*** **(.103)**	**-.909*** (.098)	**-.142** (.224)	**.815*** (.393)
1999	R² = .690 F=40.870*** N = 59	**-.502*** **(.103)**	**-.864*** (.104)	**-.138** (.219)	**1.022*** (.411)

Standard errors are in parentheses. The asterisk labels (*) stand for: * 5 percent risk level, ** 1 percent risk level, *** 0.1 percent risk level.

Table A4.   Regression analysis (OLS) of 4 countries 1996-1999.

	Dependent variable: Agglomeration of market potential (GDP per km²), 4 countries				
	Synthetic Free Trade Area				
Year	**Descriptives**	**Constant**	**Labor structure effect, LSA (labor share of agriculture)**	**Increasing returns to scale effect, IRS (patents per population)**	**Metro-politan area (NUTS1)**
1996	R² = .738 F=38.551*** N = 45	**-.075** (.068)	**-.481*** (.083)	**.211*** (.072)	**1.007*** (.312)
1997	R² = .649 F=26.494*** N = 47	**-.060** (.075)	**-.405*** (.093)	**.203*** (.079)	**1.060*** (.357)
1998	R² = 0.767 F=58.053*** N = 57	**-.110** (.067)	**-.621*** (.082)	**.185*** (.070)	**1.146*** (0.301)
1999	R² = .778 F=64.304*** N = 59	**-.066** (.080)	**-.652*** (.080)	**.208*** (.068)	**.967*** (.296)

Standard errors are in parentheses. The asterisk labels (*) stand for: * 5 percent risk level, ** 1 percent risk level, *** 0.1 percent risk level.

ESSAY 2.
Price Markups and R&D Inputs:
The Pharmaceutical Industry
in Finland and the USA[29]

Abstract

The aim of this paper is to compare the price-cost margins in the pharmaceutical industry in Finland and USA. We employ data on the Finnish and the US pharmaceutical industry. The estimation is theoretically based on a modification of the conventional growth models and its extensions under imperfectly competitive markets. The results show that the estimated price-cost margin is 0.60-0.67 in Finland and 0.51-0.67 in the US with demand-driven instruments and lagged R&D expenditure-related instruments. When R&D stock is estimated and included as one production input in the model, the price-cost margin drops to 0.43-0.55 in Finland and 0.40-0.58 in the US. Therefore, differences in regulatory environments have not altered the price-cost margins in the pharmaceutical industry within these countries. This is due either to the inefficient regulation system in Finland or it is due to the differences between market structures and the competitive environment.

Keywords: competition, market structure, price-cost margin, pharmaceuticals, price regulation.

2.1   Introduction

There is a great need for international price comparisons of pharmaceuticals particularly those being utilized in regulatory planning activities. The price comparison studies provide direct information on international price levels of pharmaceuticals. Such information is conventionally combined with information on the costs of pharmaceutical production and research and development (R&D) and then utilized in decision-making and regulatory planning.

Instead of comparing international prices directly, this article focuses on analyzing price-cost margins. There are some interesting price comparison studies (Danzon and Chao, 2000; Berndt et al., 1995). They show that international price comparison studies may provide biased results if they are based on unrepresentative samples and unweighted indices of pharmaceuticals. Furthermore, there also seems to be a lack of indispensable information on factors affecting price levels. The price comparison studies describe the situation, but do not explain why price levels differ. Factors behind the price differences can be derived from the cost structures of firms, degree of competition, regulatory practices, or domestic income levels. In order to take into account these factors, this article measures the price-cost margins.

The aim of this article is to provide information on factors influencing price levels in pharmaceutical markets. To do this, the price-cost margin of the pharmaceutical industry is estimated in two countries, Finland and the USA. These differ from each other, for instance, in regulatory and competitive settings, and the size of the pharmaceutical industry.

This paper is divided into three main sections. The following section provides some background information on pharmaceutical markets in Finland and the US. The theoretical model is set up in section 3 for the empirical analysis. Then section 4 presents the data, and the results of the estimation are given. Section 5 discusses the results compared to other studies and in the perspectives of regulation and R&D activities in the pharmaceutical industry. Section 6 concludes the paper.

2.2   Regulation and Market Structure

The pharmaceutical market in Finland has experienced strict price regulation (see e.g. Rinta 2001). Before 1995, the approval of a pharmaceutical product for the public reimbursement system was linked with the institutionally-set price. Since 1995, drug prices have been deregulated in

principle. However, if a company applies to have the drug accepted as part of the Finnish reimbursement system, the pharmaceuticals pricing board sets the price at twice the amount that will be refunded. In contrast, there has been no price regulation in the US market.

The size of the US market is 200 times larger than that in Finland. On the one hand, the large size of the markets could theoretically imply some closeness to the features of perfect competition. On the other, because there are many patent protected products with some monopoly power, one would expect that many US companies, without direct price regulation, would charge more than their counterparts in a more regulated setting.

One would expect that differences in the regulatory measures and size of the markets would cause a difference to the price-cost margin in the two countries taking into account economies of scale in production. If the industry could achieve increasing returns to scale in its production processes, the average costs of production would decrease with higher volumes of production. However, marginal costs do not necessarily decrease together with the decrease in average costs if, for instance, the cost function is linear. However, if marginal costs also decrease along with production volume, then we could expect higher price-cost margins in the US than in Finland, and vice versa, if there are increasing marginal costs. There could also exist a certain point or points in production volumes at which the marginal costs begin to decrease or increase in a given time. This can be, for instance, due to additional costs of hiring new employees from other sectors.

The method in our study is based on Solow's (1957) seminal work. The estimation procedure consists of Solow's method for measuring technical change called Solow's residual. The model ignores the question of increasing returns to scale by assuming constant returns to scale in production. Hall (1988) and Domowitz, Hubbard and Petersen (1988) developed the model and analyzed Solow's residual in both perfect and imperfect competition frameworks. They showed that Solow's residual is independent of the growth rate of the output-capital ratio if perfect competition prevails. However, if the market is imperfectly competitive, there is a correlation between the two variables and the growth of the total factor productivity is pro-cyclical.

The estimation of price-cost margin can be based on the Solow's residual setting. The method was applied by Linnosmaa, Hermans, and Hallinen (2004). They estimated the price-cost margin of the Finnish pharmaceutical industry. The estimation employed time series data and provided a fixed price cost margin over time. The present paper extends that application and utilizes R&D expenditures and estimated R&D

stock in order to take R&D stock into account as a productive input in the pharmaceutical industry. This modification is justified given the high R&D intensity of the pharmaceutical industry.

Finnish pharmaceutical markets have been highly regulated compared to US markets. On the other hand, the production capacity of the US pharmaceutical industry is over 200 times higher than the capacity in Finland. We restricted the sample to two countries because there was no further international data available which was plausible for measuring price-cost margins. We can also compare our results with other studies on the US markets (e.g. Scherer and Ross, 1990). It is also important to test the applicability of the method in two different countries with different data sources to see if the method could be utilized further in wide-scale international studies.

2.3   The Model

The model is from Domowitz, Hubbard, and Petersen (1988) and Linnosmaa, Hermans, and Hallinen (2004). The production function is the form:

$$(1) \qquad Q(t) = A(t) f\big(L(t), S(t), K(t)\big)$$

where Q signifies production, A is a measure for the technical change not captured by other factors of production, L, S and K denote labor, research and development, and capital inputs, respectively. The term t stands for time, implying that all the variables are measured at a certain time. To simplify the notation, however, the time variable is dropped from the following analysis.

Solow (1957) derived a measure for technological process, sometimes called Solow's residual. Applying the same assumptions and principles to the above production function, Solow's residual can be shown to be:

$$(2) \qquad \frac{\dot{Q}}{Q} - \frac{\dot{K}}{K} - \tilde{b}_S\left(\frac{\dot{S}}{S} - \frac{\dot{K}}{K}\right) - \tilde{b}_L\left(\frac{\dot{L}}{L} - \frac{\dot{K}}{K}\right) = \frac{\dot{A}}{A},$$

where the dotted variables stand for derivatives with respect to time.

We denote the input shares simply as:

(3) $\tilde{b}_S = \dfrac{P_S S}{cQ}$ and $\tilde{b}_L = \dfrac{P_L L}{cQ}$,

in which $\tilde{b}_S$ measures the share of R&D costs of the value of output, and $\tilde{b}_L$ stands for the share of the total labor wages of the value of output. The industry is assumed to be perfectly competitive and hence the output is valued at marginal cost c.

Under imperfect competition a firm's output is not valued at marginal cost, but the price exceeds marginal cost. Under imperfect competition, the shares of labor and R&D can be rewritten as:

(4) $\tilde{b}_S = \dfrac{p}{c}\dfrac{P_S S}{pQ} = \dfrac{p}{c}b_S$ and $\tilde{b}_L = \dfrac{p}{c}\dfrac{P_L L}{pQ} = \dfrac{p}{c}b_L$.

The terms b_S and b_L stand for the ratio of R&D expenditure to value added of production and the ratio of labor wages to value added of production, respectively. Substitution of the shares in equation 4 in Solow's residual in equation 2 provides:

(5) $\dfrac{\dot{Q}}{Q} - \dfrac{\dot{K}}{K} - \dfrac{p}{c}b_S\left(\dfrac{\dot{S}}{S} - \dfrac{\dot{K}}{K}\right) - \dfrac{p}{c}b_L\left(\dfrac{\dot{L}}{L} - \dfrac{\dot{K}}{K}\right) = \dfrac{\dot{A}}{A}$.

We define the Lerner index for monopoly power as follows:

(6) $\lambda = \dfrac{p-c}{p}$ and $1-\lambda = \dfrac{c}{p}$.

Term λ stands for the Lerner index, that is the price cost margin. The term 1- λ depicts the price -cost ratio. The generalized residual can be further rewritten as[30]

(7) $\dfrac{\dot{Q}}{Q} - \dfrac{\dot{K}}{K} - (1-\lambda)^{-1}b_S\left(\dfrac{\dot{S}}{S} - \dfrac{\dot{K}}{K}\right) - (1-\lambda)^{-1}b_L\left(\dfrac{\dot{L}}{L} - \dfrac{\dot{K}}{K}\right) = \dfrac{\dot{A}}{A}$.

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[30] This also equals Hall's (1988) specification, which is the basis of his empirical estimation procedure.

Multiplying both sides of equation 7 by $(1-\lambda)$ and rearranging it, we get:

$$(8) \qquad \left(\frac{\dot{Q}}{Q}-\frac{\dot{K}}{K}\right)-b_L\left(\frac{\dot{L}}{L}-\frac{\dot{K}}{K}\right)-b_S\left(\frac{\dot{S}}{S}-\frac{\dot{K}}{K}\right)=\frac{\dot{A}}{A}(1-\lambda)+\lambda\left(\frac{\dot{Q}}{Q}-\frac{\dot{K}}{K}\right).$$

If λ is zero, firms hav... left-hand side of equation 3) is technical change. If firms can price their products over marginal costs, Solow's residual depends on the changes in production and it fluctuates pro-cyclically (the right-hand side of equation 8).

2.4   Data

The data on the US pharmaceutical industry was collected from the OECD Health data and OECD STAN database. R&D figures for both countries were taken from the OECD ANBERD database. The data set for Finland was aggregated from the firm-level data in Statistics Finland. It contains all Finnish pharmaceutical firms, which have more than 20 workers. The firm-size restriction was made in order to avoid the problem of inconsistent data in the capital stock variable. The capital stock figures for the smallest places of business were deemed to be unreliable over time. Figures on pharmaceutical expenditures were obtained from OECD Health Data.

The US data set covers the time from 1970 to 1997 and the Finnish data from1975-1999. The R&D information covers 1973-1997. The data set contains information on nominal and real output, nominal and real value added, working hours, the number of workers, labor costs, R&D investment, and capital stock. The capital stock series was constructed from data on capital stock per labor hours. Table 1 below presents the descriptive statistics of the growth rates of the original variables used in this study. Output, value added, wages, and capital stock variables are measured in Finnish Markkas (FIM) and in US dollars (USD).

Table 1 presents the real growth rates of value added, labor, capital, R&D expenditures, estimated R&D stock, GDP, and nominal pharmaceutical expenditure.

Table 1. Descriptive statistics.

Percentage annual rates of growth in volumes (1995 prices)				
	Geometric mean	Std. deviation	Minimum	Maximum
Value added				
Finland	6.2 %	19.6 %	-14.9 %	82.9 %
USA	4.6 %	5.2 %	-4.7 %	18.4 %
Labor				
Finland (working hours)	1.9 %	5.4 %	-6.9 %	10.4 %
USA	2.7 %	3.0 %	-3.4 %	8.6 %
Capital stock				
Finland	7.6 %	15.1 %	-21.1 %	41.6 %
USA	3.1 %	6.8 %	-11.4 %	14.6 %
R&D expenditure				
Finland	6.9 %	7.9 %	-12.7 %	24.9 %
USA	7.4 %	5.8 %	-6.2 %	19.4 %
Estimated R&D stock				
Finland	7.4 %	2.7 %	3.2 %	13.8 %
USA	7.5 %	1.3 %	4.6 %	9.7 %
Domestic pharmaceutical expenditure (in current prices)				
Finland	11.0 %	4.1 %	5.3 %	21.8 %
USA	9.7 %	2.0 %	5.8 %	13.6 %
GDP				
Finland	2.2 %	3.1 %	-6.3 %	6.8 %
USA	3.1 %	2.3 %	-2.1 %	7.3 %

Volume indices for output and value added were constructed in Statistics Finland and are presented in 1995 prices for the Finnish data. Excluding the instrument variables, we received ready-made data in both value and volume terms. As instruments we used the nominal expenditure on pharmaceuticals and gross domestic income. Data for the first instrument were obtained from the Social Insurance Institution of Finland while all the other data came from Statistics Finland. The volume indices for R&D data were constructed utilizing the GDP price indices. In the US data, the volume of production was estimated utilizing pharmaceuti-

cal prices that were used as a production price deflator. The capital stock volume was formed employing the price index for investments in the US chemical industry.

The first two instruments employed in models 1 and 2 – the growth rate of the nominal expenditure on pharmaceutical products and the growth rate of real GDP – can be held as indicators which are demand-driven and do not affect the total factor productivity. Instead, a third instrument, the growth rate of real R&D expenditures with a lag of one year, is more problematic. If most of the R&D activities concentrate on improving the production processes of pharmaceutical firms, they boost the productivity. In this case, the instrument is not valid due to the causal relation with the dependent variable. But, if the R&D activities were mainly channeled to long-term drug development, they would not be mirrored closely in the short-term fluctuations in productivity. Keeping this in mind, we add the growth rate of real R&D expenditure to one of our models as an instrument.

2.5 Variable Construction

The variables are constructed straightforwardly in light of the theory. First, variables are converted from nominal to real terms. Then the annual changes are measured and contrasted with the growth rate of the capital stock (equation 8). The new and most critical part in the variable construction is the formulation of the R&D stock as part of the price-cost margin estimation procedure.

The R&D stock is applied in this study, instead of employing R&D expenditures, because our theoretical model employs the growth of stocks. The development in the growth of stocks is smoother over time than the growth of expenditure. The concept of knowledge stock is comparable to the capital stock presented in the original model. Second, R&D efforts seem to affect the knowledge stocks with lags. The stock is changing after a lag compared with R&D expenses.

About half the R&D expenditure is wages (Guellec and Ioannidis 1997). Part of the R&D costs is intermediate input and capital investment. Accordingly, half of the R&D expenditure is deducted from the total cost of labor compensation to avoid counting it twice. Part of the R&D-related investment in equipment is possibly also documented in the capital stock, which may lead to counting the same data twice. Unfortunately, the data on intermediate input and share of R&D-related capital stock were not available. If R&D stock and capital stock are counted twice, the Lerner

index in the empirical model could even be negative. When these inputs are not reduced from the estimated figures, this has two possible impacts. It can distort the growth rates of R&D stock and the share of R&D stock of the total value added. The first mentioned effect is restricted if the input changes symmetrically with the growth of the entire stock. However, the share of R&D stock can be overestimated, which in turn causes the Lerner index to be underestimated. However, when the data of both countries are treated similarly, the comparison is expected and uniformly reflects the reality. It is also illustrative to compare the results of both models, with and without the R&D stock effect.

The R&D stock is created as follows. First, the R&D stock is calculated by conventional accounting standards. The R&D stock is formed by multiplying the R&D expenditure of the first period, 1973, by a factor of five. Five years is a conventional and cautious estimate for the range of the economic influence of the expenditure on R&D activities in conventional accounting standards. This is, the research and development activities this year are expected to affect the earning prospects of the industry during the next five years on average.

The ratio between R&D investments and R&D stock is approximately 1 / 5. In other words, the actual R&D expenditure is assumed to be the best estimator for the cumulative R&D stock. In order to fill this condition, we fix the annual depreciation rates of R&D stocks in both countries. The fixed depreciation rate of real R&D stock for Finland is estimated at 14.5% and the US at 14.0%. The GDP deflator has been employed as a proxy for R&D prices. Hence, the real R&D stock grows as much as the real annual R&D expenditure and is depreciated by the fixed rate above. This corresponds to a 7.4% real rate of growth for the R&D stock in Finland and 7.5% in the US. In this setting, we can utilize the cumulative nature of knowledge, which is applied and formed in R&D activities.

2.6   Empirical Model

The empirical estimation is based on equation 8. We estimate a linear regression model:

(9) $r_t = \alpha_1 + \alpha_2 q_t + u_t$.

The left-hand side equals Solow's residual r_t and the independent variable corresponds to the output-capital ratio in the right-hand side of the equation 8. The independent variable is endogenous because the output-

capital ratio appears on both sides of equation 8. We use the 2SLS esti-
mation technique to estimate the above model.

2.7   Results

We first estimate the model (equation 9) without the R&D stock variable
and then later add this variable to the model. We utilize the nominal
growth of pharmaceutical expenditure and the real growth of the GDP
as instruments in two regression models estimated using 2SLS tech-
niques. Table 2 presents the estimation results of model 9 for both in-
strument variables. The estimates of the pooled regression model are
also shown.

The results propose that Solow's residual (left-hand side of equations
11 and 12) is strongly pro-cyclical both in the US and Finnish pharma-
ceutical industries. The correlation between Solow's residual without
R&D stock and the growth rate of the output-capital ratio is 0.978 ($p <$
.01) in Finland and 0.919 in the US. The correlation between value
added and factor productivity is 0.962 ($p <$ .01) in Finland and 0.880 ($p
<$ .01) in the US. All of the correlation estimates deviate significantly
from zero. This implies the simultaneous determination of Solow's
residual and the output-capital ratio. In other words, changes in both
variables are pro-cyclical.

Table 2 presents the estimates of the Lerner index when Solow's re-
sidual does not include the growth of the R&D stock. Estimates for the
price-cost margin in the Finnish pharmaceutical industry range between
0.597-0.668 and in the US between 0.512-0.671. According to the t-tests,
any pair of Lerner indices, obtained by different instruments, do not
differ from each other between Finland and the US ($p <$ .05).

The results obtained from the Finnish pharmaceutical industry are
equivalent to those of Linnosmaa, Hermans, and Hallinen (2004). The
estimates for the Lerner indices in the US pharmaceutical industry are
close to those obtained by Scherer and Ross (1990).

Table 3 presents the results of the model, which contains the R&D
stock in Solow's residual. The change in the R&D stock-capital ratio is
now weighted by R&D expenditure per value added (R&D share) ac-
cording to equation 8. Half the R&D share estimates are labor wages,
which are, in turn, deducted from the total wages. The price-cost mar-
gins vary between 0.43-0.55 in Finland and 0.40-0.58 in the US. Accord-
ing to the t-tests, the Lerner indices do not differ significantly ($p <$ .05)
between Finland and the US. Despite some contradictions between the

results of the models, the results of the R&D stock-corrected models clearly show that the mark-ups are lower than the estimates from models which do not take into account R&D effects. However, t-tests show that the Lerner index decreases significantly only in Finland when we use pharmaceutical expenditure as an instrument and the R&D stock effect is taken into account (Appendix 2). The values of the Lerner indices are lower in all cases when the R&D stock is considered, but the differences are not significant (p < .05).

Table 2.   Results of Solow's residual 2SLS model with labor and capital inputs.

Dependent: Solow's residual	R^2 (adjusted R^2)	Constant (α_1)	Lerner index (α_2)
Instrument: growth of GDP / capital			
Finland	.8564 (.8499)	.0193 (.0162)	.5970*** (.1437)
USA	.8010 (.7927)	.0077 (.0060)	.5120*** (.0847)
Pooled data			
Fixed effects	.8405 (within groups)	.0127 (.0085)	.5766*** (.0926)
Instrument: growth of pharmaceutical expenditure / capital			
Finland	.9001 (.8956)	.0200 (.0135)	.6683*** (.0985)
USA	.8060 (.7979)	.0076 (.0059)	.5207*** (.0868)
Pooled data			
Fixed effects	.8792 (within groups)	.0126* (.0074)	.6382*** (.0697)
Instrument: growth of lagged R&D expenditures / capital			
Finland	.8663 (.8602)	.0194 (.0157)	.6114** (.1588)
USA	.8523 (.8449)	.0094* (.0047)	.6709*** (.1044)
Pooled data			
Fixed effects	.8710 (within groups)	.0145* (.0082)	.6212*** (.1058)
Method: 2SLS and on pooled data 2SLS fixed effect model			

Standard errors are in parentheses. The asterisk labels (*) stand for the level of the statistical risk to reject the null hypothesis incorrectly: the regression coefficient is zero.

*   10 percent risk level, **   1 percent risk level, *** 0.1 percent risk level.

The results of model 1 state that the estimated Lerner indices differ significantly from zero and they are 0.44 in Finland and 0.40 in the US.

This implies the approximated price-cost ratios to be 1.79 and 1.66, respectively. Instead, the constant term does not deviate significantly from zero. The constant term partially describes the effect of technical change without the estimation of the growth of R&D stock (see equation 11). When we add the growth of the R&D stock to the model, we can expect that the R&D effects capture much of the effect of technical change. Due to the inclusion of the R&D stock in the model, it seems logical that the constant term does not differ significantly from zero.

Table 3.   Results of Solow's residual model with labor, capital, and R&D inputs.

Dependent: Solow's residual (rt)	R2 (adjusted R2)	Constant ( )	Lerner index ( )
Model 1: growth of GDP / capital as an instrument			
Finland	.7125 (.6988)	.0073 (.0234)	.4424* (.2097)
USA	.6815 (.6671)	-.0029 (.0063)	.3963** (.1133)
Pooled data			
Fixed effects	.6032 (within groups)	.0007 (.0136)	.3878* (.1530)
Model 2: growth of pharmaceutical expenditure / capital as an instrument			
Finland	.8138 (.8049)	.0093 (.0187)	.5549** (.1361)
USA	.7130 (.7000)	-.0029 (.0060)	.4355*** (.1014)
Pooled data			
Fixed effects	.7067 (within groups)	.0015 (.0117)	.5091*** (.1108)
Model 3: growth of lagged R&D expenditures / capital as an instrument			
Finland	.6979 (.6836)	.0071 (.0240)	.4287 (.2496)
USA	.8336 (.8253)	.0005 (.0048)	.5823*** (.1055)
Pooled data			
Fixed effects	.6213 (within groups)	.0027 (.0145)	.3983* (.1947)
Method: 2SLS and on pooled data 2SLS (fixed effects)			

Standard errors are in parentheses. The asterisk labels (*) stand for the level of the statistical risk to reject the null hypothesis incorrectly: the regression coefficient is zero.

*   10 percent risk level, **   1 percent risk level, *** 0.1 percent risk level.

Model 2 estimates the values of the Lerner indexes to be 0.55 in Finland and 0.44 in the US. Hence, the price-cost ratios are higher than in model 1 in both countries, 2.25 in Finland and 1.77 in the US. Models 1 and 2 imply that price-costs margins are higher in Finland than in the US. However, model 3 alters the relative ranks of the countries. The Lerner index of the Finnish pharmaceutical industry is 0.43, which equals the value of the price-cost margin of 1.75. The Lerner index of the US pharmaceutical industry is 0.58 and the price-cost margin is correspondingly 2.39.

In one case (Table 3, model 3, Finland), the Lerner index does not deviate significantly from zero. The correction of heteroscedasticity by White's robustness check altered the standard error and significance of the coefficient so that the Lerner's index became significant in this model ($p < .05$).

2.8 Interpretation of Main Findings

Carlton and Perloff (1994) list results from studies estimating price-cost margins in different industries. The highest price-cost margins appear in the regulated banking (0.88) and coconut oil industry (0.89). Our estimates on price-cost margin are below these two estimates. Scherer and Ross (1990) utilize accounting data and find that the US pharmaceutical industry has the sixth highest price-cost margin when industries are ranked according to the estimated price-cost margins. The authors estimate the price-cost margin to be 0.614. On the basis of informal discussions, Berndt et al. (1995) assess that price-cost margins for H_2 antagonists would fall into the range 0.75-0.9.

The price-cost margins of the pharmaceutical industry seem to be at a same level in Finland and the US. This is interesting because there are some noticeable differences in the pharmaceutical market environments of these countries. For instance, price regulation is stronger in Finland than in the US.

There can be two potential reasons for the similarity of price-cost margins in the pharmaceutical industry in Finland and the US. If the markets are otherwise identical in Finland and the US, but price regulation is applied in Finland, then the price regulation is not binding. In this case, Finnish authorities could either scrap the entire regulatory system or alternatively tighten price regulation. The first alternative could be optimal in the case of a costly regulatory system.

The other explanation for the result is that the markets are not otherwise identical. Market structure, technological advancement, or governmental interventions could be very different in the two countries. In this case, the price regulation may be binding. There are even other forms of regulation that have some effects on the market structure and prices. For instance, the differences in drug approval processes may imply a difference in markups.

Before 1994, price setting was linked to the market authorization of the pharmaceutical product in Finland (Rinta, 2001). Price regulation used to be tied to the reimbursement system and it aimed at defining the reasonable wholesale and retail price of pharmaceuticals. If a company wanted to include its product in the reimbursement system, Finnish authorities set a maximum price level for the product. In contrast, prices are set by the market in the US system.

The US markets are divided into two parts. First, there are drugs that are patent protected and, second, there are generic drugs without patent protection or the patent has expired. The large marketplace implies higher potential returns in the first case with high market power. The second case of generic competition implies that there might be almost perfect competition due to the large number of suppliers and consumers. In Finland, the market was relatively closed. The Finnish companies produced many compounds under license, as well as their own brands. There has also been a tradition of branding even non-prescribed generic domestically produced pharmaceuticals for Finnish markets. In other words, there exist some kind of market dichotomies in both countries.

The nature of the markets can be a partial explanation for the similar price-cost margins. In other words, high mark-ups obtained from patent-protected products can be offset by low margins within severe generic competition in the US. In Finland, regulated prices of prescribed products may imply relatively low mark-ups, which were offset by relatively high mark-ups of non-prescribed branded products in generic markets.

2.9   Conclusion

This study compared price-cost margins in the pharmaceutical industry in the US and Finland. The study applied a uniform estimation technique, based on Solow's residual, for the countries in order to get comparable results in the markets in which price regulation systems are different. According to the results, price-cost margins do not differ between Finland and the US.

This study also attempts to take into account the effects of changes in R&D expenditure. This allows us to assess the impact of specific features of R&D intensity in the pharmaceutical industry on its price-cost margin. The price-cost margin seems to decrease by over 10 percentage points in Finland when R&D stock is included in the model. However, the difference is statistically significant only in Finland, as pharmaceutical expenditure is employed as an instrument. In the US, the absolute effect was under 10 percentage points. The notion is in accordance with the theory. It also shows that conventionally estimated price-cost margins can be generally higher without implementing the impact of R&D expenditure on the measures. This particularly holds true in R&D-intensive industries, such as the pharmaceutical industry.

The results raise some questions about the efficiency of regulatory settings and the differences between the market structure. If the market structure is the same in both countries, then (price) regulation is not binding in Finland, and either the regulation should be tightened or eliminated. If there are also differences in market structure and competitive environment, as seems to be the case, the policy implication above is no longer so straightforward. For a more careful investigation of the market structure, for instance, the dichotomy in the domestic markets and the significance of foreign trade should be considered in further research.

There are some open technical questions following the above analysis. The availability of the firm-level micro-data would enhance the number of methods that could be applied when evaluating price-cost margins. If panel data were available, the results of this study could be benchmarked by other methods. Another possible path could be an international comparison of the margins. This would be important in order to assess the impacts and efficiency of different regulatory systems. The panel data would also offer an opportunity to test the main assumptions of this study, for instance, the economies of scale. In further research, it would also be important to test the impacts of policy changes on the firms' price-cost margins over time.

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Appendix 1.

Table 1.   **Results of Solow's residual OLS model with labor and capital inputs.**

Dependent: Solow's residual	R^2 (adjusted R^2)	Constant	Lerner index
Finland	.9562 (.9542)	.0220* (.0089)	.8818*** (.0402)
USA	.8453 (.8389)	.0056 (.0052)	.6640*** (.0580)
Pooled data			
Fixed effects	.9331 (within groups)	.0120 (.0053)	.8492*** (.0321)
Method: OLS and on pooled data OLS fixed effect model			

Standard errors are in parentheses. The asterisk labels (*) stand for the level of the statistical risk to reject the null hypothesis incorrectly: the regression coefficient is zero.

*   10 percent risk level, **   1 percent risk level, *** 0.1 percent risk level.

Appendix 2.
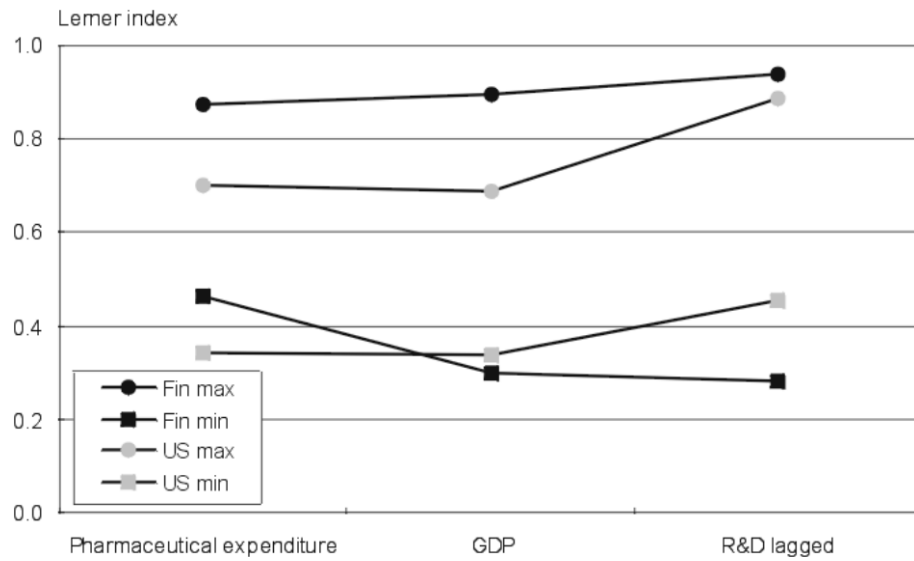
Figure A2.1. Confidence intervals (95%) of Lerner indices without R&D stock effect from Table 2.
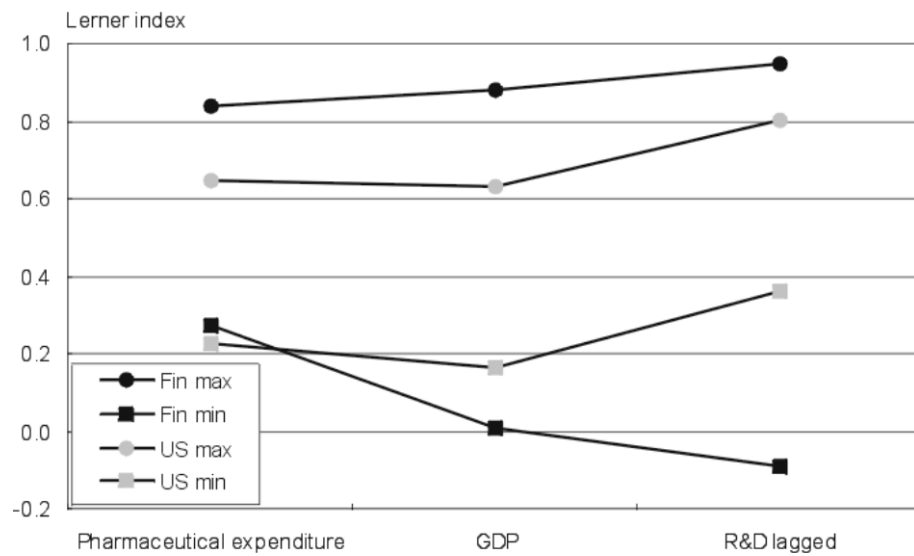
Figure A2.2. Confidence intervals (95%) of Lerner indices with R&D stock effect from Table 3.

ESSAY 3.
Finance of Small Bio-Pharmaceutical Industry in Finland – Descriptive Analysis[31]

Abstract

This study investigates the capital and ownership structures of small and medium-sized pharmaceutical-related biotechnology firms (bio-pharmaceutical companies) in Finland. These structures are also analyzed taking into account general characteristics and intangible assets of the business activities in the industry. Relatively young companies are typically owned by persons that are active in the business, private venture capital companies, and government institutions. Older firms are mostly owned by other non-financial companies. The major capital loan supplier has been Tekes, the National Technology Agency of Finland. Equity financing from private venture capital companies and governmental sources has supported growth in research and development activities in the companies examined. However, the companies owned mostly by non-financial companies have been able to generate relatively high sales. These firms are also anticipated to have the highest sales potential over the next 5 years. The results here are contrasted with explanations of the capital structure found in the literature. No single theory seems to explain the capital and ownership patterns within Finnish bio-pharmaceutical companies. Instead, the literature suggests many explanations for the observed ownership patterns. For example, different patterns can be related to the owners' willingness to monitor the managers and support activities with high earning prospects.

Key Words: Biotechnology, capital structure, finance, intangible assets, pharmaceutical industry.

3.1   Introduction

In Finland a great deal of emphasis has been placed in recent years on biotechnology research in scientific circles as well as in biotechnology companies, the number of which has grown sharply. The biotechnology sector has been an interesting one recently owing to the high growth expectations and risks related to this field. This sector is anticipated to spark a new phase of technological development that will have a pronounced impact on economic growth. ETLA carried out a survey of biotechnology companies in spring 2002. This study presents the main findings about capital structures and business characteristics of bio-pharmaceutical companies. Overviews of the Finnish biotechnology industry have been made by e.g. Kuusi (2001), Schienstock and Tulkki (2001) as well as Hermans and Luukkonen (2002). The study at hand has been influenced by a study on the capital structure of Finnish small and medium-sized companies (Hyytinen and Pajarinen, 2002), a study depicting capital structures in the biotechnology industry (Hermans and Tahvanainen, 2002) and a study on the SME sector in the US (Berger and Udell, 1998). Furthermore, Tahvanainen (2003) has analyzed the capital structures prevailing in the Finnish biotechnology industry. The study at hand focuses on the capital structure of biotechnology companies engaged in pharmaceutical-related activities at the end of 2001 (see also Hermans, 2003).

The study has two main aims. The first aim is to identify the sources of financing for Finnish bio-pharmaceutical companies. The second aim is to depict how various sources of financing are related to the intangible assets and other characteristic features of these companies. In order to fulfill the first aim the sources of financing and capital structure are evaluated with respect to the companies' age and size as well as their research intensity. In order to accomplish the second aim, principal component analysis is used to evaluate how sources and types of financing are related to the companies' intangible assets. The study also sheds light on the capital structures from the perspective of the financial literature.

The study is organized as follows. After the introduction, in Section 2 we provide an overview of the bio-pharmaceutical sector. The characteristics of the small and medium-sized companies in this sector are compared to those of the overall biotechnology industry and SMEs as a whole in the Finnish economy. Section 3 describes the capital structures of bio-pharmaceutical companies and the results of the survey are compared with those reported in the finance literature. Section 4 pre-

sents the findings of the principal component analysis and presents the interconnections between capital structures and business characteristics. Section 5 discusses the results of the study.

3.2 Characteristics of Bio-Pharmaceutical Sector

The data used in this study is derived from on a database compiled by ETLA covering financial and business-related information on 84 companies operating in the biotechnology sector. An overview of the data is presented in Hermans and Luukkonen (2002). From the database we selected 42 small and medium-sized firms that indicated they are part of the pharmaceutical industry or that their clients or subcontractors are in the pharmaceutical industry. ETLA's survey was carried out in early 2002 and its information is based primarily on the situation at the end of 2001. The information from financial statements has been cross-checked with the trade register of the National Board of Patents and Registration of Finland.

The number of personnel in small and medium-sized[32] bio-pharmaceutical companies is relatively high compared to other Finnish SMEs as a whole, but their sales revenues are lower on average than those of companies in other industries. Almost 30 percent of the bio-pharmaceutical companies employ over 20 persons while the corresponding share for all SMEs is 15 percent. Despite the fairly high number of employees, the turnover of biotechnology companies is less than other companies. The turnover of about 45 percent of the bio-pharmaceutical companies is less than EUR 200,000 while the corresponding share for SMEs as a whole is about 15 percent. The sales of the bio-pharmaceutical sector are oriented more toward foreign markets than sales of other companies on average.

The companies of the bio-pharmaceutical sector are comparatively young. Slightly more than a third of the biotechnology companies have been founded in 1997 or afterwards, while the corresponding share for SMEs as a whole is some 14%.

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[32] Below we use the term SMEs to denote small and medium-sized enterprises. A company is called small or medium-sized if two of the following three conditions are met: the company has a maximum of 250 employees, its turnover does not exceed EUR 40 million and its total assets are less than EUR 27 million.

Table 1.   **Comparison of Finnish Bio-pharmaceutical SMEs and SMEs as a whole.**

		Bio-pharmaceutrical SMEs (%)	Total SMEs (%)[33]
Number of personnel	<5	33 %	44 %
	5-20	38 %	41 %
	>20	29 %	15 %
Turnover, million euro	< 0.2	45 %	15 %
	0.2-1.5	40 %	56 %
	1.6-8.0	12 %	24 %
	>8	2 %	5 %
Exports / turnover	0 %	43 %	70 %
	0-1 %	2 %	22 %
	2-5 %	7 %	4 %
	6-10 %	0 %	2 %
	>10 %	45 %	3 %
	Unknown	2 %	0 %
Age of company, years	0-2	14 %	5 %
	3-4	21 %	9 %
	5-24	64 %	70 %
	>24	0 %	16 %
R&D expenditures / total costs (Total SMEs = R&D expenditures / turnover)	0 %	5 %	53 %
	0-1 %	2 %	23 %
	2-5 %	5 %	13 %
	6-10 %	7 %	3 %
	>10%	79 %	6 %
	Unknown	2 %	0 %
Company has patents or patent applications	Yes	74 %	6 %
	No	26 %	94 %
Company's expected turnover growth over next 5 years (Total SMEs = next 3 years	<0 %	0 %	1 %
	0-1 %	2 %	31 %
	2-5 %	0 %	20 %
	6-10 %	10 %	23 %
	>10 %	86 %	21 %
	Unknown	2 %	5 %
Total observations in sample		42	754

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[33] Hyytinen and Pajarinen (2002) used sector-specific data on Finnish companies to uncover the real structure of Finnish SMEs. This study weighted the data according to the age of the companies (as Hermans and Tahvanainen 2002). The weights are obtained as follows: $\dfrac{n_{total(t)}}{n_{sample(t)}}$. The term n denotes the number of companies in the total population and the sample. Term t denotes the three groups (t=1,2,3) in order of age. Group 1, group 2 and group 3 consist of companies founded in 1997-2001, 1991-1996, and earlier, respectively.

The nature of the bio-pharmaceutical sector as a seller of scientific research is seen especially when we look at companies' outlays on research and development (R&D) as a percentage of their total expenses. Almost eight out of ten of the biotechnology companies have R&D outlays amounting to more than 10 percent of their total expenses. Accordingly, three-fourths of the bio-pharmaceutical companies have patents or patents pending, while 94 % of all SMES have neither of these. Instead, over half of all Finnish SMEs have no R&D expenditures at all. Thus the biotechnology industry is more R&D intensive than other sectors on average.

Commercialization of products by bio-pharmaceutical companies is geared primarily toward the future, in contrast with other SMEs. Active research activity is ordinarily anticipated to generate expectations of future revenues. Otherwise it would not be worthwhile for the company to carry out R&D activity at all. On the other hand, the emphasis on commercialization geared toward the future will increase the business risks, which will in turn increase the yield requirements of investors. Given the revenue expectations of entrepreneurs and the yield requirements of investors, it is understandable that 86 percent of the bio-pharmaceutical companies expect turnover to rise over the next five years at an average annual rate exceeding 10 percent. Only about a fifth of all SMEs expect turnover to grow faster than 10 percent per annum.

3.3   Capital Structure and Financial Sources

In this section we investigate the financing received by bio-pharmaceutical companies broken down by type of capital. Because almost half of the companies made a loss in the fiscal period evaluated, the losses realized reduced the amount of equity in the balance sheet. Since we want to assess how much has been invested in the companies in the form of equity and capital loans and other forms of debt, the realized profits or losses are not taken into consideration at all in our study. Thus the capital structure presented in Table 2 does not correspond to the figures obtainable directly from the balance sheets.

Himmelberg and Petersen (1994) show using US data on older listed companies that the internal financing of companies is a significant form of financing for R&D activities. This study emphasizes the special nature of the bio-pharmaceutical sector as a young research-intensive field, and thus it investigates the financing coming from investors. Revenue financing is evaluated from the viewpoint of turnover not profitability.

Table 2.   Capital structure by age and size of bio-pharmaceutical companies.

	Equity	Capital loans	Loans	Total financing (million euro)
Total	70.6 %	18.3 %	11.1 %	225.4
0-4 years	77.1 %	10.5 %	12.4 %	134.9
5-8 years	71.0 %	27.9 %	1.1 %	59.3
9-24 years	41.4 %	33.6 %	25.0 %	31.2
Small	49.9 %	36.5 %	13.7 %	20.6
Large	72.6 %	16.5 %	10.9 %	204.8

Equity and capital loans are prominent forms of financing in all bio-pharmaceutical companies (Table 2). Equity and capital loans are both considered part of the total shareholders' equity. A company pays a dividend to shareholders and interest on capital loans only if it has profits that it can pay out. Bio-pharmaceutical companies have relatively low levels of indebtedness. Loans account for 11 percent of total financing on average. Loan financing, which is classified as a liability, is relatively higher in older companies, a fourth of whose capital comes from loans.[34] The nominal value of the equity financing of older firms is less than that of their younger counterparts at the end of 2001. Part of this may be explained by inflation and part with smaller levels of investments.

The total equity financing of SMEs operating in the pharmaceutical industry is estimated to be slightly less than EUR 160 million (Table 3). Most of the companies are owned by persons actively engaged in the business, private venture capital companies and government institutions providing venture capital, mainly Sitra.[35] Especially in older companies the owners are likely to be non-financial companies. Other companies own over 60 percent of the shares of bio-pharmaceutical companies that are more than 8 years old. The ownership of both private venture capital companies and government institutions is significant among relatively young companies. The investments of venture capitalists appear to enable companies to hire additional employees.

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[34] For an overview of theories on companies' capital structures see e.g. Myers (1984; 2001).

[35] Sitra denotes the Finnish National Fund for Research and Development.

Table 3. **Equity financing by age and size of bio-pharmaceutical companies.**

	Persons active in the business	Other persons	Private venture capital company	Other financial institution	Other company	Government institution	Other	Total share capital (million euro)
Total	25.6 %	4.8 %	31.7 %	2.6 %	10.4 %	23.6 %	1.3 %	159.0
0-4 years	27.5 %	4.1 %	42.0 %	0.3 %	0.9 %	25.0 %	0.2 %	104.0
5-8 years	22.3 %	7.6 %	13.6 %	8.5 %	17.8 %	25.9 %	4.2 %	42.1
9-24 years	21.4 %	0.6 %	8.6 %	2.0 %	62.4 %	4.9 %	0.2 %	12.9
Small	42.5 %	6.2 %	7.4 %	0.0 %	17.0 %	22.1 %	4.8 %	10.3
Large	24.5 %	4.7 %	33.4 %	2.8 %	9.9 %	23.7 %	1.1 %	148.8

The capital loans supplied to bio-pharmaceutical companies have come almost entirely from the public sector. The largest supplier of capital loans is Tekes.[36] Tekes accounts for over 80 percent of the capital loans supplied to this sector. When Sitra is taken into consideration in the calculations, the public sector's share of capital loans rises above 95 percent. The role of Sitra as a source of capital loans is especially pronounced in small companies with less than 20 employees.

The most prominent source of loans for bio-pharmaceutical companies is accounts payable from other companies and loans from Tekes. Accounts payable are usually related to business expenses. In Finland payment times for purchases are shorter than in many other countries. The relatively high portion for accounts payable tells that loan financing is not a popular means of financing in this sector where business risks (and also the risk related to repayment of the loan) are considerable. It is also typical of the bio-pharmaceutical sector that the company's revenue expectations and assets are based to a large extent on intangible assets and competencies, so companies seldom have collateral they can pledge to back loans. For example, bank loans are only taken by older bio-pharmaceutical companies, the operations of which have to a certain extent stabilized and that have accumulated tangible assets. Companies in business for over 8 years account for about 77 percent of the sector's tangible assets, such as machinery and equipment.

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[36] Tekes is The National Technology Agency of Finland.

Table 4.   Capital loan financing by age and size of bio-pharmaceutical companies.

	Private venture capital company	Foreign venture capital company	Sitra	Tekes	Finnvera	Other government institution	Other	Total capital loans (million euro)
Total	1.5 %	0.0 %	15.4 %	80.3 %	0.2 %	1.0 %	1.6 %	25.1
0-4 years	1.1 %	0.1 %	18.9 %	76.0 %	0.2 %	1.5 %	2.2 %	16.7
5-8 years	0.0 %	0.0 %	0.0 %	94.0 %	0.0 %	0.0 %	6.0 %	0.6
9-24 years	2.5 %	0.0 %	9.0 %	88.5 %	0.0 %	0.0 %	0.0 %	7.8
Small	7.0 %	0.0 %	40.0 %	41.3 %	1.5 %	8.9 %	1.3 %	2.8
Large	0.8 %	0.1 %	12.3 %	85.3 %	0.0 %	0.0 %	1.6 %	22.3

The most prominent source of capital for bio-pharmaceutical companies is equity financing. Companies obtained over 70 percent of their financing in this form. Almost all of the capital loans, i.e. subordinated loans on equity terms, came from government institutions (Table 4). Loan financing was relatively modest and over a third of the loans were related to daily business operations. In contrast, over 60 percent of the equity of older firms (founded 9-24 years ago) is held by non-financial companies (Table 3). According to Table 2, they have relatively more loan financing and over 10 percent of the loans are from banks (Table 5).

The prominent share of loan financing within older companies corresponds with the principal-agent theory regarding the relationship between a company's owners and management presented by Jensen (1986). By taking a loan the company's owner (in this case another company) seeks to monitor the behavior of the management and constrains spending by the management. On the other hand, according to Jensen and Meckling (1976), the high proportion of share capital provided by persons actively engaged in the business can be explained by constraints on fringe benefits stemming from their high ownership stakes. Owing to the pivotal role of equity financing as a whole, we will look at the significance of the ownership structure in more detail in the next section.

Table 5.   **Loan financing by age and size of bio-pharmaceutical companies.**

	Bank	Other financial institution	Other company	Other debt	Tekes	Finnvera	Other government institution	Bond	Other	Total loan financing (million euro)
Total	2.6 %	2.7 %	0.5 %	35.8 %	23.3 %	2.1 %	8.1 %	0.8 %	24.1 %	41.2
0-4 years	0.0 %	2.9 %	0.0 %	21.1 %	25.9 %	1.3 %	2.1 %	0.0 %	46.7 %	14.2
5-8 years	0.0 %	0.0 %	0.2 %	51.8 %	29.0 %	1.1 %	13.2 %	0.0 %	4.8 %	16.6
9-24 years	10.3 %	6.6 %	1.6 %	30.3 %	10.8 %	4.6 %	8.5 %	3.3 %	24.1 %	10.5
Small	9.8 %	6.1 %	0.6 %	14.3 %	14.6 %	11.4 %	18.0 %	0.0 %	25.2 %	7.5
Large	1.0 %	1.9 %	0.5 %	40.5 %	25.2 %	0.0 %	5.9 %	1.0 %	23.9 %	33.7

As a rule, few bio-pharmaceutical companies have very high levels of turnover yet. Most of the equity financing is focused on firms with turnover less than EUR 1.5 million (Table 6). Those companies that have succeeded in creating some sales are mostly owned by non-financial companies. These companies primarily export their products or services abroad. Other investor groups have made most of their investments in firms that do not yet have significant turnovers.

R&D activities and ownership of intangible assets is of key importance from the viewpoint of the companies' revenue expectations. R&D is of pivotal importance in the pharmaceutical sector owing to the long lags in product development. The time from an innovation spurring development of a drug to the launch of the final product on the market may take 10-15 years. This inevitably means that a start-up firm's R&D activities and intangible assets are of pivotal importance when assessing the firm's expected stream of revenues and consequent present value. For example, Garner, Nam and Ottoo (2002) evaluate the connection between R&D intensity and the company's market value by using growth options.

Table 6.   **Equity financing by realized turnover, i.e. sales revenue, and export intensity of bio-pharmaceutical companies.**

	Persons active in the business	Other persons	Private venture capital company	Other financial institution	Other company	Government institution	Other	Total share financing (million euro)
Turnover under 1.5 million euro	26.3 %	5.1 %	33.6 %	2.6 %	5.9 %	25.0 %	1.4 %	147.6
Turnover over 1.5 million euro	16.8 %	0.6 %	7.4 %	2.3 %	67.4 %	5.5 %	0.1 %	11.5
Exports / turnover under 10%	26.9 %	5.4 %	36.6 %	2.9 %	0.7 %	27.2 %	0.4 %	133.4
Exports / turnover over 10%	18.8 %	1.5 %	6.3 %	1.0 %	60.9 %	5.2 %	6.2 %	25.6

Table 7.   **Equity financing of bio-pharmaceutical companies broken down by realized R&D intensity[37] and possession of patents and patent applications.**

	Persons involved in company's business	Other persons	Private venture capital company	Other financial institution	Other company	Government institution	Other	Total share financing (million euro)
Low R&D intensity	4.5 %	0.2 %	0.0 %	0.0 %	93.8 %	1.5 %	0.0 %	7.5
High R&D intensity	26.6 %	5.0 %	33.3 %	2.7 %	6.2 %	24.7 %	1.4 %	151.6
No patents	25.2 %	7.8 %	0.0 %	0.0 %	46.8 %	12.8 %	7.4 %	3.4
Patents	25.6 %	4.7 %	32.4 %	2.7 %	9.6 %	23.9 %	1.2 %	155.6

Owing to the nature of the biotechnology industry, most of the companies have a relatively high level of R&D activity (Table 7). On the one hand, investors have stressed the importance of R&D activity by com-

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[37] A company's R&D intensity is high when research and development costs are over 10 percent of total costs.

panies as a way of boosting future revenue expectations (Table 7 high R&D intensity). On the other hand, the R&D intensity of the companies may be a signal to investors about future revenue expectations, which makes the company an interesting investment target.

Biotechnology R&D activity spawns patent applications but, on the other hand, companies possessing intangible assets are attractive investment opportunities. For this reason it is not clear whether most of the patent applications and patent ownership are mainly a result of research financed by equity or whether the company has been an interesting investment candidate and obtained equity financing because it has had intangible assets such as patents already when the company was founded. The investigation of cause-effect relationships between intangible assets and equity financing would require time series data. In this study we have at our disposal only cross section data from the end of 2001 so that we must satisfy ourselves with discussing the causality relationships only in general terms. However, Luukkonen (2003) states that holdings of patent applications and patents are a necessary condition for a biotechnology company to obtain equity financing from private venture capital companies.

A company's present value is based on the expectations of the future stream of revenues generated by its business activities. In Table 8 the ownership structure is broken down by the sales expectations indicated

Table 8.   Equity financing of bio-pharmaceutical companies by expected turnover in 2006 and expected annual growth in turnover.

	Persons in business	Other persons	Private venture capital company	Other financial institution	Other company	Government institution	Other	Total equity investments (million euro)
Expected sales in five years below 1.5 million euro	26.4 %	6.4 %	36.1 %	3.3 %	0.1 %	27.4 %	0.2 %	107.4
Expected sales in five years above 1.5 million euro	23.9 %	1.4 %	22.6 %	1.1 %	31.6 %	15.9 %	3.5 %	51.7
Expected rate of growth less than 25% per annum	24.1 %	4.5 %	38.6 %	0.3 %	8.7 %	23.5 %	0.3 %	90.3
Expected rate of growth greater than 25% per annum	27.6 %	5.2 %	22.8 %	5.6 %	12.5 %	23.8 %	2.6 %	68.7

by the company. First let us look at the company's own sales expectations in five years. A critical threshold of 1.5 million is set for expected sales after five years. Persons actively engaged in the business own about a fourth of the companies with both low and high revenue expectations. Private venture capital firms own slightly over a one-third stake in the companies with revenues anticipated to remain below EUR 1.5 million over the next five years but they account for slightly over a fifth of the ownership in companies with higher revenue expectations over the same time horizon. The role of government sources of venture capital, especially Sitra, will grow in connection with companies whose turnover is not expected to surpass 1.5 billion by the year 2006. On the other hand, non-financial companies have invested almost exclusively in companies whose sales expectations are relatively high.

In this section we have presented the capital structure of companies in the bio-pharmaceutical sector broken down by factors describing the nature of the business. In the next section we will seek to form a more systematic overview of the above-described capital and ownership structures using statistical means.

3.4   Financial Sources and Business Models

3.4.1   Variable Selection

The book value of a company is often below its market value determined, for example, on the financial markets (see Hall 2001). Investors seek to make investment decisions based on expectations of future returns. The future return expectations regarding a company can be assessed on the basis of financial statements and intangible assets at the disposal of the company. The intangible assets of a company are seldom booked at full value on the official balance sheet. In a broad sense the whole intellectual capital of a company can be regarded as an intangible asset. (e.g. Edvinsson and Malone, 1997; Sveiby, 1997).

A company's intellectual capital can be divided into human capital, structural capital and relational capital (Edvinsson and Malone, 1997). Human capital comprises the knowledge of the personnel. Biotechnology is a science-based sector where knowledge management is given more emphasis than in many other sectors. The total number of personnel and number of employees with doctorate degrees depict the company's internal critical mass. The business experience of the CEO in years measures the business knowledge of the management while the educational level of the CEO signifies formal or practical competence.

Structural capital includes the company's internal organizational structures and organization of activities whereby it seeks to use human capital efficiently. In this connection, structural capital is measured by R&D costs, the number of patents and patent applications as well as the age of the company (in years). In addition we look at the intensity of research and patents: the number of patents and patent applications is calculated as a percentage of the number of personnel and R&D expenditures are calculated as a share of the company's total costs.

Relational capital is comprised of the company's external relationships. The most critical aspect of relational capital is the company's possibilities to exploit the market potential of its products, i.e. client relations. Without customers the company is not viable, even if the activities of its highly educated personnel is otherwise well organized. Ahonen (2000) and Hussi (2001) list the following mechanisms of value creation. They divide intangible assets into generative intangible assets and commercially exploitable intangible assets. The value of commercially exploitable intangible assets can be measured also by the ability to generate a return. With this in mind, the sales volume of the company in 2001 is evaluated separately under the heading of business performance. On the other hand, generative intangible assets (such as intellectual capital) are not expected to generate a return until later in the future. For this reason we look at the company's expected turnover in the year 2006. The ability to take advantage of international markets is measured by exports' share of total turnover.

The return expectations of bio-pharmaceutical companies may often be several years away. For this reason market potential can be assessed from the perspective of financing received. If financiers have accepted the company's business strategy and offered the company financing, this signifies that the plan is strategically well founded and credible. Here we evaluate whether the company's activities have been financed by Sitra or Tekes, how much financing the company has received for R&D from government institutions as well as how large a share of its total R&D expenditures is financed by government institutions. Furthermore, the significance of various financing sources is depicted under the heading of capital structures by the amount of financing raised via equity capital and capital loans. The capital structure of the company is also depicted by the debt-equity ratio.

In young bio-pharmaceutical companies, there is growing emphasis on joint research with other experts in the field. The critical mass needed in R&D can be achieved also via joint research with other experts in the field. Almost all companies engage in collaboration with some do-

mestic research institutions or universities. In the statistical analysis we assess the prevalence of international collaboration by looking at whether the company collaborates with foreign academic institutions. The nature of collaboration is also depicted by whether the company engages in R&D collaboration with subcontractors or clients.

The company's external relational capital also includes possibilities to recruit skilled labor. This is measured by whether the company indicates that it has encountered difficulties in hiring employees. The company's external relations are also assessed as to whether the company's accounting is handled by one of the big five accounting firms.

3.4.2   Methodology

In the following statistical analysis we will address the features characteristic of the ownership structure of the bio-pharmaceutical sector. The analysis will make use of principal component analysis. The strength of the principal component analysis methodology in this connection is that its use does not require a theoretical model upon which the analysis is based. On the other hand, principal component analysis allows us to condense the information contained in the statistical data by using the joint variance of the variables. Principal component analysis is based on the assessment of correlations between selected variables and the mutually independent principal components.[38] The results of the principal component analysis are presented in the appendix.

The use of principal component analysis is justified by the observation that the variables appearing in the model are mutually correlated. In regression analysis the correlation of the independent variables leads to a problem of multicollinearity, which may distort the results. For example, Tahvanainen (2003) encounters this problem when using regression analysis to evaluate the debt-equity ratio of SMEs in the biotechnology sector. In contrast, in the principal component analysis the variables are grouped into different principal components and one variable can be correlated with more than one principal component. Principal component transformations are indeed supposed to be carried out so that each variable is strongly correlated with only one principal component. Thus the variable regarded as the dependent variable can be kept in the principal component analysis as one of the variables. We can therefore evalu-

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[38]   E.g. Sharma (1996) provides a detailed technical presentation of principal component analysis.

ate separately the principal component that was correlated with the debt-equity ratio in Tahvanainen (2003).

In the next section the principal components are distinguished according to whether the correlation between the selected variable and the principal component is over 0.3, which corresponds roughly to the correlation level that differs from zero taking into account the sample size and assuming a normally distributed population.

In the next section presenting the results of the statistical analysis we name five principal components, the eigenvalues of which are greater than two. The strict method is necessitated by the fact that owing to the relatively large number of variables there are ten components with eigenvalues greater than one. In order to summarize the information contained in the data, we apply stricter criteria in the selection of the principal components. The analysis makes use of the rotation of principal components, based on the varimax method. The method seeks to produce a rotated final result where each variable is prominent in only one principal component. The rotated principal components analyzed explain slightly over half of the variance of the selected variables.

3.4.3   Results

The principal components are presented in six boxes in Figure 1. Principal component 2 is presented in two parts as components 2a and 2b, which are mirror images of each other. The interpretation of the components is based on the finance literature, which we extend upon in the study. This allows us to link our approach to one of the relevant bodies of corporate finance literature.

According to the pecking order theory, the quality of companies' development projects affects capital structures in two main ways. First, because the personnel working inside the company know more about the real return expectations than foreign owners, in high quality companies (high expected return projects) the ownership share of persons actively engaged in the business is high. This means that in the first stage only loan financing is raised outside the firm. Only when the loan financing runs out does the company raise external equity financing. On the other hand, external investors can gauge the quality of the company according to either the average quality prevailing in the sector or the company's intellectual capital. Below we will analyze the principal components both with respect to the "average quality" of the sector as well as the connection between the company's intellectual capital and capital structure.

1. "Big and beautiful"
   - large personnel
   - many employees with doctorates
   - lots of tangible assets (machinery equipment)
   - many patents and patent applications
   - high R&D expenditures and considerable governmental support for R&D activities
   - R&D collaboration with foreign research institutes
   - collaboration with subcontractors
   - exports' share of turnover high in 5 years
   - owners are private venture capital companies, government institutions and persons engaged in the business
   - Tekes has provided financing

2.a "Promising subsidiaries"
   - high sales expectations in future
   - realized sales on high level
   - exports' share of turnover is high
   - owned by other non-financial companies
   - R&D collaboration with customers
   - audited by international accounting firm
   - relatively old company
   - Tekes has provided financing

   - small ownership by private venture capital companies, government institutions and persons actively engaged in business
   - few employees with doctorates
   - relatively high share of loan financing
   - located somewhere else than Turku

2.b "Doctors in Turku"
   - owned by private venture capital companies, government institutions and persons actively engaged in business
   - many employees with doctorates
   - relatively low share of loan financing
   - located in Turku
   - relatively old company

   - low sales expectations in 5 years
   - realized sales on low level
   - low share of sales are exported
   - not owned by other non-financial companies
   - no R&D collaboration with customers
   - not audited by big 5 accounting firm

3. "Sound business plan"
   - high R&D intensity
   - high R&D expenditures and considerable public support for R&D activities
   - many employees with doctorates
   - exports' share of turnover is high
   - exports' share of turnover high in 5 years
   - many patents and patent applications
   - experienced managing director

5. "Experts Sought for International Collaboration"
   - problems in obtaining skilled labour
   - considerable government support for R&D expenditures
   - exports' share of turnover high in 5 years
   - R&D collaboration with foreign research institutions
   - realized sales on low level

4. "Tekes and Sitra collaboration"
   - Tekes and Sitra have provided financing
   - lots of capital loans from government institutions
   - experienced managing director

   - no R&D collaboration with customers

Figure 1.   **Principal components numbered according to rotated component matrix (appendix).**

The original pecking order theory expects that in high quality projects the first external financing comes from loans, not equity financing (Myers and Majluf, 1984; Myers, 1984). In the biotechnology sector high quality can mean e.g. R&D-intensive activities. Nevertheless as a company's research intensity grows, so does the information asymmetry be-

tween the company's personnel and external investors. Thus, for example, the risk premium on loan financing may become surprisingly large. Hyytinen and Pajarinen (2002) maintain that in this kind of situation a reversed pecking-order may be the best model for an R&D-intensive company in practice because an R&D-intensive SME has difficulties in getting loan financing. Thus financing in the form of loans precedes financing via external equity and capital loans.

The reversed pecking order seems to appear in some of the features of the "Big and Beautiful" principal components. This principal component also features a high volume of R&D activity, a high number of employees with doctorate degrees and ownership of considerable intangible assets. The "Big and Beautiful" companies are typically owned by private venture capital firms, government institutions and persons actively engaged in the company. This principal component is strongly correlated with variables depicting company size. The companies characterizing this principal component have a lot of personnel and tangible assets. Baysinger, Kosnik and Turk (1991) find for US data on large enterprises that a high equity stake held by institutional investors increases the companies' expenditures on R&D activities. Thus the information included in the "Big and Beautiful" component is consistent with the above-mentioned study regarding the phenomenon that greater ownership by private venture capital firms and government institutions goes hand in hand with companies' R&D expenditures.

In the second principal component called "Promising Subsidiaries", a prominent role is played by equity financing from non-finance companies. For the companies of this principal component it is typical that they are already generating sales and that they expect their sales will be on a high level in five years. A considerable portion of the sales of these relatively older companies is directed abroad and they engage in collaboration with their clients. These efficient companies with growth expectations have a large international accounting company acting as their auditor. According to this principal component, the involvement of another company helps in the commercialization of products. On the other hand, it may be that other companies seek ownership in companies that have already been able to commercialize their products and services. In addition, this type of company has a higher portion of loan financing than other companies. According to Harris and Raviv (1990) the high prominence of loan financing and tangible assets reflects the real state of the company. On the one hand, a company that can service its debt conveys a message about its ability to perform to investors. On the other hand, if the company goes bankrupt it is easier to liquidate tangible assets than

intangible ones, which reduces the risk to lenders of getting their money back.

"Doctors in Turku" is an "inverse component" with respect to the preceding principal component. This means that the component is the same, but they are mirror images of each other. As the name indicates, in this type of relatively young company many of the owners are doctors and the activities are often located in Turku. The biggest owners are private venture capital companies, government institutions and persons actively engaged in the business. A prominent feature of their capital structure is the small share of loan financing. This group thus seems to be characterized by the reversed pecking order.

The "Sound Business Plan" principal component includes companies with particular emphasis on R&D activities, a large portion of which has been financed by the public sector. These companies have a large number of employees with doctorate degrees. The company has protected its expertise with patents. Their sales are directed primarily abroad, and their marketing plans are based on foreign trade also in the future. The managing directors of these companies have long business careers behind them. In other words, the companies' business plans are based on prolonged experience in business: the personnel with a high level of education carries out R&D work, the results of which are protected via patents and growth is sought from international markets.

Cooperation between Tekes and Sitra in financing the activities of biotechnology companies is seen in the "Tekes and Sitra Collaboration" principal component. The companies fitting the characteristics of this principal component have received capital loans from the public sector as the companies have an experienced managing director. On the one hand, the track record of the management means something in the financing decisions of government institutions. On the other hand the collaboration between Tekes and Sitra is not characterized by a certain type of ownership structure or, for example, certain growth expectations of the company seeking financing, but rather these government institutions have engaged in cooperation in very diverse projects. This indicates that collaboration between the institutions enhances their monitoring ability. It is efficient for many financiers to monitor simultaneously the quality of companies' projects.

In the component called "Experts Sought for International Collaboration" some companies have had problems in obtaining skilled labor. These companies have obtained a great deal of financing for R&D from the public sector. The companies are engaged in international research

projects with foreign research institutes. Even though they do not have a high turnover, they plan to commercialize their products or services and export them abroad within five years.

3.5   Discussion and Conclusions

This study analyses the capital structure of biotechnology companies that develop pharmaceutical products. The financing received from the company's investors is usually equity financing and to a lesser extent capital loans, i.e. subordinated loans on equity terms. On the other hand, ordinary loan financing is not a very popular form of financing in the bio-pharmaceutical sector.

The classic pecking order theory by Myers and Majluf (1984) does not appear to explain the forms of financing prevalent in the Finnish bio-pharmaceutical sector. The pecking order theory predicts that external equity financing is too expensive for R&D-intensive start-ups. According to this theory, external equity financing would be available on unfavorable terms. Thus entrepreneurs, i.e. the persons actively engaged in the business, fund the project themselves. After this the company can take a risk-free or low-risk loan and only after this is equity financing sought from external investors. In the Finnish bio-pharmaceutical sector, external financiers such as private venture capital firms and government institutions are participating as owners of the company in a rather early stage.

Bhagat and Welch (1995), Hall (2002) as well as Hyytinen and Pajarinen (2002) showed that SMEs are less dependent on loan financing the more R&D intensive their activities are. This decision gains only partial support in the descriptive principal component analysis, but this phenomenon can be observed in certain individual bio-pharmaceutical companies. Many older bio-pharmaceutical companies owned by other companies have relatively low R&D intensity and solidity ratios. Furthermore, the reversed pecking order theory predicts high shares for external equity and capital loan financing and low shares of loan financing in young but relatively large R&D-intensive companies.

Ang, Cole and Wuh Lin (2000) observed that the owners' cost of monitoring the management of the company grows when the number of foreign investors increases and the ownership share of the management decreases. The management knows more about the situation of the company than outside investors. This empirical observation by Ang, Cole and Wuh Lin (2000) regarding the asymmetry with respect to the cost of infor-

mation based on the principal – agent theory supports the hypothesis that the management's share of ownership is comparatively important in companies with many different owners. On the other hand, this also explains the relatively large share of bank loans in bio-pharmaceutical companies owned mainly by other companies. Banks are able to lower the costs stemming from the asymmetry of information costs between the owners and the management by monitoring the company with its own resources. The willingness to provide a loan gives the owners a signal about the sound shape of the company and thus reduces the cost of gathering information.

The "Big and Beautiful" principal component is marked by the following phenomenon: the more a company has intellectual property rights and R&D activity, the greater are its financial resources. This observation corresponds with the findings of Lerner and Merges (1998) obtained using international data. The more financial resources a company has, the more influence a company engaged in R&D collaboration has over decisions (e.g. about intellectual property rights).

Lerner, Shane and Tsai (2002) studied the equity financing cycles prevailing in the US biotechnology industry. According to them, companies seeking to finance their R&D activities are obliged to settle for partnership agreements on unfavorable terms when the stock market is in a slump. These kinds of partnership agreements appear to be difficult to change when the situation in the stock market improves. In future studies it would be worthwhile to analyze at what stage do the non-financial companies obtain stakes in biotechnology companies that are already generating revenues.

In the current situation prevailing in the financial markets, obtaining a listing on the stock exchange does not seem a realistic option. The licensing and royalty payments as well as mergers and acquisitions are the most common way of securing second round financing for commercialization projects. Thus technological expertise does not appear to suffice alone to achieve commercial success, but rather the start-up needs to engage in close-knit collaboration with another company and to invest in marketing competencies.

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Appendix. Results of Principal Component Analysis

Communalities			
	Variable	Initial	Extraction
Sources of financing			
Capital structure	Solidity (equity per total debt & equity)	1	0.6863903
Equity financing			
Equity financing from individuals active in business (log euros)	LNACTIV€	1	0.8010382
Equity financing from other non-financial firms (log euros)	LNFIRM€	1	0.838017
Equity financing from government institution (log euros)	LNPUBVC€	1	0.9035721
Equity financing from private venture capital organization (log euros)	LNPRVC€	1	0.8556579
Capital loan financing from government institution (log euros)	LNPUVCL€	1	0.8724937
Capital loan financing from private venture capital organization (log euros)	LNPRVCL€	1	0.7909272
Intangible assets			
Human capital			
Number of personnel	LNPERSON	1	0.9271824
Number of doctors on staff	LNDOCS	1	0.8224857
CEO's experience (in years)	LNCEOEXP	1	0.8187757
CEO is a doctor (=1)	post-graduated CEO	1	0.7225567
Structural capital			
Research and development (R&D) costs (log euros)	LNRDCOST	1	0.9164357
Number of patents and patent applications (log)	LNPATENT	1	0.8928357
Age of firm (log years)	LNAGET	1	0.7991473
Patent per number of personnel	Patents / total personnel	1	0.8508303
R&D costs per total costs	R&D costs per total costs	1	0.8566066
Relational capital			
Public support to R&D activities (log euros)	LNPBRD	1	0.9210542
Problems in skilled labor supply (=1)	Problems in skilled labor supply	1	0.7373992
Sitra has financed a firm (=1)	Sitra has financed a firm	1	0.7982579
Tekes has financed a firm (=1)	Tekes has financed a firm	1	0.8500641
Public supports to R&D activities per R&D costs	public r&d support per r&d costs	1	0.8427616
Firm has top-5 auditor (=1)	Top5 Auditor	1	0.7072709
Collaboration with foreign academic institutions (=1)	collaboration with foreign academic institutions	1	0.7907651
Principal customer's share of total sales over 1/3	principal customer (>1/3)	1	0.660605
Principal subcontractor's share of total purchases over 1/3	principal subcontractor (>1/3 out of purchases)	1	0.7711855

Communalities, cont.			
	Variable	Initial	Extraction
R&D collaboration with customers	rd collaboration with customers	1	0.7862258
R&D collaboration with subcontractors	rd collaboration with subcontractors	1	0.6515332
Tangible assets Tangible assets (log euros)	LNTANG	1	0.8908755
Background dummies Location in Turku region	Turku	1	0.7502396
Firm announces its core branch in pharmaceutical industry	Pharma=1	1	0.8309156
Firm has spun out from academic research	research spin-off	1	0.8221582
Business performance			
Present turnover			
Turnover (log euros)	LNTO	1	0.8679751
Exports per turnover	exports per turnover	1	0.7579612
Anticipated future turnover			
Anticipated future turnover in 2006	LNTO5	1	0.8479678
Exports per turnover in 5 yrs	exports per turnover in 5 yrs	1	0.7962595
	Extraction Method: Principal Component Analysis.		

Appendix, cont.

Total Variance Explained

Component	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loadings		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	7.5500655	21.571616	21.571616	7.5500655	21.571616	21.571616	5.155834	14.730954	14.730954
2	5.3737336	15.353525	36.92514	5.3737336	15.353525	36.92514	4.6588054	13.310872	28.041827
3	2.94936	8.4267429	45.351883	2.94936	8.4267429	45.351883	2.9549013	8.4425752	36.484402
4	2.49134	7.1181144	52.469997	2.49134	7.1181144	52.469997	2.6240589	7.4973112	43.981713
5	2.3085172	6.5957633	59.065761	2.3085172	6.5957633	59.065761	2.4885319	7.1100911	51.091804
6	1.8265491	5.2187116	64.284472	1.8265491	5.2187116	64.284472	2.4314193	6.9469122	58.038717
7	1.713833	4.8966657	69.181138	1.713833	4.8966657	69.181138	2.1736823	6.2105208	64.249237
8	1.5897537	4.5421534	73.723292	1.5897537	4.5421534	73.723292	2.0816619	5.9476053	70.196843
9	1.3767422	3.9335492	77.656841	1.3767422	3.9335492	77.656841	1.9519456	5.5769874	75.77383
10	1.256533	3.5900944	81.246935	1.256533	3.5900944	81.246935	1.9155867	5.4731049	81.246935
11	0.9546938	2.7276966	83.974632						
12	0.8947182	2.5563376	86.530969						
13	0.7623783	2.1782236	88.709193						
14	0.6166829	1.7619513	90.471144						
15	0.5806536	1.6590104	92.130155						
16	0.485015	1.3857572	93.515912						
17	0.4084618	1.1670338	94.682946						
18	0.3978799	1.1367997	95.819745						
19	0.3459201	0.9883432	96.808088						
20	0.2866466	0.8189902	97.627079						
21	0.2544	0.7268571	98.353936						
22	0.1755862	0.5016749	98.855611						
23	0.1269336	0.3626674	99.218278						
24	0.0909274	0.2597925	99.478071						
25	0.0701375	0.2003928	99.678463						
26	0.0523641	0.1496117	99.828075						
27	0.0361161	0.1031889	99.931264						
28	0.0240576	0.068736	100						

Extraction Method: Principal Component Analysis.

Appendix, cont.

Component Matrix(a)

	Component									
	1	2	3	4	5	6	7	8	9	10
LNPBRD	**0.835376**	0.0252071	-0.2069432	0.2053087	-0.070921	0.1636177	-0.0939433	0.2266713	-0.185606	-0.1055139
LNPERSON	**0.7879374**	0.2794558	0.1143391	-0.2723011	-0.2206523	0.0715007	-0.1096641	-0.1289529	-0.2416936	-0.0122283
LNRDCOST	**0.7759517**	0.1031488	0.1089786	**0.3185527**	-0.1969846	**0.3173479**	-0.1802982	0.0204263	-0.0809058	0.1065824
LNTANG	**0.7202918**	**0.4721778**	0.1247984	-0.0386221	-0.1927352	-0.1965564	0.0007183	0.2001652	-0.0306558	0.1234882
exports per turnover in 5 yrs	**0.7163789**	0.0215664	-0.1772552	0.1610748	**0.4120551**	0.1806152	0.1025551	-0.0709282	0.0662257	0.0537179
LNPRVC€	**0.6647698**	-0.1850622	0.2686114	0.1372457	-0.329148	-0.0821671	0.2533517	-0.069659	-0.0561944	**-0.3181437**
Pharma=1	**0.664488**	0.1729131	0.0517115	-0.298995	0.1082562	**0.3099998**	0.0887926	-0.166412	**0.3497015**	0.041387
LNPATENT	**0.6620579**	0.027499	**0.3243345**	**0.4140451**	**0.3715953**	-0.1045055	-0.1411523	0.0551501	-0.0622035	0.0359632
LNPUBVC€	**0.6367867**	**-0.5238026**	**0.3248937**	-0.2624533	-0.1976269	-0.074481	0.0182423	-0.0005234	-0.0647269	0.0118982
Tekes has financed a firm	**0.6028728**	0.2934693	**-0.4023608**	-0.2034334	-0.2321291	-0.2284507	-0.2918567	0.0468323	0.0164862	-0.059041
collaboration with foreign academic institutions	**0.5982522**	-0.2007331	0.270147	-0.227369	0.2343139	-0.0785412	0.251482	0.0940137	**-0.3058899**	-0.2028977
LNDOCS	**0.5716328**	**-0.4507345**	-0.0152973	-0.0254594	-0.1445188	0.2939711	0.2747969	-0.1340867	-0.0361689	0.2992867
principal customer (>1/3)	**-0.4821565**	0.079205	-0.1479131	0.2873072	-0.1990086	0.0786958	**0.3999769**	0.1238526	0.223197	0.2156329
Top5 Auditor	**0.4693151**	0.1864997	0.0658002	**-0.4660462**	0.085417	0.0794999	0.0710998	**0.3245882**	0.2461685	0.2146519
R&D collaboration with customers	**-0.4453923**	**0.4349214**	**0.4031327**	-0.1258584	-0.1247647	0.3322012	0.1989025	0.0112225	-0.1535042	-0.1765303
LNFIRM€	0.1168886	**0.8314251**	-0.0617772	-0.2159564	-0.0797035	0.0527135	-0.2398101	0.1262628	0.0044691	0.005504
LNTO	-0.1397957	**0.8238015**	0.3038595	0.0547549	-0.0879529	-0.170912	-0.0755769	0.1280682	-0.1037487	0.0680508
LNTO5	-0.0498077	**0.8015217**	0.171901	-0.0200594	-0.0012865	-0.030703	-0.0248733	0.2461485	-0.1270213	0.307914

Component Matrix(a), cont.

	Component									
	1	2	3	4	5	6	7	8	9	10
Solidity (equity+caploans per equity+debt)	-0.0932296	**-0.6076626**	0.1421402	0.0190996	**0.3914056**	0.0042876	-0.1350439	0.0566011	-0.1674337	0.2918642
exports per turnover	0.1979669	**0.600224**	-0.0250352	0.1656018	**0.4533727**	0.2450149	0.1930316	-0.0704757	-0.0121435	0.149987
LNAGET	**0.4011932**	**0.5650278**	-0.086716	**0.3083616**	0.1486892	-0.2353651	0.1784457	-0.2292884	0.010929	-0.2329972
Turku	-0.0649344	**-0.5416871**	**0.4156239**	0.2654928	0.0234006	0.0037162	-0.2023419	0.39512	0.0571787	-0.0920635
Patents / total personnel	0.083628	-0.0702626	**0.6226724**	0.1606211	**0.4523547**	-0.2815908	0.0171916	-0.0720497	**0.3380963**	-0.1471932
public r&d support per r&d costs	0.277179	-0.118166	**-0.5765545**	-0.108299	**0.4580709**	-0.1073287	0.2360473	0.1670207	0.041851	**-0.3179817**
r&d collaboration with subcontrac-tors	0.2943375	0.0855758	**0.4879632**	-0.080664	0.1636947	0.2297912	**-0.3300587**	0.0207895	0.2556993	-0.2420902
LNPUVCL€	**0.4031676**	-0.16951	**-0.4600136**	**-0.4152867**	-0.0963217	**-0.3454972**	-0.1796908	-0.1311583	**0.3032186**	0.1645031
LNCEOEXP	**0.3772668**	0.1353715	-0.2036257	**0.6224144**	0.0757296	-0.409694	-0.1574782	-0.0104657	0.1740758	0.0214843
r&d costs per total costs	**0.3788936**	-0.2948607	-0.2396302	**0.4707054**	-0.0914218	**0.3929414**	-0.1629073	-0.0634095	**0.3003204**	0.2521991
LNACTIV€	0.2982501	-0.494674	-0.0731743	0.2816268	**-0.5705111**	0.069478	0.0366376	0.0065268	-0.1662174	-0.1529424
Problems in skilled labor supply	0.1372081	-0.2096243	**-0.4168142**	**-0.3987663**	**0.4441255**	0.2608603	-0.0352393	0.0232762	-0.1998419	-0.1867252
Sitra has financed a firm	0.2893369	-0.3762562	0.1851437	-0.2175391	-0.0552852	**-0.6349818**	0.1367405	-0.0392827	-0.0119025	0.2544223
principal subcontractor (>1/3 out of purchases)	-0.2665188	-0.2494189	-0.0557795	-0.1255829	-0.0624053	0.1173653	**-0.5855763**	**0.4014793**	0.2143348	-0.2266436
LNPRVCL€	0.0906612	0.27056	-0.1896088	0.0773904	**-0.3233272**	0.014803	**0.4332726**	0.2885319	**0.4294154**	**-0.3277673**
research spin-off	0.0166507	-0.0577288	**-0.4153908**	0.2546267	0.1593404	-0.1004921	0.1028986	**0.6477881**	**-0.3309965**	0.0768097
post-graduated CEO	0.1791031	-0.2795362	**0.3235305**	-0.2171556	-0.0011761	0.043945	0.354817	**0.5098706**	0.222261	0.1526898

Extraction Method: Principal Component Analysis. 10 components extracted.

Appendix, cont.

Rotated Component Matrix(a)

	Component									
	1	2	3	4	5	6	7	8	9	10
LNPERSON	**0.832105**	0.2927441	0.1322656	0.180942	0.0462707	-0.1308048	0.0440874	0.0070351	0.1437658	-0.238616
LNPRVC€	**0.7291953**	**-0.3422608**	0.0792421	0.0064245	-0.1433218	0.1884379	0.0927141	0.3199159	0.175508	-0.0517098
LNPBRD	**0.7101219**	0.0501616	**0.5062112**	0.1233892	0.225571	-0.002955	-0.0012586	0.1455102	-0.0218343	0.2650426
LNPUBVC€	**0.6670803**	**-0.4215487**	0.020469	0.2328429	-0.0756838	0.067368	0.4044034	-0.1631527	-0.021218	-0.159249
collaboration with foreign academic institutions	**0.6567743**	-0.1521017	-0.1534355	-0.0386123	**0.3175246**	0.2453286	**0.3108132**	-0.1121465	0.1972234	0.0464505
LNTANG	**0.6246222**	**0.5027768**	0.1568919	0.2824646	-0.1366767	0.1098646	0.1902878	0.2139946	0.158399	0.0754496
principal customer (>1/3)	**-0.57591**	-0.040821	0.0843069	-0.1881027	-0.2728226	-0.1732368	0.1070723	0.305578	0.1828322	0.2050922
LNTO5	-0.006055	**0.864019**	-0.0464692	-0.1264676	-0.2136363	-0.0258714	0.0799704	0.0188733	0.126698	0.1188911
LNFIRM€	0.1428114	**0.8464874**	-0.0173129	0.0546188	0.0339195	-0.1441155	-0.1054838	0.2068893	-0.0905611	-0.1172471
LNTO	0.0291054	**0.79202**	-0.2188257	-0.171917	**-0.3374104**	0.1128627	-0.1133996	0.1310833	0.0677008	0.0343902
LNACTIV€	**0.4347158**	**-0.5968364**	0.2226056	0.0136435	-0.276302	-0.2360336	-0.0760071	0.1685198	-0.0785015	0.1836142
exports per turnover	-0.0411783	**0.5636498**	0.3084346	-0.2282227	0.2911241	0.1947704	-0.0299139	0.0272842	**0.4077601**	-0.0273975
r&d costs per total costs	0.0155806	-0.2737867	**0.8721311**	0.1137428	-0.0511727	-0.019355	-0.019818	0.0158407	-0.0649228	-0.0016541
LNRDCOST	**0.6625738**	0.1217836	**0.667052**	-0.0188419	-0.119805	0.0400348	0.0036206	0.0252775	0.0233005	-0.0116585
exports per turnover in 5 yrs	**0.3262775**	0.0422603	**0.5481452**	0.1334425	**0.4599682**	0.265756	0.072584	-0.0068137	0.2866655	0.007586
LNDOCS	**0.3737643**	**-0.4185263**	**0.452299**	0.0917618	0.0323151	-0.1930273	**0.369102**	-0.1238913	**0.3084555**	-0.0979447
LNPUVCL€	0.0957648	-0.0782173	0.051416	**0.871425**	0.1926413	-0.1574209	0.0848235	0.0380141	-0.0222846	-0.1554057
r&d collaboration with customers	-0.0988364	**0.3205146**	**-0.3216521**	**-0.6730545**	-0.157989	-0.1502506	0.0307584	0.1322626	0.017216	-0.2258172

Rotated Component Matrix(a)

	Component									
	1	2	3	4	5	6	7	8	9	10
Tekes has financed a firm	**0.4804135**	**0.3164**	0.1268402	**0.6067572**	0.1458177	-0.1723796	-0.1465169	0.2320941	-0.0884225	0.0280044
Sitra has financed a firm	0.2277767	-0.2745604	-0.2896162	**0.5429067**	-0.2159746	0.2069765	0.3146271	-0.2103515	0.2323552	0.0752054
Problems in skilled labor supply	0.0682695	-0.1059925	-0.016068	0.03663	**0.7935515**	-0.203855	0.0225136	-0.2045395	-0.0791886	-0.0030356
public r&d support per r&d costs	0.0119703	-0.1388794	0.0049292	0.2532655	**0.7797234**	0.1012485	0.013735	0.2280527	0.0924603	0.283192
Patents / total personnel	-0.022539	-0.0549271	-0.110751	-0.0663038	-0.0724985	**0.8671487**	0.1419462	-0.0759983	0.0130615	-0.2175898
LNPATENT	**0.4857428**	0.108746	**0.3886552**	0.020334	0.026577	**0.651337**	0.0035202	-0.190605	0.1079503	0.1437197
LNCEOEXP	0.090693	0.0722876	**0.384487**	**0.3856561**	-0.1303531	**0.4596008**	**-0.3474778**	0.1888537	0.1079087	**0.335393**
post-graduated CEO	0.0816593	-0.1379678	-0.0219097	-0.0478006	-0.0347189	0.1257641	**0.8108388**	0.0799661	-0.0640511	0.0954442
Top5 Auditor	0.2383208	**0.3611944**	0.1064743	0.2526889	0.2135282	-0.0054789	**0.6101852**	0.071895	-0.0328619	-0.1436143
LNPRVCL€	-0.0366105	0.0500265	0.0405761	-0.006474	0.0095817	-0.0297627	0.1843589	**0.863081**	0.0174781	0.07222
Solidity (equity+caploans per equity+debt)	-0.1295055	**-0.3693148**	0.0521086	-0.0143842	0.0852078	0.1630511	0.1945555	**-0.6540476**	-0.0847032	0.1537927
principal subcontractor (>1/3 out of purchases)	-0.1552291	-0.0732395	-0.0232133	0.0431879	0.0461608	-0.0514284	0.0051391	-0.0359976	**-0.8558859**	0.0261279
Turku	0.0512032	**-0.3970463**	0.0541722	-0.2059953	-0.2337155	**0.3542439**	0.2311848	-0.1812437	**-0.4786035**	0.2216635
LNAGET	0.2536022	**0.3464313**	0.0975618	0.0790874	0.1188756	**0.3572686**	**-0.3592118**	**0.3764894**	**0.4309932**	0.027215
research spin-off	-0.0219012	0.0591175	0.0876454	-0.001883	0.2292833	-0.0873727	0.0910199	0.0066571	-0.0656426	**0.8588688**
Pharma=1	**0.3442345**	0.1808318	**0.3743293**	0.1663415	**0.3054103**	0.0694434	**0.3180964**	0.1564287	0.1566771	**-0.5134446**
rd collaboration with subcontractors	**0.2986942**	0.1568297	0.1381328	-0.1610257	0.0497592	**0.4044891**	0.1120648	-0.0251105	**-0.3591931**	**-0.4294338**

Extraction Method: Principal Component Analysis. Rotation Method: Varimax with Kaiser Normalization. Rotation converged in 13 iterations.

Appendix, cont.

Component Transformation Matrix

Component	1	2	3	4	5	6	7	8	9	10
1	0.765137	0.0320552	0.4182002	0.3246962	0.185007	0.1786928	0.1698277	0.0863262	0.170267	-0.0421375
2	0.0041987	0.8961063	-0.0413413	-0.1074283	-0.036804	-0.0028326	-0.2072486	0.310354	0.1910855	-0.0811058
3	0.2510253	0.0512936	-0.2182918	-0.4258171	-0.474671	0.4777384	0.3123501	-0.2221041	-0.0531567	-0.3195603
4	-0.1009028	-0.1457236	0.5150882	-0.2530077	-0.3350404	0.3769598	-0.4109835	0.1339238	0.1150647	0.429908
5	-0.253488	0.1436023	0.0241452	-0.0893324	0.6552395	0.5479868	0.0291465	-0.3973281	0.1224651	0.0566903
6	-0.0052714	0.0039702	0.5298768	-0.6185944	0.2438627	-0.3808337	0.1289322	-0.0278712	-0.1533289	-0.301852
7	-0.0966353	-0.2193818	-0.161648	-0.2498701	0.0969588	-0.0375094	0.4021617	0.4030768	0.709077	0.1271416
8	0.0313192	0.2129071	-0.0161276	-0.097486	0.0476708	0.0217245	0.5248059	0.1678152	-0.480637	0.6376413
9	-0.4404811	-0.0381713	0.283704	0.319553	-0.0556658	0.3249916	0.2730393	0.4633235	-0.2121321	-0.4230602
10	-0.2696773	0.237797	0.3495738	0.270197	-0.3511029	-0.2119103	0.3640848	-0.5147954	0.3179943	0.0929881

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.

ESSAY 4.
Intellectual Capital and Anticipated Future Sales in Small and Medium-Sized Biotechnology Companies:
Empirical Evidence from Finland[39]

Abstract

The objective of the study was to empirically verify impacts of intellectual capital to the anticipated future sales of small and medium-sized companies within the biotechnology industry. The Finnish biotechnology industry is used as an example of an industry with high growth prospects but long and insecure product development phases. Theoretically, intellectual capital is divided into the following three categories: human capital, structural capital, and relational capital. In the empirical setting, survey data of small and medium-sized Finnish biotechnology companies are used. In the econometric analyses the interactions, or empirically co-variation, between the three categories of intellectual capital explain two thirds of the variance in the anticipated future sales of the sample companies. Thus, it seems that a well-balanced combination of human capital, structural capital, and relational capital implies value creation potential and high anticipated future sales.

Key words: Biotechnology, intellectual capital, knowledge management, sales anticipations.

4.1   Introduction

4.1.1   Background

In valuation of the company or a single business project, prevailing methods in accounting and finance are based on assessing the worth of today's investment in relationship to the positive cash flows in the future. The net present value of the project or the company is derived from these future cash flows. Strictly speaking, the net present value of the investment is the difference between the discounted, or present, value of the future income and the amount of the initial investment (see e.g. Brealey and Myers, 2003). Both theoretically and in practice, the valuation of on-going companies or business projects, in contrast to their liquidation value, is linked to their ability to generate positive cash flows in the future.

In management literature, the value of companies is often explained by the impact of intellectual capital, e.g. Edvinsson and Malone, 1997; Sveiby, 1997; Hall, 2001 and Mayo, 2001. Adequate intellectual capital enables the company to create new innovations and to exploit them commercially. This is a prime source for future sales especially in high technology industries.

The anticipated future sales are determining the market valuations of companies. High present value estimates are characteristic of industries that have high prospects for future sales. The biotechnology industry is an archetype of industries with prospects for extraordinary high future sales. Because of its high future prospects, the biotechnology industry has attracted large infusions of private venture capital. Government agencies enhancing promising industries have also heavily supported the development of biotechnology.

Despite the high impact of intellectual capital on the anticipated sales and, accordingly, on the valuation of companies, there have been only a few empirical contributions in these matters in the knowledge management literature. Attempts to empirically measure the impact of intellectual capital on value creation have been rare (Gu and Lev, 2001). Even though the biotechnology industry offers tempting future prospects and sets demanding challenges for venture capital industry and for public industry development agencies, there is a lack of research studies exploring the special characteristics of companies in the biotechnology industry (Cumby and Conrod, 2001).

4.1.2   Objective and Scope of the Study

The fact that the market valuation of companies is mainly based on antici-
pated growth prospects, challenges the reliability of the anticipated future
cash flows disclosed by the companies. This study attempts to offer a tool
on how these kinds of speculative future prospects can be assessed in a
way that controls for individual and subjective biases of future anticipa-
tions. The intellectual capital framework offers insights into how the pre-
sent resources of companies can be used in empirical evaluations of future
anticipations disclosed by companies themselves. This is especially rele-
vant in growth-oriented industries such as the biotechnology industry.

The objective of the present study is to empirically verify impacts of
intellectual capital to the anticipated future sales of small and medium-
sized enterprises (SMEs) within the biotechnology industry. It is im-
portant that the drivers behind the business logic and the valuation of
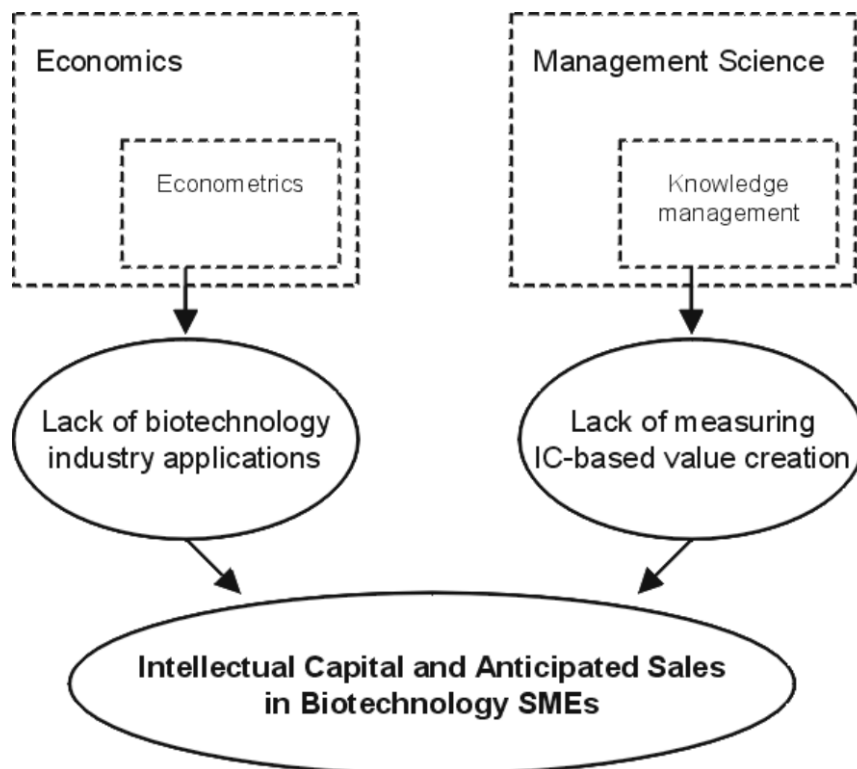
Figure 1.   **The positioning of the present study in relationship to
different research methods and research traditions (IC =
Intellectual Capital).**

companies within the biotechnology industry can be well understood. The present study combines econometric discipline of research methods and knowledge management research traditions to reach the present research objective, Figure 1.

The present study employs a well-representative survey sample of small and medium-sized Finnish biotechnology companies. The interviews were carried out at the beginning of 2002.[40] Many of the Finnish biotechnology companies are research-based spin-offs, having at the time of the interviews low or no sales. The sample of companies constitutes a good case for studying how anticipated future sales and corresponding valuations are built on the intellectual capital of the companies. Accordingly, in the present study we empirically test the intellectual capital approach presented in the knowledge management literature (e.g. Sveiby, 1997; Edvinsson and Malone, 1997; Stewart, 1997; Ahonen, 2000; Hussi and Ahonen, 2002) by applying statistical tools.

4.2   Theoretical Background

The knowledge management literature has flourished since the mid 1990s. Nonaka and Takeuchi (1995) laid a foundation in the discussion on knowledge creation in companies. In the literature the intellectual capital of the companies was used as an explanation for the fact that the book values of companies are often lower than the market valuations of the companies. (Edvinsson and Malone, 1997; Stewart, 1997).

In the knowledge management literature, intellectual capital is usually grouped into three partly overlapping categories. For example, Sveiby (1997) defines the following three categories: individual competencies, internal structures, and external structures. Edvinsson and Malone (1997) list the following three categories: human capital, organizational capital, and customer capital, respectively. Hussi (2001) and Hussi (2004) combine these definitions and puts forward the idea that intellectual capital contains the following three categories: human capital, internal structures, and external structures. Hussi argues that the category of individual competencies is too narrow a definition for human capital. According to Hussi, human capital contains other aspects besides individual competencies. Such additions can include, for example, the health of individu-

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[40] The paper draws on the ETLA and Etlatieto Ltd survey of Finnish biotechnology companies, conducted in March-May 2002. Descriptive survey findings have been reported in Hermans and Luukkonen (2002) and Hermans and Tahvanainen (2002).

als. On the other hand, external structures can include a wider scope than only customer relations. For example, many companies are closely linked to their suppliers or academic research networks.
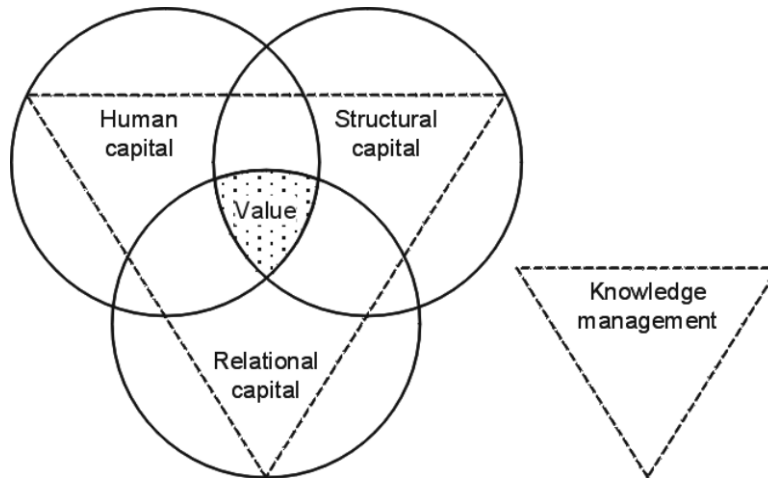
Figure 2. **Intellectual capital and knowledge management (Edvisson and Malone, 1997).**

In the present study, we apply a recent consensual definition of intellectual capital (e.g. MERITUM project, 2002; Bontis, 2002a), which also groups intellectual capital into three categories, Figure 2. The first category is human capital, which is composed of the skills and competencies of the company's personnel. The second category is structural capital, which signifies the company's ability to organize its activities in a way that tacit knowledge can be converted into intellectual property rights owned by the company.[41] The third category is relational capital, which stresses the importance of external networks, for example, with customers and other partners. According to the knowledge management approach, when there is a close interaction between these three categories of intellectual capital, the firm is able to create value from its business activities and growth can be anticipated. A well-balanced combination of human capital, structural capital, and relational capital is needed and this requires proper knowledge management. For example, even if a compa-

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[41] Nonaka and Takeuchi (1995) define their seminal model in which they interpret how the tacit knowledge is converted to explicit knowledge and back to the tacit knowledge of other individuals and groups. In the present study we do not focus on the so-called SECI model but instead we focus on measuring the interactions between different categories of intellectual capital and its impact to anticipated sales.

ny has ample human capital represented by labor with a high level of expertise, the value creation is not guaranteed if production or marketing processes are not well organized or customers are not reached.
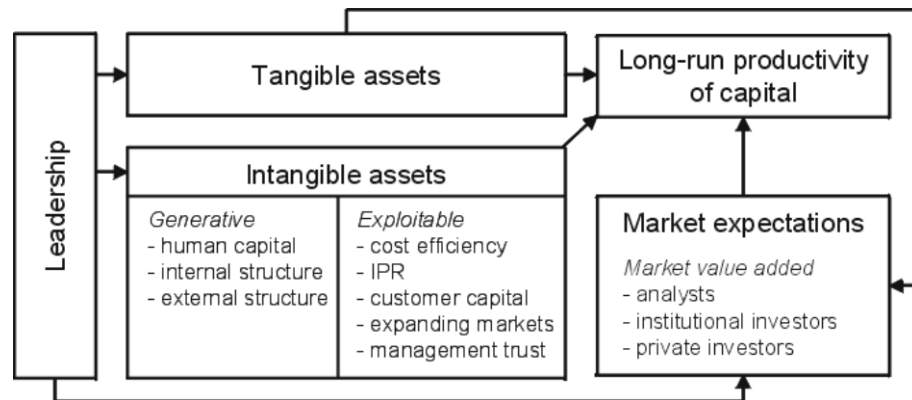
Figure 3.   Intangible assets and long-run productivity of capital (Hussi, 2001).

Ahonen (2000) and Hussi (2001) deepen the description behind the value creation mechanism, Figure 3. They divide intangible assets into generative assets and commercially exploitable intangible assets. The scheme in Figure 3 emphasizes the generative intangible assets as an enabler for the development of commercially exploitable intangible assets. The commercially exploitable intangible assets, in turn, enable the present value creation. The value creation is depicted as the interaction between human capital, structural capital (internal structure), and relational capital (external structure) in Figure 2. Generative intangible assets prepare the way for the commercially exploitable intangible assets in the future and affect the long-run productivity of capital in Figure 3.

4.3   Data and Research Methods

4.3.1   The Survey Companies

At the end of 2001 there were approximately 120 biotechnology companies actively operating in Finland (Kuusi, 2001; Hermans and Luukkonen, 2002). The companies were interviewed by telephone in the spring of 2002 and sufficient data was obtained from 84 companies. Of the companies interviewed, 12 companies were classified as large companies. A company was classified as a large company if two out of the following three condi-

tions were fulfilled: the company has more than 250 employees, its sales are more than 40 million euros, or its total balance sheet exceeds 27 million euros. Thus, 72 of the interviewed biotechnology companies were small or medium-sized and formed the research sample of companies.

Using only small and medium-sized companies in the study increases the reliability of the study. Many of the large companies are multifunctional with only a (small) part of their sales coming from biotechnology products. Also some of the large sample companies are a part of a consolidated company and their financial reports are not given in a uniform manner.

The survey data includes information about ownership, financial accounting, input-output networks, as well as research and development activities. The survey also includes the company managers' expectations about the future development of the companies. The survey contained 120 questions of which about one third are used in the present study.

Specific measures were taken in order to get undistorted answers from the company managers. For example, at the beginning of each interview, a confidentiality assurance was given to the respondents, assuring, for example, no data that could identify a single company would be published. The psychological implications behind the sales anticipations would be an interesting research topic in itself, but in the present study these anticipations are taken as given.

4.3.2 Variable Construction

In the present study, we follow the definition of intangible assets (IA) presented in Figure 3, in which intangible assets are divided into two categories: generative intangible assets and commercially exploitable intangible assets. The amount and quality of generative intangible assets are measured in the present empirical study by several variables describing intellectual capital. Commercially exploitable intangible assets are measured by the present sales of the companies. Accordingly, by studying separately generative intangible assets and commercially exploitable intangible assets, we can identify the impact that these two categories of assets have on the anticipated sales. In the present study, intangible assets are studied as stocks but intellectual capital through interaction (see e.g. Hussi, 2004).

Many of the values of the variables in the present study have a very wide distribution and the distributions can be skewed. This can distort such analyses, which are based on linear correlations. Thus, as a common research procedure, variables are logarithmized before performing the

analyses. This transformation is not needed for variables that are ratios or that are dichotomous dummy variables.

4.3.2.1 Generative Intangible Assets

Variables to measure generative assets are constructed mainly based on Sveiby's (1997) notion that intellectual capital can be measured by using three categories of variables, namely

- a) growth and renewal
- b) efficiency
- c) stability.

In biotechnology industry, large investments have been made in intensive research and development activities to commercialize innovations or sell intellectual property rights. Only few of the anticipated potential innovations have been successfully developed, and even less of them commercialized. Thus, the importance of efficiency and stability is not as remarkable as it is when there is something to sell. Accordingly, in the present study the focus is on the first category of variables, growth and renewal.

Intellectual capital is grouped into three categories: human capital, internal capital, and relational capital. These categories are used when conceptualizing the variables in the theoretical knowledge management framework. Theoretically, the interactions between human capital, internal capital, and relational capital are important in the value creation in companies. These categories of intellectual capital can be applied at the firm level (Mouritsen et al., 2000) and at the economy level representing groups of companies (Bontis, 2002b). The econometric procedures can be based on the viewpoint of the business management literature, and the variables of knowledge management models can be linked to data on the biotechnology industry.

Human capital (HC)

Human capital is more central to the core of intellectual capital than the other two categories of intellectual capital (Edvinsson and Malone, 1997). We modify Sveiby's (1997) classification in the construction of the three variables, which we will use to measure human capital in the companies:

- a) the total personnel
- b) the education level of the personnel (the number of persons holding doctoral licentiate degrees)
- c) the business experience of the CEO (in years).

The total personnel measure the quantity and the critical mass of human capital in the companies. Biotechnology is a knowledge intensive industry and, thus, the total personnel is a relevant variable measuring the critical mass of human capital. The number of personnel in the companies is connected to the age of the companies within the data. On the one hand, over half of the youngest companies in the sample employed less than 10 persons. On the other, almost half of the oldest companies had more than 250 employees.

The two other variables attempt to capture features describing the quality and the skills of the personnel. The education level of the personnel measures the general quality of the human capital and the specific quality of the human capital in the form of the research training of the personnel. This variable measures the formal knowledge stock and the ability to process the knowledge stock.

Table 1.   Description of the human capital variables.

Statistics	N					
HC	Valid	Missing	Mean	Median	Std. Deviation	Sum
Personnel	72	0	29.4	8	104.4	2 119
Doctors and licentiates	72	0	3.0	2	3.8	215
CEO's business experience in years	71	1	10.6	10	7.6	756

The business experience of the company's CEO attempts to measure the skills related to the business performance. It is interesting to note that the youngest biotechnology companies have hired many employees with doctoral degrees but CEO's with doctoral degrees do not have long careers in business.

Structural capital (SC)

Structural capital includes the way of organizing the company's activities and also the intellectual property rights of the company. The present study operates with three variables describing structural capital:

  a)   research and development input (research and development costs in euros)

  b)   patent intensity (the number of patent applications and patents)

  c)   the age of the firm (in years)

In the present study, we deviate from the mainstream measures (Sveiby, 1997), which focus on the information technology inputs. However, Deeds (2001) brings out research and development expenditure as a focal source of innovation potential. Within the data at hand, research and development intensity is strongly connected to the age of the companies. Over half of the young companies spend over 50 percent out of their total expenditure on research and development activities. This expresses clearly the nature of the biotechnology industry. Companies, which had a low research and development expenditure percent, were on average older than other companies in the sample. Such older companies were often owned by other non-financial companies.

Lev and Sougiannis (1998) discuss the impacts of different reporting methods on the relation of research and development expenditure and realized earnings. In the present study, we do not use figures taken from the financial statements of the companies, but rather figures given directly by the companies in the interviews. In Ahonen's (2000) terms, research and development expenditure can be regarded as a generative intangible asset whereas the patent portfolio is a commercially exploitable intangible asset. A key question related to a company's structural capital and value creation is how its research and development expenditure can generate patent applications and patents that are commercially exploitable. Stewart (1997) also highlights the intellectual property rights as a way to create value with (internal) structural capital. The number of patents and patent applications is used to measure the future potential of the company. However, the interaction between the internal capability to produce patent applications and the external regulatory environment is essential. Because the variable measuring patenting intensity is the quantity of patent applications and the patents a company holds, it also reflects the future sales potential arising from the innovation portfolio of the company.

Table 2.   Description of the internal structure variables.

Statistics	N					
SC	Valid	Missing	Mean	Median	Std. Deviation	Sum
Research and development costs in million euros	72	0	1.39	0.17	3.40	100.34
Patents and patent applications	72	0	11.8	4	26.6	849
Age of company	72	0	7.2	6	4.9	521

The age of the company is employed as a variable measuring structural capital. Some factors, for example, the stability of the organizational structures are often difficult to measure, and they can be quantified by using age as an estimator (Sveiby, 1990 and Sveiby, 1997). The age of the company can affect how the internal affairs have been organized in a company in many ways. Organizational cultures differ from each other in old companies, on the one hand, and in young companies, on the other.

Age can also contain some other specific features with high relevance for market valuation and sales potential. For instance, the drug development process carries out a tightly regulated drug approval process with pre-clinical and clinical phases (1-3). Furthermore, even if a drug is approved, it will not self-evidently become a bestseller in the marketplace. It can be expected that when the company passes a single phase of the approval process, this affects positively the anticipations of the future sales and, thus, the valuation of the company.

However, only 35% of the companies in the sample have disclosed that their core business is drug development. Thus, in order to control for the impact of special features within the drug development business, we added a dummy (0-1) controlling variables in the analysis. These variables indicate whether a single company belongs to some specific branch (=1) or not (=0). Accordingly, we were able to control for the impact of differences of business logics within separate branches (pharmaceuticals, diagnostics, biomaterials, industrial enzymes, food and feed, agro, services, other).

Relational capital (RC)

Edvinsson and Malone (1997) and Stewart (1997) define the company's relational capital as customer capital. Sveiby (1997) also takes into account supplier networks in relational structures. Market potential and catering to customer needs are fundamental requirements for success in any business. Most of the future of the market potential in small open economies results from the anticipated sales in international markets. Foreign exports are, thus, essential to companies acting in a small open economy that does not have a large home market, and the anticipated future sales of companies can be related to their plans to internationalize their operations. The present level of foreign exports varies among different age groups of the sample companies. The younger sample companies, in particular, anticipate a relatively rapid increase in their exports in the future. Accordingly, the demand-pull of the global markets can be considered a key external driver for anticipated future sales of the Finnish biotechnology companies. However, the variable "anticipated change in

exports" is not utilized in the present study due to a simultaneity and feasibility problem. Anticipated exports growth is deemed to occur simultaneously with anticipated sales growth. Both are based on the companies' own articulations and this could raise a danger of explaining anticipations by anticipations from the same source.

Many of the early-stage biotechnology companies have no customers. Thus, their success rests on future anticipations. Potentials in research and development increase a company's anticipated sales that, in turn, draw financial investments necessary to continue research and development activities aiming at commercialization. When speaking of the early-stage biotechnology companies, a most important aspect of relational capital is research and development collaboration and investor networks. A strong science base is necessary in order to attract large investments. (Darby and Zucker, 2002.)

In order to obtain financing the company should be credible and trustworthy in the investors' eyes. Guiso, Sapienza and Zingales (2001) state, "Whether such an exchange [financing] will take place depends upon not only the enforceability of contracts, but also the extent the financier trusts the financee. Thus, higher level of trust improves the efficiency of financial contracts and increases their use." In this sense the definition of relational capital above is closely related to the concepts of social capital and trust.

Relational capital is measured in the present study by seven variables, which are divided into the following three groups

a) university collaboration intensity (university research and development paid from governmental research and development support in euros)

b) sources of equity financing (in euros, equity financing received from individuals active in business, private venture capitalists, governmental venture capitalists and other firms),

c) sources of capital loan financing (in euros, capital loan financing received from private venture capitalists and governmental venture capitalists).

The equity financing from persons who are actively involved in business, private and governmental venture capital institutions and other firms measure ownership structures. Hermans and Tahvanainen (2002) showed that the ownership-related variables are loaded with expectations for value creation. Some investors are willingly involved in business activities as board members. At best, the investors can contribute

to the businesses of the investee company significantly with their relations and experience. Capital loan financing is measured as money flows from private and governmental venture capital institutions to the biotechnology companies.

Table 3. **Description of the external structure variables (in millions of euros).**

Statistics	N					
Million euros	Valid	Missing	Mean	Median	Std. Deviation	Sum
University research and development in collaborating projects	68	4	0.11	0.001	0.36	7.66
Equity financing from individuals active in business	71	1	0.42	0.03	1.37	29.96
Equity financing from other non-financial companies	72	0	0.56	0.00	2.28	40.04
Equity financing from private venture capital companies	72	0	0.41	0.00	2.12	29.23
Equity financing from governmental venture capital institutions	72	0	0.35	0.00	1.44	25.46
Capital loan financing from private venture capital companies	71	1	0.28	0.00	1.00	19.69
Capital loan financing from governmental venture capital institutions	70	2	0.56	0.02	1.70	39.54

In the science-based industry, research collaboration with academic institutions seems to be an essential form of relational capital. It also reflects the external governmental research and development support intensity. This is because Finnish authorities have typically set a condition of university collaboration for granting their own research and development support to companies. In Stage 2 of the regression analysis, we choose academic collaboration and governmental equity financing and capital loan financing separately as variables measuring relational capital.

4.3.2.2 Commercially Exploitable Intangible Assets

In order to avoid circular argumentation, we exploit the present sales as a measure of the company's present ability to exploit its structural and relational capital. This decision is made following the argumentation of Ahonen (2000) and Hussi and Ahonen (2002). The above thinking predicts that value creation occurs in the interaction between all of the three categories of intellectual capital and, therefore, present sales cannot be taken as a predictor for relational capital only.

The present sales are taken as a present measure of how effectively commercially exploitable assets have previously been utilized. To a great extent, the anticipated sales seem to rely on the market potential of the future, and not on the present sales and present market share. Almost one third of the sample companies had annual sales of less than 100 thousand euros (see Table 4). The oldest companies had relatively high sales volumes.

Table 4.   **Description of the present and anticipated sales (in millions of euros).**

Statistics	N					
Millions of euros	Valid	Missing	Mean	Median	Std. Deviation	Sum
Sales in 2001	72	0	1.80	.20	4.96	129.85
Anticipated sales in 2006	70	2	11.73	1.40	31.78	821.12

Present sales are an estimator to measure the part of the intangible assets that are already exploited commercially. Among the sample companies, the anticipated sales in the years 2001 - 2006 were on average expected to grow at about a 45 percent annual rate. The anticipated sales are a prime determinant in the valuation of the company. In the next section, anticipated sales will be the dependent variable in the regression analysis and will be explained by the indicators of intellectual capital.

4.3.3   Statistical Procedure

A methodological contribution of the present study is the combining of econometric analyses with the knowledge management approach.

Econometric modeling is used as our main tool. Factor analyses are applied as an important analysis method. The factor scores resulting from the factor analyses are fed into regression analyses. The anticipated sales of the companies are explained by these regression models.

Thus, there are two stages in the statistical procedure:

Stage 1: Factor analysis is used to identify the three intellectual capital factors and produce factor scores for each company.

Stage 2: Regression analysis is used to explain the companies' anticipated sales in 2006. The intellectual capital factors are formed by factor scores produced in Stage 1. The factor scores are used as variables in the regression model. In other words, the output of the factor analysis is used as predictors that explain the anticipated sales of the sample of biotechnology companies.

First, we try to find the forms of interactions between the three categories of intellectual capital (IC). According to the knowledge management theory, this is important for two reasons. First, the value creation in business activities is connected to the interactions between the three categories of intellectual capital. Second, there can be interactions that are not strictly connected to the value creation. It is important to separate the latter kind of interactions from those that create value. In statistical terms, the interaction between the three categories of intellectual capital is measured as the co-variation of the intellectual capital based variables.

The idea in the first stage is to find the common variation between the variables and form the intellectual capital factors discussed above. Because an orthogonal factor analysis method is applied, the factors are uncorrelated with each other, which is an advantage in regression analysis. This lowers the risk of multicollinearity between the independent variables. Factor scores are constructed from the factors and they are used as new variables in Stage 2.

Our attempt is to explain the anticipated sales of the companies based on the knowledge management approach. Regression analysis is used to produce three alternative models. Firstly, we use original variables without the results of the factor analysis. Secondly, we construct a regression model with all the factors received from Stage 1. Thirdly, we regress only statistically significant factors and add some significant dummy variables found in the data.

Despite the fact that we employ cross-sectional data, the analysis is dynamic in a similar sense as Bounfour (2002). We are interested in the valuation of assets and the input-output relations of intellectual capital.

4.4   Results

4.4.1   Stage 1: Factor Analysis

Factor analysis produced four factors in Stage 1. Applying the generalized least squares (GLS) method the factors interconnected the variables within three intellectual capital components mentioned above (see e.g. Sharma, 1996). We took natural logarithms from other than ratio variables or dummy variables. Appendix 1 presents the communalities for each variable. It shows that the factor model explains 28 - 78 % of the variance of a single variable. The model can explain 73 % of the total variance of all the initial variables (see eigenvalues in Appendix 2).

Then, using the rotated factor solutions presented in Table 5, we produced factor scores for each case company and factor by multiplying the factor loadings by the values of the initial variables. Factor rotation was chosen instead of the initial factor solution due to the clarity of the interpretation of the factors. The factor rotation was done using the varimax method, which is a rotation method that minimizes the number of variables that have high loadings on each factor. Thus in order to simplify the interpretation of the factors, we utilize the results of the rotated solution.

One factor indicates how different categories of intellectual capital interact, or co-vary with each other. For example, the loadings of Factor 1 in Table 5 presents co-variation between the three categories: critical mass of personnel (human capital), large patent portfolio and R&D expenditures (structural capital), and university collaboration and equity financing from private venture capital companies (relational capital). Table 5 implies also that Factor 1 is related to the pharmaceutical industry and negatively with the service sector.

Table 5.   Factor matrix.

	Factor								
	1	2	3	4	5	6	7	8	9
Patents and patent applications (log)	**0.813**	0.137	-0.014	-0.094	-0.087	0.161	0.002	0.007	0.117
R&D expenditures (log)	**0.810**	0.125	0.159	**0.298**	0.064	0.059	0.082	0.092	0.011
Expenditures on university collaboration (log)	**0.764**	0.148	-0.162	0.153	0.083	0.217	0.050	0.115	-0.109
Personnel (log)	**0.704**	0.159	**0.441**	0.244	0.050	0.028	-0.051	-0.088	-0.020
Services (=1)	**-0.357**	0.020	0.132	0.237	0.275	-0.018	0.165	0.166	-0.047
Pharma (=1)	**0.327**	0.162	-0.107	**0.299**	0.067	-0.112	-0.028	-0.121	-0.038
Equity financing from government VC (log)	0.200	**0.779**	-0.050	0.155	0.055	-0.171	0.139	0.270	-0.086
Equity financing from private VC (log)	**0.307**	**0.754**	-0.045	0.099	-0.134	0.054	-0.011	-0.054	-0.130
Equity financing from persons active in business (log)	-0.015	**0.609**	-0.117	0.091	0.032	0.185	-0.106	0.010	0.065
Industrial enzymes (=1)	-0.104	-0.164	0.058	-0.022	0.045	-0.121	-0.092	0.039	0.094
Present sales (log)	0.102	-0.092	**0.975**	0.000	0.007	0.160	0.030	-0.050	-0.007
Anticipated change in exports per turnover	0.249	0.245	**-0.499**	0.061	0.223	-0.198	0.116	0.203	0.028
Equity financing from other companies (log)	**0.395**	-0.174	**0.422**	-0.161	0.133	0.021	0.018	-0.158	-0.152
Doctors and licentiates (log)	**0.357**	0.273	-0.033	**0.888**	0.023	-0.016	-0.027	0.040	-0.063
Agriculture (=1)	0.173	-0.137	0.167	-0.206	0.151	0.019	-0.081	-0.120	-0.063
Diagnostics	-0.034	0.031	0.029	-0.023	**-0.993**	0.008	-0.023	0.078	-0.052
CEO experience (log years)	**0.313**	-0.002	0.156	0.061	0.043	**0.779**	0.070	0.026	0.150
Age of company (log years)	0.055	0.101	**0.376**	-0.237	-0.190	**0.526**	-0.152	-0.175	-0.004
Biomaterials (=1)	0.167	-0.084	0.065	-0.145	0.150	0.287	0.188	0.049	-0.118
Capital loan financing from private VC (log)	0.011	-0.003	0.008	-0.011	0.007	0.000	**0.999**	0.034	-0.002
Capital loan financing from government VC (log)	0.122	0.155	-0.182	0.002	0.211	0.184	**0.350**	0.064	-0.011
Turku (=1)	0.069	0.121	-0.142	0.017	-0.081	-0.014	0.045	**0.939**	-0.261
Helsinki (=1)	0.000	-0.088	-0.048	-0.059	0.043	0.121	-0.003	-0.238	**0.955**
Problems in skilled labor supply (=1)	0.145	-0.114	0.043	0.259	0.067	-0.215	-0.027	-0.063	0.282

Factor loadings ≥ 0.30 bolded.

Extraction Method: Generalized Least Squares.

A   9 factors extracted. 18 iterations required.

B   Only cases for which SME biotechnology firm = 1 are used in the analysis phase.

4.4.2   Stage 2: Regression Analysis

The outcome generated by the intangible assets is the anticipated future sales in Figure 4 instead of the long-run productivity of capital in Figure 3. The anticipated sales approximate the productivity of capital and the present value of the company due to the following reasoning. The biotechnology industry resembles the pharmaceutical industry in the sense that both have extremely long product development processes. Consequently, as many as one third of the companies in the sample are involved in the development of pharmaceutical products. Furthermore, when Scherer and Ross (1990) and Linnosmaa, Hermans, and Hallinen (2004) analyzed price-cost margins in the pharmaceutical industries in the USA and Finland, they found relatively high price-cost margins in both countries. This implies that physical capital does not play a pivotal role in the value creation process of the pharmaceutical industry. If this is also typical for the biotechnology industry, it seems reasonable to assume that the anticipated future sales imply growth in productivity of capital and the present value of the company. Hence, the original theoretical framework by Hussi and Ahonen (2002) holds for the framework in Figure 4.
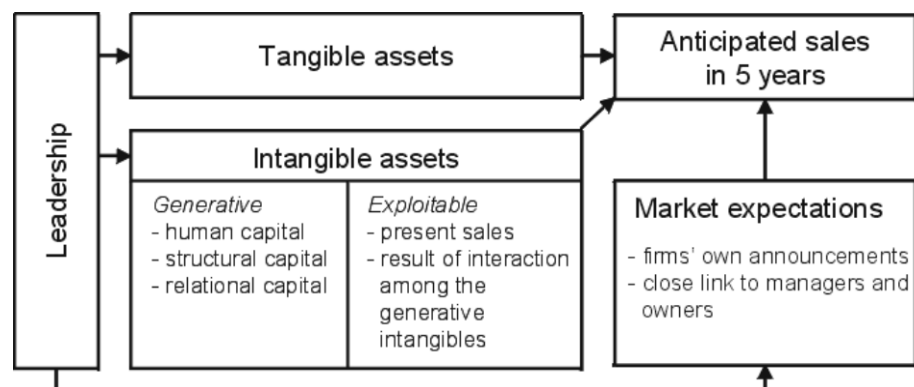
Figure 4.   Intellectual assets and anticipated future sales of the company. Modified from Hussi (2001).

The regression analysis exploits the theoretical models presented above. First, we utilize the initial variables without factor scores in the regression analysis. The results of the initial variable models are shown in Table 6. Generally speaking, the initial R^2 ratios show that model 3 explains most of the variance of the variables in the model. However, when the adjusted R^2 is observed, model 2 holds the best

fit.[42] In this setting, the anticipated sales are almost entirely explained by the present sales. This describes a size effect (or scale economies) of the companies. Simplifying, if you are big now, you will be expected to be big in the future.

When we regress the anticipated sales, explaining the sales in 2006 by the initial variables, only a few of the variables are statistically significant. The model does not contain the interaction effects of intellectual capital trying to relate intellectual capital measures directly and separately to the value creation (anticipated sales).

Next we conduct the second phase by employing the factor scores formed above in the factor analysis. These factors describe how the three forms of intellectual capital are interlinked to each other. The results of the factor-based models 4, 5, and 6 are presented in Table 7.

In model 4, we employ all the factors received from the generalized least square (GLS) method factor analysis in Stage 1. It implies that factors 2, 4, 5, 6, 8, and 9 do not significantly explain the anticipated sales. Therefore, we drop these factors from model 5. Then we add intangible assets to the analysis in model 6.

Models 4, 5 and 6 are able to explain about 70 percent of the regressors' variance. For example, according to the adjusted R2, the independent variables in model 6 are able to predict systematically 70 percent of the variation of anticipated sales.

The successful predictors are the chosen intellectual capital factors. As a result, the company anticipates high sales if the company's intellectual capital is well balanced according to factors 1 and 3 in models 4, and 5. Factor 1 deviates also significantly from zero in models 4 and 5, but remains insignificant in model 6. Model 6 contains a severe problem of multicollinearity: the independent variables Factor 1 and Tangible assets correlate significantly ($r = 0.439$, $p = 0.001$). This indicates that research-intensive activities require also significant investments in equipment and loan financing (relational capital) with the anticipated future sales in Models 4, 5 and 6. The next section discusses on results of the empirical analysis.

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[42] Conventional R[2] increases with the variables included in the model and decreases with the number of cases included in the analysis. The adjusted R[2] takes those matters into account .

Table 6. **Regression model: Explaining anticipated future sales of small and medium-sized biotechnology companies by initial variables.**

Dependent variable: Anticipated sales in 2006.			
Variable Logarithmized variable (log) Dummy variable (d)	Model 1: without dummies	Model 2: extended model	Model 3: extended model with tangible assets
R²	.744	.817	.837
Adjusted R²	.672	.705	.691
F-test	10.384***	7.267***	5.732***
Constant	**1.880** (.909)**	1.666 (1.070)	1.112 (1.644)
Present commercially exploitable assets			
Present sales (log)	**.914*** (.126)**	**.956*** (.144)**	**.912*** (.183)**
Human capital			
Personnel (log)	-.131 (.291)	-.477 (.313)	**-.684* (.385)**
Doctors and licentiates (log)	-.174 (.343)	-.529 (.391)	-.367 (.546)
CEO experience (log)	-.019 (.330)	.070 (.401)	-.697 (.566)
Structural capital			
R&D expenditures (log)	.156 (.154)	.230 (.160)	.284 (.193)
Patents and patent applications (log)	-.037 (.215)	-.121 (.256)	.160 (.331)
Age of company (log)	-.368 (.371)	-.397 (.396)	.152 (.672)
Relational capital			
Equity financing from other companies (log)	.066 (.081)	-.089 (.088)	.122 (.104)
Equity financing from persons active in business (log)	.123 (.087)	-132 (.091)	**.222* (.114)**
Equity financing from private VC (log)	-.130 (.105)	**-.200* (.118)**	-.202 (.135)
Equity financing from government VC (log)	.092 (.098)	**.282** (.118)**	.185 (.168)
Capital loan financing from private VC (log)	.151 (.108)	.029 (.090)	.058 (.162)
Capital loan financing from government VC (log)	.004 (.087)	.055 (.114)	.123 (.119)
Expenditures on university collaboration (log)	.047 (.132)	.136 (.143)	-.039 (.184)
Anticipated change in exports intensity (% units)		.002 (.812)	-.419 (1.063)
Problems in employing skilled labor (d)		**1.136** (.519)**	.797 (.613)
Pharmaceuticals (d)		.217 (.471)	-.153 (.550)
Diagnostics (d)		.566 (.544)	.287 (.721)
Biomaterials (d)		.667 (.553)	.884 (.646)
Industrial enzymes (d)		-.592 (.843)	.203 (1.260)
Agriculture (d)		.152 (.959)	-.171 (1.122)
Services (d)		.569 (.595)	-.129 (.755)
Helsinki (d)		-.064 (.570)	.058 (.657)
Turku (d)		**-1.211* (.632)**	-.746 (.872)
Tangible assets (log)			.108 (.177)

Standard errors are in parentheses. The asterisk labels (*) stand for the level of the statistical risk of rejecting the null hypothesis incorrectly: the regression coefficient is zero.

* 10 percent risk level, ** 5 percent risk level, *** 1 percent risk level.

Table 7. **Regression model: Explaining anticipated future sales of small and medium-sized biotechnology companies by interacting factor scores.**

Dependent variable: Anticipated sales in 2006.			
Variable	**Model 4: all the factors**	**Model 5: focal factors**	**Model 6: focal factors and tangible assets**
R^2	.724	.703	.722
Adjusted R^2	.678	.688	.700
F-test	15.736***	47.273***	31.869***
Constant	**7.001*****	**7.009*****	**5.800*****
	(.180)	**(.177)**	**(1.313)**
Factor 1: RC + HC	**.461****	**.468****	.297
	(.192)	**(.188)**	(.270)
Factor 2: HC + RC + SC + non commercial exploitability	-.100		
	(.195)		
Factor 3: RC + HC + SC + commercial exploitability	**2.137*****	**2.125*****	**2.029*****
	(.193)	**(.188)**	**(.260)**
Factor 4: HC + SC + commercial exploitability	.010		
	(.185)		
Factor 5: RC + HC	.194		
	(.183)		
Factor 6: RC + HC	.135		
	(.214)		
Factor 7: HC + SC + RC	**.461****	**.458****	**.371***
	(.178)	**(.175)**	**(.198)**
Factor 8: RC + HC	-.217		
	(.181)		
Factor 9: HC + SC	.155		
	(182)		
Tangible assets			.100
			(.118)

Standard errors are in parentheses. The asterisk labels (*) stand for the level of the statistical risk of rejecting the null hypothesis incorrectly: the regression coefficient is zero.

* 10 percent risk level, ** 5 percent risk level, *** 1 percent risk level.

4.4.3   Discussion on Empirical Results

Factor analysis measured interaction through statistical correlation (load-ings) between initial variables and new factors obtained in the analysis. The loadings of these factors implied how different categories of intel-lectual capital correlate with a single factor. Then factor scores were used in creation of new variables for each factor in the final solution. This formed the basis for measurement of interaction between the three cate-gories of intellectual capital. In other words, high scores within some factor implied that the company has a high (low) amount of all these forms of intellectual capital that have high (low) loadings to this specific factor, respectively.

The intellectual capital (IC) driven value creation of Factor 1 is depict-ed in Figure 5. There is the following co-variation within the three intel-lectual capital categories explaining high anticipated sales. A critical mass of personnel and doctors are directed to research and development activ-ities, which are supported by a large patent portfolio. These companies are financed by private venture capital companies and other compa- nies. The most promising companies, within Factor 1, are partially related to the pharmaceutical sector.

Factor 1
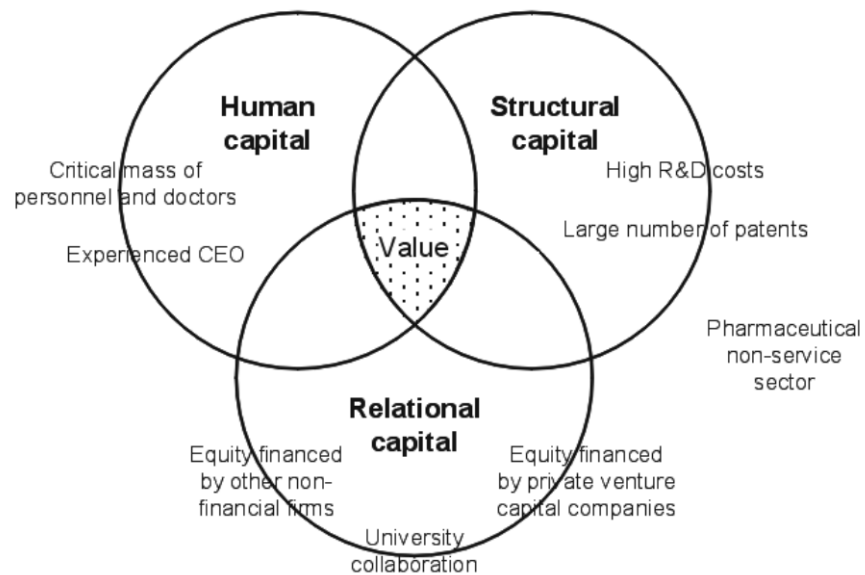
Figure 5.   Intellectual capital (IC) driven value creation within the small and medium-sized biotechnology companies (factor 1).

In other words, Factor 1 implies that if the bio-pharmaceutical company holds a critical mass of personnel and an experienced CEO (human capital); high R&D costs and a large patent portfolio (structural capital); and it has intensive collaboration with universities and it is equity financed by other firms and private capital companies (relational capital), the company achieves high factor scores for Factor 1. The regression analysis models how these IC factor scores are linked with the anticipated future sales of the companies. The model results indicate that a high (low) Factor 1 score predicts high (low) anticipated sales in 2006, respectively.

The same logic applies to Factor 3. The critical mass of personnel (human capital); high age of the company (structural capital); and significant equity financing from other firms together with a low change of anticipated export intensity (relational capital) predict a high volume of anticipated future sales in 2006 (Figure 6).
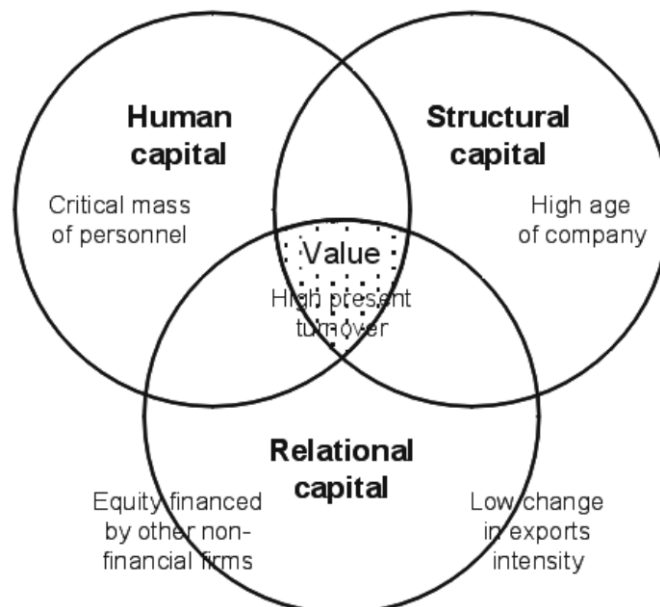
Figure 6.   **Intellectual capital (IC) driven value creation within the small and medium-sized biotechnology companies (factor 3).**

Factor 1 emphasizes the significance of holding a patent portfolio in the drug development business. Patents and patent applications form a necessary base of intellectual property rights for commercial exploitation.

It is critical to hold patents related to those technologies which are the basis of the company's own drug development. Without patent protection any other company can develop a generic drug based on the same chemical compound as a treatment for some specific disease. Without patent protection another company can take a free ride and get the same drug into the market by completing the generic drug approval process. In such a case the free-rider company can accomplish this with a very limited amount of R&D expenditures compared to the companies which invent new potential drugs.

Factors 1 and 3 present how Saint-Onge's et al. value platform is concretized within the Finnish biotechnology industry (Figure 6). These companies have an above normal present sales level as was not the case in factor 3. Factor analysis seemed to be able to divide the size effect more effectively than the first regression model with the initial variables. For example, Factor 3 is closely related to the present sales and the critical mass of personnel in models 4, 5 and 6 as initial separate variables are in Models 1, 2 and 3, too. In contrast, Factor 1 is not loaded with the present sales level at all, but rather with research and development activities, number of patents, or university collaboration.

In this empirical setting Factor 7 implies that capital loan financing from both private and governmental sources is strictly connected to the anticipated sales volumes of the biotechnology companies. However, the sensitivity of the solution of Factor 7 should be investigated, because the results of the factors, which explain a minor part of the variance of the initial variables, can be sensitive to the method used. However, the link between capital loan financing and anticipated sales remains interesting. Factor 7 may refer to dynamic impacts of financing. For instance, it would be important to investigate to what extent a company, when approaching potential financiers, raises its own estimates of anticipated future sales in order to get capital loan financing, and to what extent the company's capabilities to exploit the market potential is strengthened as a result of being successful in raising new financing.

4.4.4 Sensitivity Analyses

In order to test how sensitive the results presented above are in relation to the compressing method we employ the principal component analysis (PCA) instead of the generalized least square (GLS) method factors. Then we apply the principal component scores in regressing the intellectual capital interactions towards the anticipated sales of the biotechnology companies. The results remain mainly parallel in the principal compo-

nent analysis. The R2 of the regression model applying the principal component analysis is 61.4 %, which is somewhat lower than in the analysis applying the factor analysis. Four significant principal components were found instead of the three (or two) factors explaining the anticipated sales.

The principal component analysis comprises qualitatively similar basic features as the factor analysis. For example, in the principal component analysis, components related to factors 1 and 3 could be identified. The variables related to the region of the companies do not seem to be robust in this benchmark model. The Helsinki region with business experienced leaders and capital loans from government institutions explain part of the anticipated sales in the benchmark model. Part of the anticipated future sales is explained by service companies that are already generating some sales and are owned by individuals active in the business.

Another sensitivity analysis was made by performing the same research analyses using relative measures instead of the absolute measures. The relative measures were attained from the absolute measures by dividing each of the values of the original variables by an appropriate variable representing the size of the corresponding company. Obviously, this transformation was not needed for dummy variables or variables which already are ratios. Appropriate variables for dividing the values of original variables were, for example, total costs or the number of personnel of the company.

In the generalized least square (GLS) factor analysis done with the relative measures, three factors significantly explained the anticipated sales. The R^2 of the regression model utilizing relative measures is 29.8 %. The first factor had positive loadings with the variable describing other companies' relative equity share and with the company's innovation intensity, which was measured by the ratio of patents and patent applications to labor involved in research and development activities. The first factor had a negative loading with the relative equity share of individuals active in business. The second factor had a positive loading with the ratio of present sales to labor, with the logarithmized age of the company and with government venture capitalists' relative equity share. The third factor had a high loading with the ratio of present sales to labor. The factors 1, 2, and 3 were related to the branches of agriculture, service, and diagnostics, respectively.

The factor analysis applying the relative measures was not able to reveal the detailed structures behind the anticipated sales. This analysis stressed the importance of the present sales per labor and of branch spe-

cific features. These results, together with the results of the principal component analysis above, raise a need for a closer look at branch specific phenomena within the biotechnology industry.

4.5 Conclusions

The present study relates the knowledge management theory and the measurement of intellectual capital (IC) to the anticipated sales that small and medium-sized biotechnology companies have articulated. According to the literature, value is created by the interaction of the three categories of intellectual capital, namely human capital, structural capital and relational capital.

We tested the theoretical framework among small and medium-sized Finnish biotechnology companies. In the first stage of empirical analyses, we identified factors that present interaction between the variables measuring the different categories of intellectual capital.

In Stage 2 of the empirical analysis, we constructed two kinds of regression models that explained the anticipated sales of the companies. Firstly, we utilized the initial variables. Secondly, we exploited factor scores from Stage 1. The regression models implied that the strict effects of single initial variables without interaction explained the anticipated sales at a general level as much as the factor-based variables that take into consideration the interaction between the categories of intellectual capital. The initial variable model stressed the present ability of commercialization as an explanation for anticipated future sales.

The factor-based model seemed to be able to separate some size-effect features. Particularly, two intellectual capital related factors were found that systematically explain the anticipated future sales. Both of these factors link to some degree human capital, structural capital, and relational capital. According to the first factor, the companies owing the highest anticipated sales levels have the critical mass of highly educated personnel and doctors directed to research and development activities. These companies hold large patent portfolios and they are partially owned by private venture capital companies and by other companies. According to the second factor, the critical mass of labor of an aged company has already generated sales. The company was mainly owned by other companies. Third significant factor was related to capital loans offered by private and governmental venture capital companies.

Three paths for further research are evoked by the present study. Firstly, in the present study some preliminary results concerning explana-

tions for the anticipated future sales of Finnish biotechnology companies were obtained. Deeper analyses could help to build various economic forecast models. These could be, for example, macroeconomic, industry specific or region-based. Secondly, a follow-up study of the same sample of companies would be very attractive. In it the real sales of 2006 could be compared to the anticipated sales, which were projected by the company managers in 2002. What kind of companies were the most successful in realizing their anticipated sales? Thirdly, it would be interesting to investigate to what degree various kinds of investors have been able to select the companies that have turned out to be the most successful in terms of economic profitability and in terms of continuous intellectual capital development.

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Appendix 1. Communalities and total variance explained by factor analysis.

Table A1.1   Communalities of the factor analysis

Communalities(a,b)		
	Initial	Extraction
Sales	0.751	0.999
RDcost	0.779	0.841
Person	0.778	0.833
Ceoexp	0.570	0.788
Patent	0.692	0.811
Age	0.568	0.669
Docs	0.691	0.999
Firminv	0.552	0.661
Activinv	0.456	0.611
PrVCinv	0.652	0.789
GovVCinv	0.683	0.855
GovVCL	0.420	0.526
PrVCL	0.415	0.999
UnivRD	0.717	0.802
Dexport	0.622	0.730
ProbPers	0.335	0.447
Pharma	0.378	0.480
Diagnost	0.498	0.999
Biomater	0.305	0.410
IndEnz	0.287	0.457
Agricult	0.276	0.356
Service	0.449	0.552
Helsinki	0.546	0.999
Turku	0.631	0.999

Extraction Method: Generalized Least Squares. Only cases for which SME biotech firm = 1 are used in the analysis phase.

One or more communality estimates greater than 1 were encountered during iterations. The resulting solution should be interpreted with caution. Appendix 1, continues.

Table A1.2   Total variance explained by generalized least square (GLS) method factors.

Total Variance Explained(a)									
Factor	Initial Eigen-values			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loadings		
	Total	% of Variance	Cumula-tive %	Total	% of Variance	Cumula-tive %	Total	% of Variance	Cumula-tiv e %
1	4.546	18.943	18.943	2.246	9.360	9.360	3.332	13.885	13.885
2	3.238	13.493	32.435	1.872	7.802	17.162	1.951	8.128	22.013
3	1.889	7.869	40.305	1.988	8.284	25.446	1.932	8.049	30.062
4	1.745	7.270	47.575	1.932	8.049	33.495	1.382	5.760	35.822
5	1.523	6.345	53.920	1.393	5.804	39.299	1.319	5.496	41.319
6	1.400	5.834	59.754	0.733	3.053	42.352	1.298	5.407	46.726
7	1.242	5.175	64.929	2.618	10.907	53.259	1.288	5.367	52.092
8	1.083	4.514	69.443	1.191	4.963	58.221	1.222	5.091	57.184
9	1.023	4.261	73.704	0.949	3.956	62.177	1.198	4.994	62.177
10	0.849	3.537	77.241						
11	0.829	3.455	80.697						
12	0.754	3.144	83.840						
13	0.673	2.803	86.643						
14	0.518	2.158	88.802						
15	0.475	1.980	90.781						
16	0.450	1.875	92.656						
17	0.345	1.436	94.092						
18	0.318	1.326	95.418						
19	0.278	1.158	96.576						
20	0.228	0.950	97.526						
21	0.194	0.809	98.335						
22	0.177	0.736	99.072						
23	0.113	0.471	99.543						
24	0.110	0.457	100						

Extraction Method: Generalized Least Squares.

Only cases for which SME biotech firm = 1 are used in the analysis phase.

Appendix 2. Financial structure
(Equity and capital loan financing from different sources)

Table A2.1.   Estimated distribution of aggregate equity, capital loans, and debt by firm size and age (Hermans and Tahvanainen, 2002).

	Equity	Capital loans	Debt	Total
A: All (N=72)				
%	43.6 %	31.5 %	24.9 %	100.0 %
(amount, mill.€)				305.3
B: Breakdown by size of SME				
Small	-6.9%	70.9 %	36.0%	100.0 %
(amount, mill.€)				32.7
Large	49.3 %	27.1 %	23.6 %	100.0 %
(amount, mill.€)				274.7
C: Breakdown by age of SME				
Infant	39.5 %	46.2 %	14.3 %	100.0 %
(amount, mill.€)				162.7
Adolescent	41.0 %	27.0 %	32.0 %	100.0 %
(amount, mill.€)				64.1
Middle-aged	54.4 %	4.6 %	41.0 %	100.0 %
(amount, mill.€)				78.4
Old	n.a.	n.a.	n.a.	n.a.
(amount, mill.€)				n.a.

Table A2.2.   Estimated distribution of equity by firm size and age (Hermans and Tahvanainen, 2002).

| | Individuals | | Institutions | | | | | Total sources of equity |
	Active in business	Other individ.	Public VC	Private VC	Financial instit.	Other companies	Other equity	
A: All (N=72)								
%	22.8 %	5.2 %	19.4 %	24.3 %	2.2 %	22.0 %	4.2 %	100.0 %
(amount, mill.€)								215.0
B: Breakdown by size of SME								
Small	32.1 %	2.8 %	27.1 %	7.3 %	1.8 %	24.9 %	4.0 %	100.0 %
(amount, mill.€)								14.4
Large	22.1 %	5.3 %	18.8 %	25.5 %	2.2 %	21.8 %	4.2 %	100.0 %
(amount, mill.€)								200.7
C: Breakdown by age of SME								
Infant	28.9 %	6.1 %	24.0 %	37.8 %	0.5 %	2.4 %	0.3 %	100.0 %
(amount, mill.€)								116.1
Adolescent	22.7 %	7.7 %	25.8 %	14.2 %	7.6 %	18.1 %	3.7 %	100.0 %
(amount, mill.€)								50.8
Middle-aged	8.2 %	0.2 %	1.3 %	2.3 %	0.5 %	73.3 %	14.2 %	100.0 %
(amount, mill.€)								48.2
Old	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
(amount, mill.€)								n.a.

Table A2.3.   Distribution of capital loans by firm size and age (Hermans and Tahvanainen, 2002).

	Private				Public						
	Dom. fin. instit.	Foreign fin. instit.	Foreign VC	Private VC	Public VC	Sitra	Finn-vera	Tekes	Other govt. & public	Other	Total
A: All (N=72)											
%	0.6 %	0.0 %	4.0 %	18.1 %	0.4 %	13.7 %	0.3 %	53.4 %	0.0 %	9.6 %	100.0 %
(amount, mill.€)											96.2
B: Breakdown by size of SME											
Small	2.5 %	0.0 %	16.9 %	18.4 %	0.0 %	37.7 %	1.4 %	19.2 %	0.0 %	4.0 %	100.0 %
(amount, mill.€)											21.7
Large	0.0 %	0.0 %	0.3 %	18.0 %	0.6 %	6.7 %	0.0 %	63.3 %	0.0 %	11.2 %	100.0 %
(amount, mill.€)											74.5
C: Breakdown by age of SME											
Infant	0.7 %	0.0 %	5.1 %	22.5 %	0.6 %	11.4 %	0.2 %	48.0 %	0.0 %	11.4 %	100.0 %
(amount, mill.€)											75.2
Adoles-cent	0.0 %	0.0 %	0.0 %	1.4 %	0.0 %	20.1 %	0.7 %	76.1 %	0.0 %	1.7 %	100.0 %
(amount, mill.€)											17.3
Middle-aged	0.0 %	0.0 %	0.0 %	5.4 %	0.0 %	29.9 %	0.0 %	55.4 %	0.0 %	9.3 %	100.0 %
(amount, mill.€)											3.6
Old	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
(amount, mill.€)											n.a.

ESSAY 5.
Projected Growth Effects of the Biotechnology Industry in Finland – The Fourth Pillar of the Economy?[43]

Abstract

This study aims to assess the impact of the Finnish biotechnology industry on the economic growth in Finland. The study employs official data from Statistics Finland and new survey data covering 84 Finnish biotechnology companies. The study offers methodological insights into how a new emerging industry can be treated as a statistical branch in an input-output forecast model and how probability distributions can be utilized in the model instead of point estimates. An econometric forecast for the economy-wide growth impact of the biotechnology industry in Finland is estimated. In the estimation procedure this study employs the survey data both in forming growth anticipations within a new emerging industry and assessing inter-industrial growth effects. Applied Monte Carlo simulations predict that the contribution of the biotechnology industry to annual GDP growth in 2002-2006 will be in the range of 0.05-0.09 percentage points per annum with a probability of 90%. In comparison with the major sectors of the Finnish industry – forest industry, metal products and machinery industry, and electronics industry – this implies that it will rather take decades instead of years for the biotechnology industry to become a fourth pillar of the Finnish economy.

Key words: biotechnology, economic forecast, growth contribution, input-output model, Monte Carlo simulation.

5.1 Introduction

5.1.1 Background

There have been growing expectations concerning the economic potential of biotechnology during the last two decades in Finland. Biotechnology is anticipated to become an important driving force in the economy after the era of information and communications technologies. Schienstock and Tulkki [1] have even raised a question whether the biotechnology industry will become a fourth pillar of the Finnish economy, next to the forest industry, the metal products and machinery industry, and the electronics industry.

In Finland, the number of dedicated biotechnology firms has grown rapidly in the 1990s and is estimated to be one tenth of such firms in Europe (Kuusi [2]).The public sector has expended considerable resources in training and R&D in this field. Private investments and venture funding have also grown decisively (Hermans and Tahvanainen [3]).The main application areas of biotechnology in Finland include pharmaceuticals, diagnostics, functional food, biomaterials, enzymes, and the food and chemistry businesses, as well as services related to these fields (see *e.g.* Hermans and Luukkonen [4]).

Biotechnology is not easy to define as an industrial branch. The OECD Ad Hoc Meeting on Biotechnology Statistics defined biotechnology as *"the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services"* [5].Public attention is usually paid to small dedicated biotechnology firms, but they are not the only ones to make and commercialize biotechnological discoveries. Some established larger firms are also involved in biotechnology R&D and commercialization. The entire field is closely related to scientific research, where many of the discoveries are made. The commercialization of the discoveries is, however, uncertain and the process is slow compared with, for example, the information and communications technologies (Luukkonen and Palmberg [6]).

The high risk nature of the development processes of the biotechnology industry must be taken into consideration when forecasting its economic impacts. The delays in the development processes of biotechnology companies as well as the risk of technological failure have to be included as part of the forecasting model.

5.1.2   Objectives and Motivation of the Study

Despite the high investments and expectations regarding the biotechnology sector, there has not been much effort expended in estimating the economic growth impacts of the sector in the near future. It is well known that biotechnology firms report high growth potentials for sales, but the spill-over effects on other industrial branches and the growth contributions to the gross domestic product (GDP) have sparsely been analyzed. Ernst & Young [7] analyze the growth contributions of the biotechnology industry in the US in 1999.

The objective of the study is to assess the impact of the Finnish biotechnology industry on the economic growth in Finland. There were two obstacles to overcome in the construction of a forecast model. First, biotechnological applications span over several statistical subgroups in the official statistical classification, and thus the conventional statistical classes are not applicable for this new emerging industry – the official statistics and classification procedure within this area are still under construction in OECD [5]. Second, the exceptional risks related to both the technological feasibility and delays in research and development processes are not reflected in the anticipated future sales disclosed by the biotechnology companies.

In order to overcome the first obstacle, it was necessary to create a new industrial class of biotechnology in the conventional input-output table of Statistics Finland. The second obstacle was overcome by the application of Monte Carlo simulation, which simultaneously allows the implementation of the stochastic features of failure vs. success, and the probability distributions for anticipated future sales of the biotechnology companies.

5.1.3   Research Procedure

The forecasting procedure consists of 3 phases (**Figure 1**).

1. Survey data that covers production and patterns of purchases and sales in the biotechnology industry are used in the formation of input-output tables estimating linkages to other industries.

2. The biotechnology sector is added to the official input-output tables of Statistics Finland as a new branch. This enables the estimation of backward linkages to other industries. The

backward linkages depict how much the biotechnology sector increases purchases from other branches when its own sales grow, and *vice versa*. This enables estimation of the economy wide growth potential; the estimation is based on the Monte Carlo simulation using probability distributions of firms' anticipated future sales and bankruptcy risk during 10,000 iterations.

3. The results of forecast impacts are presented and discussed in the context of the Finnish economy.
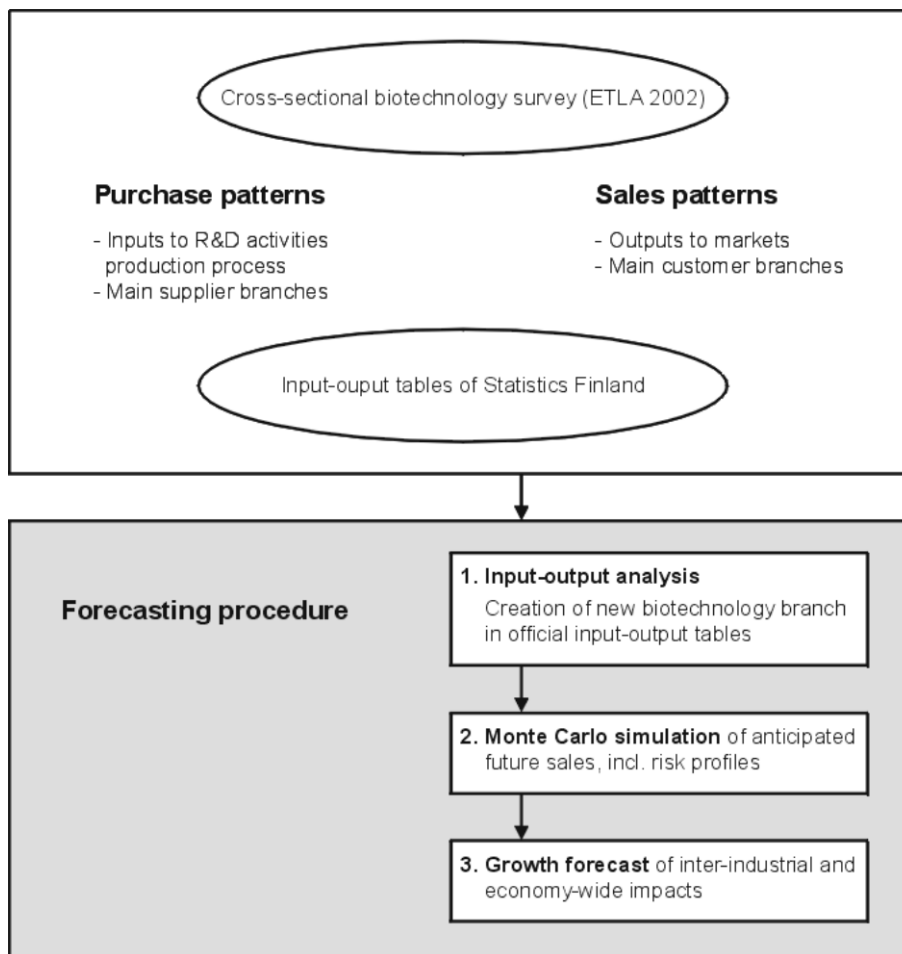
Figure 1. **Framework of the forecast model.**

The biotechnology sector is classified under many statistical branches in official statistics (e.g. chemical production, food stuff production, business services). However, the biotechnology companies differ a lot from other Finnish companies on average (Hermans and Tahvanainen [3]; Hermans [8]). For example, there are many biotechnology companies which do not have sales yet but which expect to have high sales in the future, based on relatively high expenditures on research and development (R&D). The utilization of survey data is necessary in order to be able to estimate the input-output structures of these companies and their inter-industrial linkages and economic impacts. In the survey, small and medium-sized biotechnology companies announced their input-output structure (patterns of purchases and sales) at the end of 2001. They also disclosed their sales expectations.

Most large biotechnology-related companies did not reveal their patterns of purchases and sales. Consequently, they could not be included in the new statistical branch of the biotechnology industry described above. The majority of the large companies represent more mature entities compared to the biotechnology SMEs; thus, their input-output structures are closer to the average industrial classes than the biotechnology SMEs. Therefore, the large companies are treated as part of the existing statistical classes.

Input-output modeling reveals supply and demand linkages between different branches. An industry uses the outputs of other industries as intermediate inputs in its own production processes. The industry sells its own output to another industrial branch, which uses that, in turn, as an intermediate input in its production. Input-output tables conclude these inter-industry linkages, and they have been used in many contexts, such as industrial forecast models (e.g. Burridge [9]), regional forecast models (Rickman [10]), and forecasting the dynamics of production within a pharmaceutical company (Marangoni and Fezzi [11]).

The word simulation refers to any analytical method which attempts to imitate a real-life system; usually other types of analyses are mathematically too complex or too tedious to produce (Drakos [12]). One type of simulation is the Monte Carlo simulation, which randomly generates values for uncertain variables to simulate a forecast model using numerous iterations. The Monte Carlo simulation is used in a multitude of applications; examples thereof are nuclear reactor design, radiation cancer therapy, traffic flow, oil well exploration and econometric Dow-Jones forecasting (ibid.). Monte Carlo simulation has also been used in the estimation of the input-output multipliers (see e.g. Bullard and Sebald [13]; Roland-Holst [14]).

This study constructs input-output multipliers from the cross-sectional data, and the simulation is utilized in the forecasting procedure. Without the use of simulation, an input-output model would result only in a single outcome: a scenario in which all the positive expectations of the biotechnology companies are realized. However, such a scenario does not reflect the most probable outcome.

The presented forecast procedure uses both the input-output model and Monte Carlo simulation to numerically analyze the effect of varying uncertainty factors. The first factor is the threat of bankruptcy. It is defined as a stochastic outcome: bankruptcy or continuing business at the end of 2006. Exogenous foreign demand constitutes the second uncertainty factor. It is included as a probability distribution of anticipated exports by the Finnish biotechnology companies. These uncertainties are included in the simulation. Instead of a single outcome, the model produces a distribution of all the potential outcomes given the assumptions behind the initial probability distributions. The assumptions are discussed in detail below.

This study is divided into four sections. The present section introduces the background, objectives and rationale of the forecasting procedures. Data employed in this study and assumptions behind the model are examined in Section 2. The input-output relations between the biotechnology sector and other branches, those that use biotechnology in their processes and products and those that are suppliers to the biotechnology firms are also depicted. Section 3 employs a numeric Monte Carlo simulation-based input-output analysis to construct a growth contribution scenario for the Finnish economy as a whole. Section 4 concludes the results of the forecast and relates the projected growth of the biotechnology industry to the three main pillars of the Finnish economy.

5.2   Biotechnology Industry in Finland

5.2.1   Data

This study employs a survey conducted by ETLA. The survey contains financial and business activity information on 84 Finnish biotechnology firms. A problem of the representativeness of the survey data arises because there were 131 biotechnology firms active at the end of 2001, and thus survey data represent only 64% of the sector. Furthermore, the sample seems to be slightly biased toward the older age groups: the sample contains three-fourths of the companies founded during 1991-1996 as well as companies founded earlier than 1991, but only 49% of the

companies founded during 1997-2001 (Table 1). In order to form a plausible estimation to depict the entire biotechnology sector in Finland, weights were constructed reflecting the age groups of the firms; the weights are inverses of the percentage shares of the sample in different age groups.

Table 1. **Number of biotechnology firms in the sample of the ETLA survey respective to total population sorted by age groups.**

	before 1991	1991-1996	1997-2001
ETLA sample	25	34	25
Total number	34	46	51
Percentage share of sample	74 %	74 %	49 %
Weight	1.36	1.35	2.04

The survey contains information on purchase and sales patterns of 72 small and medium-sized enterprises (SMEs): from which main branches did they purchase their inputs, and to which main branches did they sell their outputs. This information was integrated as a new branch in the official input-output tables of Statistics Finland. The SMEs disclosed only the three most significant branches that they trade with, and thus there was not enough detailed information on all of the subclasses. This problem was eliminated by aggregation of branches, in which the entire input-output table was condensed to a 7x7 table.

Detailed purchase and sales data were not disclosed by the large companies, and therefore they were placed in the conventional industrial and service branches best fitting their activities. The existing structures of the branches of large companies were assumed to adequately illustrate their input-output patterns. The large companies are often multi-functional in the sense that they also have more conventional products. These estimates contain only the share of biotechnology related sales disclosed by the companies, not their entire conventional production.

A stochastic feature was included in the forecasting model. A discrete dichotomous setting for the probability of going bankrupt was added to the model. The bankruptcy risk was set at 5.7% for small and medium-sized firms according to US experience in the biotechnology industry, and 1% for large-sized firms [15]. In Finland, the relative share of bankruptcies has been slightly above 5% according to the ETLA biotechnology database.

The growth forecast was based on the future sales figures according to the firms' announcements. All biotechnology firms expect successful growth potential in the next 5 years, in 2002-2006. The estimation of exogenous foreign demand set into the input-output model was based on the anticipated future exports disclosed by the companies (**Table 1**).

Instead of relying only on the estimates announced by the firms, probability distributions were utilized to create weighted anticipated future exports for every single firm. It was assumed that all the firms have the same risk of either delays in entering the marketplace with new products, or a market penetration that will not evolve as optimistically as expected. Thus, the probable anticipated future sales were formed by applying a uniform distribution. The lower limit of the distribution was set by current exports (in the end of 2001). The upper limit was set by the anticipated future exports in 2006 as announced by the company. Finally, a Monte Carlo simulation with 10,000 iterations was run using the parameters above.

5.2.2 Input-Output Structure

The Finnish biotechnology industry is based on intensive international relations and foreign trade; two thirds of the sales are exported and almost one third of the purchases are imported (Figure 2). The biotech-

Biotechnology SMEs 2001
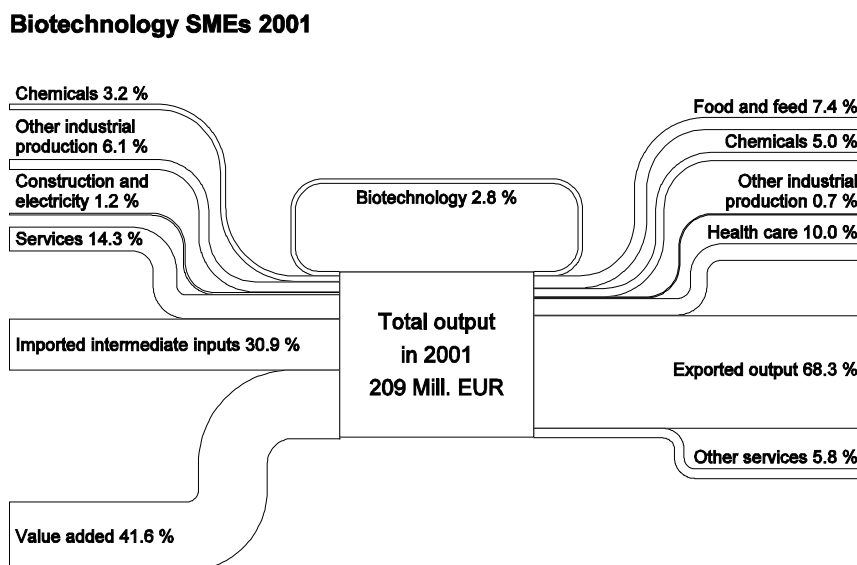
Figure 2. Input-output structure of the Finnish small and medium-sized biotechnology companies.

nology industry purchases most of its domestic intermediate inputs from the service sector. Other domestic inputs contain the wages of labor and the profits or losses of the companies. The great losses, almost 100 million euros in 2001, reduce the net domestic inputs. The inputs add up to 209 million euros.

In input-output models inputs always equal outputs, and thus total output is 209 million euros. The largest domestic customer branches to which the output is sold are health care services, the food and feed industry, and the chemical industry (incl. pharmaceuticals). Over 60% of the total output of services and products are exported. Thus, the foreign trade intensity is relatively high within the Finnish biotechnology SMEs.

5.2.3 Growth Prospects

Biotechnology firms are active in many industrial sub-branches. Most of the companies are related to pharmaceuticals or diagnostics, or both. There is also a significant number of firms involved in service activities, biomaterials, and the food industry. A few of the companies are focused on enzyme production or agriculture.

The biotechnology companies seem to anticipate high growth in demand for their products. The global market potential appears to be particularly attractive. Table 2 presents the anticipated growth rates of sales of the Finnish biotechnology industry by sub-branches.

Table 2.   **Anticipated annual growth rates of biotechnology sales of products and services for the 5 consecutive years, as anticipated by the Finnish biotechnology companies in 2002.**

Growth rate in %	Domestic sales	Exports	Entire sales
Pharmaceuticals	4 %	36 %	22 %
Diagnostics	4 %	17 %	14 %
Biomaterials	17 %	94 %	49 %
Food and feed	3 %	11 %	7 %
Industrial enzymes	7 %	5 %	5 %
Agriculture	21 %	24 %	23 %
Services	12 %	101 %	38 %
Other	6 %	19 %	18 %
Total	7 %	27 %	21 %

The table shows how the growth prospects vary among each sub-branch of the biotechnology sector. The companies believe their sales will grow annually 21% on average over the next five years. The growth is expected to be realized mainly on the international markets. It seems that most of the firms expect that they can exploit a market potential throughout the world (Figure 3).

A rather surprising finding is that the enzyme related industry expects only a moderate 5% growth. Finland is regarded as a giant in pulp and paper production, which is a heavy user of enzymes, and thus it would be expected to stimulate the demand for new enzyme applications (see Laestadius [16]). At the other extreme, biomaterials production is anticipated to grow almost 50% annually.
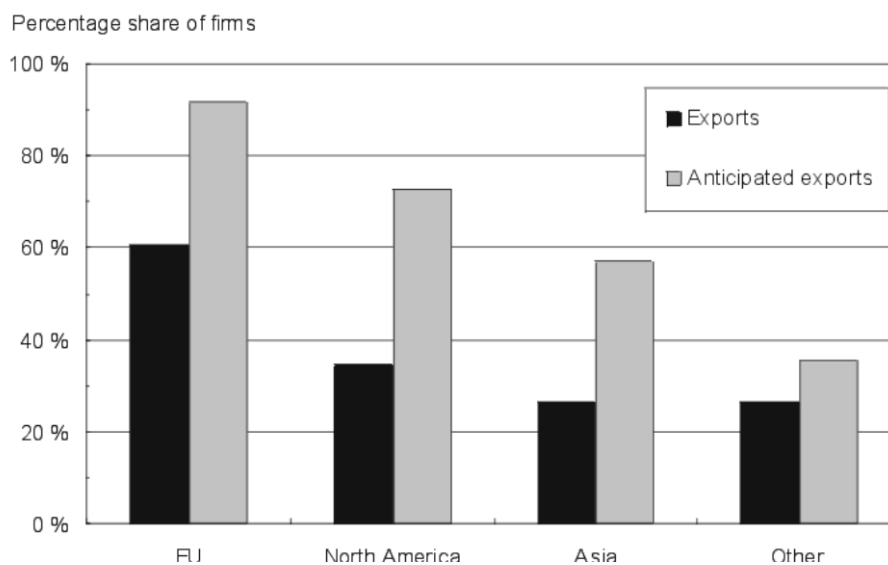
Figure 3.   Export areas of the Finnish biotechnology firms in 2001 and in 2006 (projections).

The forecast procedure utilizes the companies' expectations regarding their future exports growth. However, using the companies' own expectations introduces two possible types of bias to the model

1. randomness at the company level: an arbitrary assessment of anticipated future exports

2. systematic error at the industry level: a tendency of the entire biotechnology sector to over-estimate systematically the level of anticipated future exports over the period of the survey.

Hermans and Kauranen [17] have analyzed the first type of bias. They related the measurable intellectual capital factors to the anticipated future sales of the biotechnology SMEs in Finland. The intellectual capital theory suggests that the interrelation of human, structural, and relational capital acts as a driver for value creation in a knowledge-intensive business (see e.g. Edvinsson and Malone [18]). In the study, they were able to construct an intellectual capital model, which explained 70% of the variance of anticipated future sales. Consequently, measurable intellectual capital was tightly related to the anticipated future sales of the biotechnology SMEs: if a company holds a relatively high (low) level of intellectual capital, it also has high (low) growth prospects, respectively. Therefore, it seems well-reasoned to rely on the companies' expectations in the ordinal sense, that is, the companies with highest anticipated future sales are those that will probably sell more than those with lower expectations.
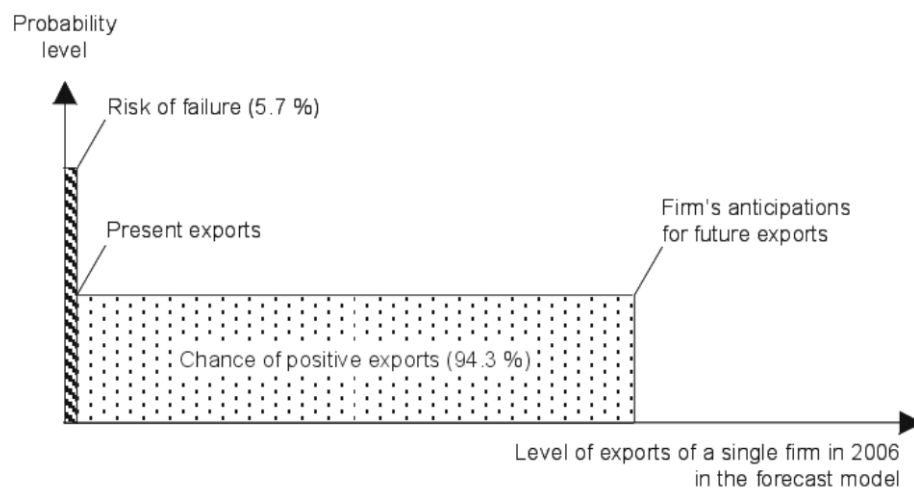
Figure 4.   Probability distribution of an individual firm's exports.

Despite the ability to explain the variance of anticipated future sales of the biotechnology SMEs, the second bias remains. There are two main reservations. The first is related to the high risk in developing new biotechnology innovations, and particularly in converting them into commercially exploitable products. Second, there are doubts about the expected short time interval (here 2002-2006) for converting large losses into a flourishing business. The companies seemed to disclose their anticipated future sales within the most optimistic scenario, probably omitting the possibility of technical failures or severe time delays in product development. An example of this optimistic approach is visible in Figure 2, in which approximately 70% of the companies plan

to have access to the highly competitive North American marketplace within five years.

In order to control for the second bias, probability distributions were applied while forecasting the economic impacts: a discrete probability distribution covering the bankruptcy risk, and a uniform distribution covering the sales expectations between the present and anticipated future exports (Figure 4). In other words, there is a 5.7% chance that a single firm will go bankrupt and 94.3% chance that its exports will be between the exports of 2001 and the anticipated future exports for 2006 [15].

5.3 Economic Forecast

5.3.1 Input-Output Analysis

The econometric modeling procedure is initiated by input-output analysis. Input-output tables are utilized in order to estimate growth prospects covering inter-industrial linkages as well as contributions to the whole economy until the end of 2006. A conventional Leontief-type input-output matrix was constructed (see *e.g.* Forssell [19] and Giaschini [20]). The input-output model describes the interlinkages between all branches of industry.

Horizontal rows imply how the output of a single industry is used: as intermediate inputs in production processes of other industries and as end products to satisfy the domestic and foreign demand. Vertical columns depict how much an industry uses intermediate inputs from other industries and from imported inputs, and how much value added it produces. The method used in this study assumes that these structural multipliers, depicting the shares of input and output usage out of output, are fixed over the period that is analyzed. Equation 1 states the above relation formally:

(1)

$$x_i = \sum_{j=1}^{n} a_{ij} x_j + y_i = x = Ax + y = \begin{bmatrix} x_1 \\ x_2 \\ \dots \\ \\ \\ x_n \end{bmatrix} = \begin{bmatrix} a_{11} & a_{12} & \dots & & a_{1n} \\ a_{21} & a_{22} & & & \\ \dots & & \dots & & \\ \\ \\ a_{n1} & & & & a_{nn} \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ \dots \\ \\ \\ x_n \end{bmatrix} + \begin{bmatrix} y_1 \\ y_2 \\ \dots \\ \\ \\ y_n \end{bmatrix}$$

The multiplier *a* is derived from a ratio: $a_{ij} = \dfrac{x_{ij}}{x_j}$, in which x_j is the total (intermediary and final) output produced by the industry. The term x_{ij} measures how much the industry *j* uses the production of the industry *i* as an input. When *i* equals *j*, the multiplier *a* measures the intermediate inputs used within the companies of the same industry itself. The term *y* denotes a value of end products in an industry *(1,…,n)*. Capital letters without subscripts are matrix notations referring to the terms above.

Because $X = AX + Y \Leftrightarrow Y = (I - A)X \Leftrightarrow X = (I - A)^{-1}Y$. Therefore,

(2)

$$x_i = \sum_{i=1}^{n} b_{ij}\, y_i = X = (I - A)^{-1} Y = \begin{bmatrix} x_1 \\ x_2 \\ \dots \\ \\ \\ x_n \end{bmatrix} \begin{bmatrix} b_{11} & b_{12} & \dots & & b_{1n} \\ b_{21} & b_{22} & & & \\ \dots & & \dots & & \\ \\ \\ b_{n1} & & & & b_{nn} \end{bmatrix} \begin{bmatrix} y_1 \\ y_2 \\ \dots \\ \\ \\ y_n \end{bmatrix},$$

when $[b_{ij}] = (I - A)^{-1}$. Presented another way:

(3)

$$(I - A)^{-1} = \begin{bmatrix} \begin{bmatrix} 1 & 0 & \dots & & 0 \\ 0 & 1 & & & \\ \dots & & \dots & & \\ \\ \\ 0 & & & & 1 \end{bmatrix} - \begin{bmatrix} a_{11} & a_{12} & \dots & & a_{1n} \\ a_{21} & a_{22} & & & \\ \dots & & \dots & & \\ \\ \\ a_{n1} & & & & a_{nn} \end{bmatrix} \end{bmatrix}^{-1}$$

$$
=\begin{bmatrix} 1-a_{11} & -a_{12} & ... & & & -a_{1n} \\ -a_{21} & 1-a_{22} & & & & \\ ... & & ... & & & \\ & & & & & \\ & & & & & \\ -a_{n1} & & & & & 1-a_{nn} \end{bmatrix}^{-1} = \begin{bmatrix} b_{11} & b_{12} & ... & & & b_{1n} \\ b_{21} & b_{22} & & & & \\ ... & & ... & & & \\ & & & & & \\ & & & & & \\ b_{n1} & & & & & b_{nn} \end{bmatrix}
$$

where b_{ij} expresses how much industry i needs to produce so that industry j could produce one unit of final product j.

These matrix operations enable the use of the multipliers of the inverse matrix when estimating the effects of the growth in the biotechnology industry in Finland. The input and output structure of small and medium-sized biotechnology firms were added to the model as a new branch. Large-sized enterprises were treated as a part of their conventional branch because they did not disclose any information on their purchase and sales patterns.

Table 3.   Inverse matrix derived from input-output table.

Inverse matrix	Agriculture and other primary production	Bio-techno-logy	Food industry	Chemical industry	Other industrial production	Construc-tion and electricity	Health care services	Other services
Agriculture and other primary production	1.2410	**0.0084**	0.4465	0.0310	0.0637	0.0422	0.0064	0.0151
Biotechnology	**0.0002**	**1.0518**	**0.0020**	**0.0018**	**0.0001**	**0.0001**	**0.0013**	**0.0002**
Food industry	0.0641	**0.0082**	1.2768	0.0294	0.0193	0.0159	0.0085	0.0223
Chemical industry	0.0247	**0.0363**	0.0178	1.0772	0.0263	0.0131	0.0092	0.0051
Other industrial production	0.0966	**0.1028**	0.2030	0.1995	1.3697	0.3564	0.0617	0.1202
Construction and electricity	0.0494	**0.0263**	0.0460	0.0484	0.0362	1.0779	0.0245	0.0652
Health care services	0.0111	**0.0034**	0.0052	0.0014	0.0016	0.0017	1.0239	0.0054
Other services	0.2439	**0.2260**	0.3688	0.2765	0.2640	0.3295	0.1898	1.3531

Table 3 depicts the inverse matrix derived from the general form of Equation 3. The coefficients are interpreted as follows. The exogenous

increase of 1 unit in demand of biotechnology products and services will add 1.0518 units to the total output of the biotechnology industry due to the usage of intermediate products from the companies in its own industry. A one unit increase in the output of the biotechnology industry is reflected by a 0.226 unit increase in the demand of other services (vertical column "Biotechnology" in Table 3). However, only 0.0002 units of biotechnology outputs are produced for the other services (horizontal row "Biotechnology" in Table 3).

Table 3 also shows that an exogenous change in demand for the output of other sectors results only in a negligible increase of demand for the biotechnology products and services. This reflects the fact that the biotechnological applications are not yet tightly linked with other sectors' production processes. For example, a one unit increase in production of health care services induces only a 0.0013 unit increase in purchases of inputs from the biotechnology industry.

The input-output linkages can and probably will vary with time. For example, biotechnology products can replace some conventional chemical products in consumer and intermediate input markets, leading to an increase in the coefficients of the biotechnological inputs in the inverse matrix. However, this replacement, or crowding-out effect is not taken into account in the fixed coefficient input-output model based on cross-sectional data.

The multipliers are estimated from the cross-sectional data obtained through the ETLA biotechnology survey. The survey is the first of its kind in Finland. Thus, time series data are not available for the Finnish biotechnology sector, which at the moment excludes the construction of a time series model.

5.3.2   The Monte Carlo Simulation

This section presents the results of two simulation procedures. The first simulation contains only the predicted growth impacts of biotechnology SMEs on other industries. In addition to SMEs, the second simulation contains also the large biotechnology related multifunctional companies. The twofold approach was necessary in order to avoid blurring between the inter-industrial linkages and growth contribution to GDP.

The input-output model estimates spill-over effects, and thus it reveals the impact of potential growth in the biotechnology industry on other sectors in the table. However, these spill-over effects could not be assessed with a single simulation because the large companies are part of

the official branches, and SMEs are part of the newly formed branch of the biotechnology industry. The first simulation, containing only SMEs, indicates how large the spill-over effect is on other branches.

The second simulation, which contains also the large biotechnology-related companies, enables the estimation of the growth contribution of the entire biotechnology industry to GDP. However, it does not offer an insight into the spill-over effects on the specific branches since the output growth effects of the large companies and spill-over effects cannot be distinguished from each other.

Results of simulation 1

The value added of small and medium-sized biotechnology companies was approximately 90 million euros in 2001. According to the results of our forecast model, the predicted nominal growth contribution of the biotechnology SMEs to the GDP in 2006 will be in the range of 181-446 million euros with a 90% probability (Figure 5). This corresponds to the growth contribution of .03-.07 percentage points on annual average between 2002-2006. This prediction contains the multiplier effects from input-output tables to non-biotechnology branches. The value added of the biotechnology SMEs is predicted to be 125-309 million euros in 2006 with a 90% probability.
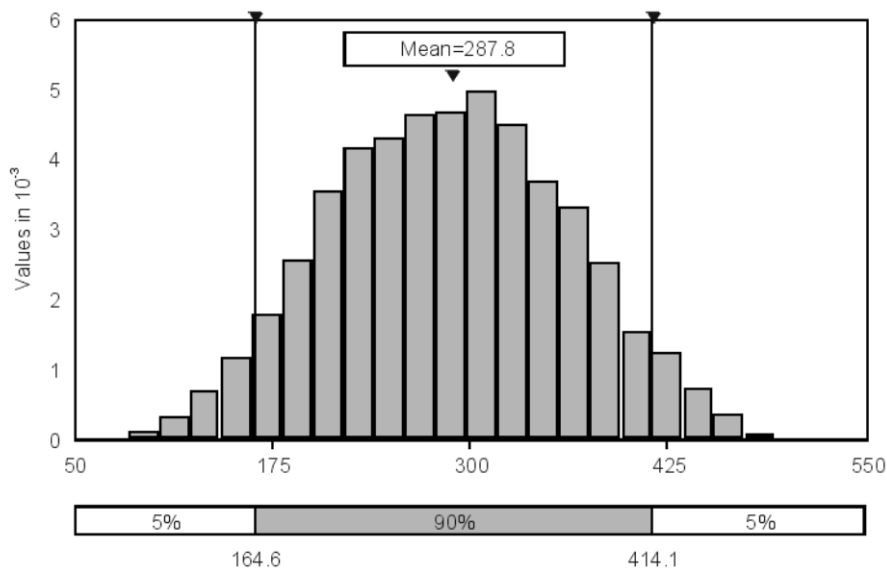
Figure 5.   **Distribution of the forecast nominal contribution of the small biotechnology industry to the GDP in 2006.**

Table 4 presents the main results of the forecast procedure. The overall contribution of the biotechnology business is slightly positive for the economic growth in Finland. As mentioned above, the gross domestic product (GDP) is expected to grow an additional 0.02-0.06 percentage units on annual average by the impact of the growth of biotechnology industry. The biotechnology industry is forecast to grow 18-34% on annual average between 2002-2006. The spill-over effects produced by the biotechnology industry are distributed unevenly among other branches.

The spill-over effects are highest in the chemical industry, corresponding to an increase in production of 0.04-0.09 percentage points in annual terms. The production of Other Industry (including production of instruments and food industry) is predicted to be stimulated by 0.01-0.02 percentage points on an annual average.

Table 4.   Monte Carlo simulation-based anticipated nominal growth contributions of small and medium-sized biotechnology companies in annual terms.

Branch	1. Annual growth contribution to a single branch (2002-2006), percent, range of 90 % probability	2. Annual growth contribution to GDP (2002-2006), percentage units, range of 90 % probability	3. Nominal contribution to the growth of the value added in 2006, million euros, range of 90 % probability
Agriculture, forestry, and other primary production	0.01 – 0.02 %	0.00 – 0.00 %	1 - 3
Biotechnology SMEs	18.1 – 33.7 %	0.02 – 0.04 %	114 – 286
Chemicals	0.04 – 0.09 %	0.00 – 0.00 %	3 - 7
Other industry	0.01 – 0.02 %	0.00 – 0.00 %	10 – 25
Construction	0.01 – 0.02 %	0.00 – 0.00 %	3 – 7
Services	0.01 – 0.02 %	0.01 – 0.01 %	34 – 86
GDP	0.02 – 0.06 %	0.02 – 0.06 %	**165 – 414**

The service sector forms the largest sector in the Finnish economy; it produces 63% of the GDP. Despite a relatively low growth contribution of 0.01 percentage points, the contribution corresponds to 34-86 million euros during 2002-2006; this is the largest contribution to any other branch in monetary terms. The impacts on construction, and agriculture and forestry remain low both as percentage points and in monetary terms.

As a whole, the high relative economic growth of value added of small and medium-sized biotechnology firms have only a low spill-over effect on the entire economy over the next five years according to the forecast model. There are two potential reasons for the low spill-over effects. First, there is a lack of the input-output data of large companies in the survey. This has been discussed above. Second, the volume of purchases and sales was still very low in 2001.

It must be born in mind that even a single company showing significant success and consequently purchasing higher volumes would have a significant impact on the entire input-output structure over time. In the second simulation, the classification of the large biotechnology related companies as a part of the conventional branches counteracts the effects of a single company affecting the input-output structure of the entire biotechnology industry.

Results of simulation 2

After predicting only the economic impacts of small and medium-sized biotechnology companies, a second forecast model was constructed combining SMEs and large multi-functional biotechnology companies. The multi-functional companies are those that also have essential production activities in branches other than biotechnology. All the large
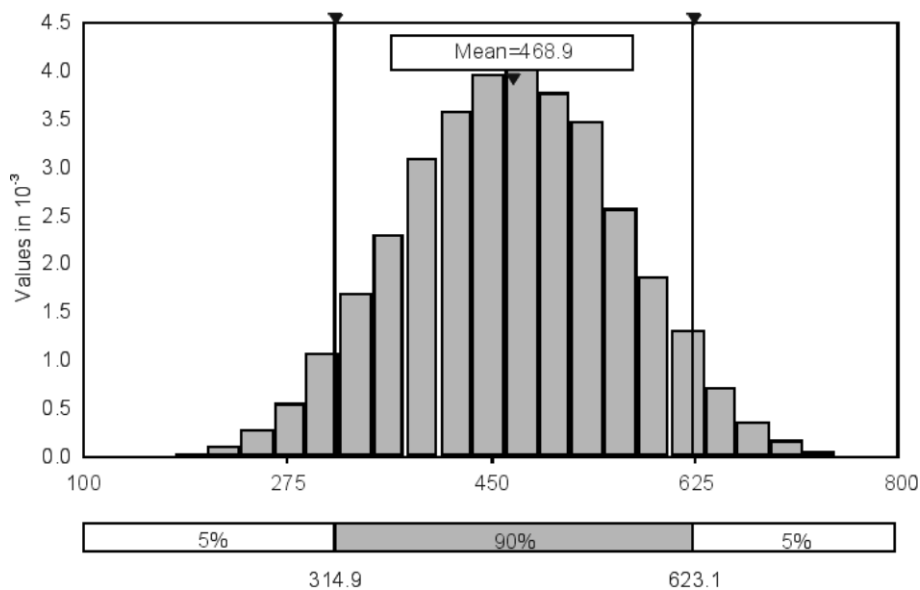
Figure 6. **Distribution of forecast nominal contribution of the entire biotechnology industry to the GDP in 2006.**

companies are placed in their conventional branches (not the biotechnology industry) in the input-output model.

The value added of the entire biotechnology industry with production that utilizes biotechnology-based products or processes, was about 500 million euros in 2001. The forecast model estimates that the growth of the entire biotechnology industry will contribute 315-623 million euros to the growth of the GDP in 2006 (Figure 6) with a 90% probability. This corresponds to a growth contribution of 0.05 – 0.09 percentage points to the GDP growth rates per annum.

Table 5. **Monte Carlo simulation-based anticipated nominal growth contributions of entire biotechnology industry (incl. large companies) in annual terms.**

Branch	1. Annual growth contribution to a single branch (2002-2006), per-cent, range of 90 % probability	2. Annual growth contribution to GDP (2002-2006), percentage units, range of 90 % probability	3. Nominal con-tribution to the growth of the val-ue added in 2006, million euros, range of 90 % probability
Agriculture, forestry and other primary production	0.03 – 0.06 %	0.00 – 0.00 %	6 – 14
Biotechnology SMEs	18.3 – 33.7 %	0.02 – 0.04 %	115 – 285
Chemicals	0.18 – 0.99 %	0.00 – 0.01 %	15 – 81
Other industry	0.03 – 0.10 %	0.01 – 0.02 %	51 – 134
Construction	0.01 – 0.03 %	0.00 – 0.00 %	6 – 13
Services	0.02 – 0.04 %	0.01 – 0.02 %	79 – 155
GDP	**0.05 – 0.09 %**	**0.05 – 0.09 %**	**315 – 623**

Table 5 presents the growth contributions of the entire biotechnology sector to other branches and the total GDP growth. The impact on the production of chemicals and chemical products is greatest: the annual growth contribution of biotechnology-related value added is forecast to reach the range of 0.18 – 0.99 percentage points. The entire biotechnology industry contributes to the growth of the production of Other Industry by 0.03 – 0.10 percentage points on annual average. Growth contributions to other sectors are not as significant.

The growth rates of production of a single branch can be very different from the growth contribution rates presented in Table 5. For example, the growth rate of value added in agriculture and other primary production can even be negative covering the years of the forecast and thus its contribution to the GDP would also be negative.

This study considers anticipated exports to be an exogenous variable. In other words, the increase in domestic demand resulted from an increase in the use of inputs in domestic production. If part of the domestic production had also been considered exogenous, the growth rates would have been slightly higher.

5.4   Conclusions

5.4.1   Summary

This forecast study is intended to offer insights on the impacts of the Finnish biotechnology industry on the economic growth in Finland. The study focuses on converting expected growth potential into impacts on economy-wide growth. The use of Monte Carlo simulation enabled the use of probability distributions instead of point estimates in order to model risks related to the failure of a single company as well as time delays in its product development and market launches.

The present purchase-sales patterns of the small and medium-sized biotechnology companies were added as a new industrial sector to official statistics. This procedure employed an input-output analysis, which enabled the estimation of economy-wide growth impacts. An inverse matrix with fixed multipliers was constructed, and the impact of exogenous foreign demand between 2002-2006 was assessed using a Monte Carlo simulation with 10,000 iterations.

The high percentage growth prospects of the Finnish biotechnology industry remained relatively moderate on an aggregate macroeconomic level. The growth contribution for the Finnish nominal GDP growth was 0.05-0.09 percentage points annually. This equals the growth impacts of 315-623 million euros in nominal terms during 2006.

A noticeable impact on the chemical industry was seen. According to the simulations, the biotechnology companies add 0.2-1.0 percentage points to the annual nominal growth of chemical production in Finland. Many of the biotechnology firms act in chemical-related sub-industries.

5.4.2   Further Studies

This study opens views for further research:

1. The sub-branches of the biotechnology industry differ from each other concerning their risk profiles. For example, the predicted time span from innovation to product launch is exceptionally long in drug development as compared to development of biomaterials and industrial enzymes. The drug development is strictly regulated requiring extensive pre-clinical and clinical testing before approval to initiate marketing. The Monte Carlo simulation can be refined by using sub-branch-specific risk profiles which would add to the accuracy of the model.

2. This study employed fixed input-output multipliers because only cross-sectional survey data was available. As time series become available, the changes of multipliers can be estimated over time using historical data. This would enable the incorporation of the evolvement of industrial structures into the model.

3. Rantala [21] estimates a change of input coefficients over time with the help of R&D intensities of industrial branches. In the R&D-intensive biotechnology industry, the inclusion of these dynamic procedures to the input-output models could offer another way of estimating the changes of input-output multipliers behind the forecast.

4. This study does not analyze labor effects. However, the identification of labor effects induced by the growth of the biotechnology industry would be valuable in the macro-economic context (see e.g. Menrad et al. employing German data [22]).

The forecast model presented in this study can be refined to support these four research set-ups.

5.4.3   Biotechnology – the Fourth Pillar?

Industrial history shows us that if a region or a country has no previous industrial tradition in a certain sector, successful businesses and new growth emerge slowly or only seldom. Finland has pinned high hopes on biotechnology as a source of new research-intensive growth. Almost all industrialized countries have the same goal, and many of them have already long traditions in this sector, whereas Finland has a short history in biotechnology. In Finland, the biotechnology sector's volume of produc-

tion measured by value added is about 500 million euros. In order to get a perspective on the growth possibilities, the biotechnology sector can be compared to the development of the currently strong sectors in Finland – the forest, machinery and electronics industries.

In the early 1950s, the value of pulp and paper industry production was 500 million euros in 2000 prices (Figure 7). The electronics industry reached that level in the mid-1970s. If the biotechnology sector achieved the same growth as that of the electronics industry, it would reach the position of the "fourth pillar" of Finnish industry in about 30 years. If the life cycle of the biotechnology industry as an independent sector is comparable to the forest industry, the time span would be 50 years. Finally, if the growth rate of production of the biotechnology sector was sustained at the same level as in the forecast period 2001-2006, it would take 15-30 years to reach the same production level as the electronics, machinery and metal products, or pulp and paper industries have today.
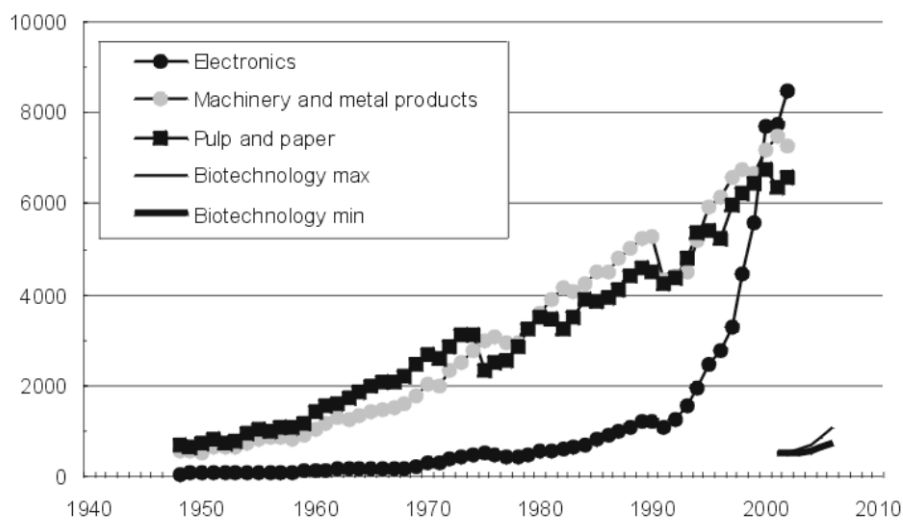
Figure 7. **Industrial production by sector 1948 – 2002, in year 2000 prices (Hermans and Ylä-Anttila [23]).**

Even with a swift growth, it will take more than a decade for the biotechnology industry to become one of the main pillars of the Finnish economy. It is likely that the Finnish economy's new engine of growth will emerge from a combination of new and old sectors. In such a scenario, biotechnology would play a significant role.

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Appendix.   Simulation report of the model of small and medium-sized biotechnology enterprises.

Summary Information	
Workbook Name	SME_4.xls
Number of Simulations	1
Number of Iterations	10000
Number of Inputs	144
Number of Outputs	27
Sampling Type	Monte Carlo
Simulation Start Time	9.3.2004 11:04
Simulation Stop Time	9.3.2004 11:05
Simulation Duration	00:00:28
Random Seed	1692226105

Output		Statistics						
Name	Cell	Minimum	Mean	Maximum	x1	p1	x2	p2
Agriculture and other primary production / Value added io	D31	0.7	2.2	4.0	1.3	5 %	3.2	95 %
Agriculture and other primary production / Contribution to own branch	G31	0.003 %	0.010 %	0.018 %	0.006 %	5 %	0.015 %	95 %
Agriculture and other primary production / Contribution to GDP	I31	0.000 %	0.000 %	0.001 %	0.000 %	5 %	0.000 %	95 %
Biotechnology / Value added io	D32	58.5	198.7	353.2	113.6	5 %	285.8	95 %
Biotechnology / Contribution to own branch	G32	10.811 %	26.454 %	38.247 %	18.151 %	5 %	33.732 %	95 %
Biotechnology / Contribution to GDP	I32	0.009 %	0.029 %	0.052 %	0.017 %	5 %	0.042 %	95 %
Food industry / Value added io	D33	0.3	0.9	1.5	0.5	5 %	1.2	95 %
Food industry / Contribution to own branch	G33	0.003 %	0.009 %	0.016 %	0.005 %	5 %	0.013 %	95 %
Food industry / Contribution to GDP	I33	0.000 %	0.000 %	0.000 %	0.000 %	5 %	0.000 %	95 %
Chemical industry / Value added io	D34	1.5	5.1	9.1	2.9	5 %	7.4	95 %
Chemical industry / Contribution to own branch	G34	0.019 %	0.064 %	0.113 %	0.036 %	5 %	0.091 %	95 %
Chemical industry / Contribution to GDP	I34	0.000 %	0.001 %	0.001 %	0.000 %	5 %	0.001 %	95 %
Other industrial production / Value added io	D35	4.8	16.1	28.7	9.2	5 %	23.2	95 %
Other industrial production / Contribution to own branch	G35	0.004 %	0.012 %	0.021 %	0.007 %	5 %	0.017 %	95 %

Other industrial production / Contribution to GDP	I35	0.001 %	0.002 %	0.004 %	0.001 %	5 %	0.003 %	95 %
Construction and electricity / Value added io	D36	1.4	4.8	8.6	2.8	5 %	6.9	95 %
Construction and electricity / Contribution to own branch	G36	0.003 %	0.011 %	0.019 %	0.006 %	5 %	0.015 %	95 %
Construction and electricity / Contribution to GDP	I36	0.000 %	0.001 %	0.001 %	0.000 %	5 %	0.001 %	95 %
Health care services / Value added io	D37	0.3	1.1	2.0	0.6	5 %	1.6	95 %
Health care services / Contribution to own branch	G37	0.001 %	0.002 %	0.004 %	0.001 %	5 %	0.003 %	95 %
Health care services / Contribution to GDP	I37	0.000 %	0.000 %	0.000 %	0.000 %	5 %	0.000 %	95 %
Other services / Value added io	D38	17.3	58.9	104.7	33.7	5 %	84.7	95 %
Other services / Contribution to own branch	G38	0.004 %	0.014 %	0.026 %	0.008 %	5 %	0.021 %	95 %
Other services / Contribution to GDP	I38	0.003 %	0.009 %	0.015 %	0.005 %	5 %	0.013 %	95 %
Total / Value added io	D39	85	288	512	165	5 %	414	95 %
Total / Contribution to own branch	G39	0.013 %	0.043 %	0.076 %	0.024 %	5 %	0.061 %	95 %
Total / Contribution to GDP	I39	0.013 %	0.043 %	0.076 %	0.024 %	5 %	0.061 %	95 %

Appendix. Simulation report of the model of small, medium, and large-sized biotechnology enterprises.

Summary Information	
Workbook Name	SME_LE_03_2004.xls
Number of Simulations	1
Number of Iterations	10000
Number of Inputs	180
Number of Outputs	27
Sampling Type	Monte Carlo
Simulation Start Time	8.3.2004 15:13
Simulation Stop Time	8.3.2004 15:14
Simulation Duration	00:00:41
Random Seed	1069949287

Output		Statistics						
Name	Cell	Minimum	Mean	Maximum	x1	p1	x2	p2
Agriculture and other primary production / Value added io	D50	2.8	9.6	16.4	5.5	5 %	13.7	95 %
Agriculture and other primary production / Contribution to own branch	G50	0.013 %	0.045 %	0.076 %	0.026 %	5 %	0.063 %	95 %
Agriculture and other primary production / Contribution to GDP	I50	0.000 %	0.001 %	0.002 %	0.001 %	5 %	0.002 %	95 %
Biotechnology / Value added io	D51	58.1	199.7	351.3	114.9	5 %	284.9	95 %
Biotechnology / Contribution to own branch	G51	10.753 %	26.556 %	38.130 %	18.304 %	5 %	33.665 %	95 %
Biotechnology / Contribution to GDP	I51	0.009 %	0.030 %	0.052 %	0.017 %	5 %	0.042 %	95 %
Food industry / Value added io	D52	0.7	2.4	4.1	1.5	5 %	3.3	95 %
Food industry / Contribution to own branch	G52	0.007 %	0.025 %	0.042 %	0.015 %	5 %	0.034 %	95 %
Food industry / Contribution to GDP	I52	0.000 %	0.000 %	0.001 %	0.000 %	5 %	0.000 %	95 %
Chemical industry / Value added io	D53	5.2	48.5	90.9	14.9	5 %	81.4	95 %
Chemical industry / Contribution to own branch	G53	0.065 %	0.593 %	1.102 %	0.184 %	5 %	0.990 %	95 %
Chemical industry / Contribution to GDP	I53	0.001 %	0.007 %	0.013 %	0.002 %	5 %	0.012 %	95 %
Other industrial production / Value added io	D54	22.5	87.7	154.8	44.1	5 %	130.9	95 %
Other industrial production / Contribution to own branch	G54	0.017 %	0.065 %	0.115 %	0.033 %	5 %	0.097 %	95 %

Other industrial production / Contribution to GDP	I54	0.003 %	0.013 %	0.023 %	0.007 %	5 %	0.019 %	95 %
Construction and electricity / Value added io	D55	2.9	9.7	16.1	6.4	5 %	13.0	95 %
Construction and electricity / Contribution to own branch	G55	0.006 %	0.021 %	0.035 %	0.014 %	5 %	0.028 %	95 %
Construction and electricity / Contribution to GDP	I55	0.000 %	0.001 %	0.002 %	0.001 %	5 %	0.002 %	95 %
Health care services / Value added io	D56	0.7	3.7	6.8	1.6	5 %	5.9	95 %
Health care services / Contribution to own branch	G56	0.001 %	0.008 %	0.014 %	0.003 %	5 %	0.013 %	95 %
Health care services / Contribution to GDP	I56	0.000 %	0.001 %	0.001 %	0.000 %	5 %	0.001 %	95 %
Other services / Value added io	D57	33.1	107.4	178.7	72.9	5 %	142.0	95 %
Other services / Contribution to own branch	G57	0.008 %	0.026 %	0.044 %	0.018 %	5 %	0.035 %	95 %
Other services / Contribution to GDP	I57	0.005 %	0.016 %	0.026 %	0.011 %	5 %	0.021 %	95 %
Total / Value added io	D58	150	469	776	315	5 %	623	95 %
Total / Contribution to own branch	G58	0.022 %	0.069 %	0.115 %	0.047 %	5 %	0.092 %	95 %
Total / Contribution to GDP	I58	0.022 %	0.069 %	0.115 %	0.047 %	5 %	0.092 %	95 %