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# Evolution of the Location of Innovation in the International Pharmaceutical Industry

**John Cantwell**
Rutgers Business School
International Business
john.cantwell@rutgers.edu

**Sarah Edris**
Rutgers University
International Business
sarah.edris@rutgers.edu

## Abstract

This paper examines the effects of location specific interaction between university science and technological effort on the location of technological activity in the international pharmaceutical industry. We propose, as the primary sources of growth in the pharmaceutical industry have shifted towards the life sciences, and away from chemistry, locations that are more specialized in the life sciences will attract more pharmaceutical research. We predict that locational technological specialization coevolves with location specific expertise in the life sciences, university commitment to these fields, and the openness and quality of scientific systems. We also

contend that the locations with greater industry-university interactions will become more attractive. The empirical analysis consists of a dynamic cross-section model applied to the location of invention of patents in the pharmaceutical field between 1976 and 2015.

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## ABSTRACT

This paper examines the effects of location specific interaction between university science and technological effort on the location of technological activity in the international pharmaceutical industry. We propose, as the primary sources of growth in the pharmaceutical industry have shifted towards the life sciences, and away from chemistry, locations that are more specialized in the life sciences will attract more pharmaceutical research. We predict that locational technological specialization coevolves with location specific expertise in the life sciences, university commitment to these fields, and the openness and quality of scientific systems. We also contend that the locations with greater industry-university interactions will become more attractive. The empirical analysis consists of a dynamic cross-section model applied to the location of invention of patents in the pharmaceutical field between 1976 and 2015.



**Keywords:**

National Innovation Systems; University-Industry relationships

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## INTRODUCTION

This paper examines the effects of location specific interaction between university science and technological effort on the location of technological activity in the international pharmaceutical industry. We propose, as the primary sources of growth in the pharmaceutical industry shifts towards sciences in which a given country happens to be specialized in, that country benefits from the shift, and gains technological specialization in the international innovation network. We examine the effect of university-industry linkages on the shift in the technological paradigm from chemistry to the life sciences within the industry, as well as the effects of the quality and openness of scientific systems across different national systems of innovation.

We draw on various strands of literature to form the context of our research. First, we draw on the literature that examines the shifts in technological paradigms within industry to test whether pharmaceutical research has been affected. Second, there is a large literature which uses patents to explore various aspects of technological specialization and development efforts over time. Third, we make use of the discussion on the significance of university-industry relations for the historical evolution of both science and technology. Drawing upon this research, we form our predictions about, and undertake a broad comparison of linkages between university science and technological efforts to interpret how differences in the patterns of these relationships have shaped the development of the technological specialization of countries. We predict that locational technological specialization coevolves with location specific expertise in the life sciences, university commitment to these fields, and the openness and quality of scientific systems. We also contend that the locations with greater industry-university interactions will become more attractive.

We develop a dynamic cross-section econometric analysis to examine the interrelationship between the specialization of countries in pharmaceutical activity and the changing significance of the scientific stock the industry relies on between 1976 and 2015. Notwithstanding the evidence and theory which suggest the relationship between science and technology is strongest in the pharmaceutical industry, the pharmaceutical sector is appropriate for this type of analysis because it is an industry in which activity in large firms is geographically dispersed, and also because the structure of the industry has changed markedly over the period, and where intellectual property rights really matter. In the evolutionary process of substantial change that has characterized this sector, the technological specializations of countries in pharmaceutical activities have shifted between them, and institutions related to both science and public policy have strongly interacted with one another. Hence, in examining the changing location of pharmaceutical activities, the interaction between the shift in the relevance or use of different forms of scientific systems, and with the wider growth of the international pharmaceutical industry, has been critical.

The paper therefore not only contributes to the international business literature, but also contributes to the broad literature in evolutionary economics and economic geography conceptually, in that countries don’t stand in isolation as a principal source – or a beneficiary of innovation and growth—they coevolve with both, their institutional environment (narrowly defined) and in relation to other countries. Indeed, our study demonstrates that the technological specialization of countries depends on the knowledge and demands of the environment for which they host their operations, and also integrate knowledge across networks relating to science. The paper also contributes empirically by analyzing complex interrelations between technological efforts and university science, accounting for dynamic processes over time. To be sure, technological specialization, university-industry relations, and the geographical space hosting productive activity have been previously analyzed separately in the literature. The theme of this project addresses the interconnectedness between these factors.

The paper is structured as follows. First, in Section 2, we reason about the historical coevolution of technological and scientific specialization of countries in the international pharmaceutical industry, as well as the increasing significance of international openness to research. In Section 3, we describe the empirical research methodology, the data employed and the specifications of the econometric model. We report the results in Section 4. In section 5, we summarize the project, propose future directions of research, and concluding remarks.

## HYPOTHESES

The literature suggests that a wide range of national institutions affect the structure of the pharmaceutical industry, its' rate of technical advance, and performance. For this reason, theoretical and empirical studies of the industry have paid attention to the structure of the health care system, the institutional arrangements surrounding health-related research, and the role of intellectual property protection in affecting the processes of innovation. Surprisingly, scant attention has been paid to the shift in the technological paradigm from chemistry to the life sciences within the industry, the effect of university-business linkages on this shift over time, as well as the effects on change in the industry of the quality and openness of scientific systems across different national systems of innovation. We therefore hone in on the characteristics of countries that necessarily entail a strong interaction between the technological efforts and the sciences upon which the industry relies on.

**Scientific Specialization**

This paper examines the effects of location specific interaction between university science and technological effort to explain the relative technological position of countries as sources of pharmaceutical inventions. In the context of the recent evolution of the international pharmaceutical industry, the technological specialization of countries in pharmaceutical activities have shifted between them, and remained highly uneven and distinct. We propose, as the primary sources of growth in the pharmaceutical industry have shifted towards the life sciences, and away from chemistry, locations that are more specialized in the life sciences will attract more pharmaceutical research.

Indeed, as Chandler remarks in much of his work on the evolution of business activities in response to shifts in the technological environment, the science essential to the continuing growth of high-technology industries can peter out (Chandler, Jr., 2009). If the structure of scientific endeavor ceases to match industry needs, it may no longer serve as a major source of opportunities for commercialization. This is most evident in the pharmaceutical industry, in which perceived limits to learning resulted in a break from the conventional association of the industry with chemistry and moved it towards biology and related disciplines, leading to a shift in the relative attraction of countries specialized in either one or other of these different streams of science.

For example, at one time, pharmaceutical companies had very little detailed knowledge about the causes, much less of the biological underpinnings of specific diseases. These companies relied on "random screening" as a method for finding new drugs, by which the specific biochemical and molecular roots of many diseases were not well understood. However, biology and related disciplines deepened the understanding of drugs and diseases, making possible the transition to "drug development by design," and redefining the strategic boundaries of long-established drug producers. We therefore predict that locational technological specialization coevolves with location specific expertise in the life sciences, and university commitment to these fields. We therefore form our hypotheses around three related disciplines in the life sciences. Thus:

*Hypothesis 1a: Increase in the level of scientific specialization in biochemistry, genetics, and molecular biology is likely to attract more pharmaceutical research and to increase technological specialization in the pharmaceutical field.*

*Hypothesis 1b: Increase in the level of scientific specialization in immunology and microbiology is likely to attract more pharmaceutical research and to increase technological specialization in the pharmaceutical field.*

*Hypothesis 1c: Increase in the level of scientific specialization in pharmacology, toxicology, and pharmaceutics is likely to attract more pharmaceutical research and to increase technological specialization in the pharmaceutical field.*

**University-Industry Linkages**

As is well known to innovation scholars, research activities result in publications and knowledge embodied in technological inventions and innovations. For this reason, access to research and knowledge produced by universities can be an essential input for innovative business firms. Universities also nurture person-embodied knowledge and skills; not only do many research students seek long-term careers in business firms, businesses also draw on the skills in universities to compensate internal resources and infrastructure for conducting R&D. Indeed, pharmaceutical technology transfers often result from industry access to formal meetings, e.g. university consulting arrangements provided for industry, attending academic conferences that disperse information or the informal interactions with university researchers who can readily share their research findings. We therefore aggregate this insight to the country level to examine the way in which institutional characteristics—defined narrowly to include university and industry linkages—have played out in the evolution of the location of innovation. Specifically, we are interested in the extent to which university has helped provide businesses with international linkages, and the interaction between business and university networks.

This line of reasoning can be traced back to the 19$^{th}$ century in continental Europe, where Germany and Switzerland were leaders of the synthetic dye industry, in part because of the strong university research and training in chemistry. It was thus initially Swiss and German core chemical companies which exploited competencies and knowledge they accumulated in organic chemicals and dyestuff to commercialize drugs and enter what became the pharmaceutical industry. At this time, the science of chemistry was providing new learning and generating new product opportunities. And so, other countries, including the US—before the impact of WWI, during which the US ceased importing German products—relied on German and Swiss firms to supply new drugs. It is the coincidence between World War II crash programs—which provided the financing necessary to expand research and facilities—and the relative strength of American and British positions in the science of biology that differentiated the pattern of development of pharmaceutical activities in the English-speaking world. These countries witnessed the birth of specialized pharmaceutical producers who leveraged on the technical experience and organizational capabilities accumulated through wartime efforts to develop penicillin–discovered along with its antibiotic properties by Alexander Fleming in 1928.

Nonetheless, the willingness to exploit the results of academic research commercially distinguishes the pattern of development in the American environment. Indeed, links between the academy and industry, particularly the ability to freely exchange personnel, appears to have been the strongest in the US at this time. We therefore contend that the countries with greater industry-university interactions will become more attractive locations as sources of pharmaceutical inventions. Thus:

*Hypothesis 2: Greater industry-university interactions are likely to attract more pharmaceutical research and to increase technological specialization in the pharmaceutical field.*

**International Openness**

In more recent years, the quality of science has become directly associated with international openness, since quality scientists are more likely to engage in research communities that are international. We predict that countries which are more specialized in the related life science disciplines are more likely to be associated with this effect. In other words, we predict the interaction between the scientific specialization in the related disciplines in the life sciences and the state of scientific development of countries is likely to attract pharmaceutical research. Thus:

*Hypothesis 3a: The interaction between the scientific specialization in biochemistry, genetics, and molecular biology and international openness to research in the life sciences is likely to attract pharmaceutical research and to increase technological specialization in the pharmaceutical field.*

*Hypothesis 3b: The interaction between the scientific specialization in immunology and microbiology and international openness to research in the life science is likely to attract pharmaceutical research and to increase technological specialization in the pharmaceutical field.*

*Hypothesis 3c: The interaction between the scientific specialization in pharmacology, toxicology, and pharmaceutics and international openness to research in the life sciences is likely to attract pharmaceutical research and to increase technological specialization in the pharmaceutical field.*

## EMPIRICAL RESEARCH METHODOLOGY

We develop a dynamic cross-section econometric analysis to examine the interrelationship between the relative importance of locations as sources of pharmaceutical inventions allied with the relative strength of scientific knowledge. We construct measures of technological specialization of pharmaceutical inventions connected to countries. We then examine the scientific fields each country specializes in, the quality and international openness of their scientific systems, and the university and industry involvements in those countries. These institutions change over time, relying on a previous history which we intend to recognize in our analysis.

### Technological Specialization Over Time

We analyze the evolving patterns of pharmaceutical technology development efforts at the national level using patents granted from 1976 to 2015 from USPTO data on patent grants. The use of patents as an indicator of technological specialization is the most commonly used method to estimate the patterns of innovative activity. Indeed, the application and limitation of the data to the context of technological specialization studies is well known in the literature. For the purpose of this study, the use of patent records provides information on the inventor, allowing us to identify the country of residence of the invention. We then restricted our analysis to countries with more than 1000 patents granted in the pharmaceutical field over the period to allow for a more meaningful statistical analysis of the distribution of pharmaceutical inventions around the world. In doing so, we were also able to control for the size of the countries.

To investigate the emergence and growth of pharmaceutical technologies in various countries, we developed and used the revealed technological advantage (RTA) index, a proxy for technological specialization (Cantwell, 1989). To be sure, the country analysis herein refers to the patenting activity of national actors and the institutional influences on pharmaceutical inventions, not countries as individual actors per se. The RTA index is therefore defined as a country's share of patents in the pharmaceutical technology field divided by the country's share in all patent fields as follows, where i=country, j=field, t=period:

$$\mathrm{RTA}_{ijt} = \left(\frac{P_{\mathrm{ijt}}}{\Sigma_i P_{\mathrm{ijt}}}\right) / \left(\frac{\Sigma_j P_{ijt}}{\Sigma_{ij} P_{ijt}}\right)$$

We calculated an RTA index of country-level technological specialization for the period 1976 to 2015 (broken down into 5 year periods) to provide an indication of the relative position of countries as sources of pharmaceutical inventions over time. An RTA index greater than one suggests a comparative technological advantage in pharmaceuticals, while an index less than one indicates a comparative technological disadvantage. The RTA index normalizes for differences in the propensity to patent across fields, or in this context for the relatively high level (high absolute numbers) of the propensity to patent in the pharmaceutical field.

However, because we are interested in the change of specialization over time, we report in Table 1 the shifts in the RTA index of locational specialization between periods and over time. First, we calculated the RTAs in the form of cumulated stocks of patents over five-year periods, and then the difference in that stock compared to the previous five-year period. In doing so, we constructed 8 period-specific observations between the years 1976 to 2015 (over 40 years). We then calculated the shifts between these periods, constructing 7 observations of changes from one period to the next. For clarification, the shift between Period 1 and 2 reported in Table 1 reflects the shift between 1976-1980 to 1981-1985, and so on. Hence:

$$\Delta \mathrm{RTA}_{ijt} = \mathrm{RTA}_{ijt-1} - \mathrm{RTA}_{ijt}$$

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Insert Table 1 about here

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Table 1 reports the shifts in the RTA index of country-level technological specialization in pharmaceuticals over time. In North America, the United States and Canada have been gaining technological specialization in modest increments between periods, over time. In Europe, the UK seems to have, on average, maintained its technological position in pharmaceuticals. Germany has been losing technological specialization relative to its historical high from the earlier era, during which the industry had relied predominantly on chemistry, the German strength. Switzerland, France, Netherlands, and Belgium experienced a decrease in their specialization in earlier periods, before increasing in specialization in stable increments in later years. Austria, Sweden, Denmark, Italy, and Spain show patterns of increase and decrease in specialization, none of which are consistent over time. In Asia, Japan has been losing specialization in this field. South Korea shows patterns of increase and decrease in specialization between periods, over time. Though China and India have either been absent or low in their level of technological activity in this field, their technological specialization fluctuates markedly, reflecting lower absolute numbers.  The decline in Japan’s RTA in the pharmaceutical field may reflect its comparative weakness in the life sciences.

To be sure, the postwar pharmaceutical industry was dominated by companies from the US, Switzerland, Germany, and the UK. So, in maintaining their competencies in chemistry, Swiss and German companies also had to absorb molecular biology and related techniques.

However, the Swiss and German position eroded, perhaps because they were unable to break the convention with chemistry—American companies had often relied on German firms to supply new drugs up until WWII. The impact of WWI, during which the US ceased importing German products coupled with the overall superiority of the American scientific systems when taken as a whole helped to establish the US industry on a firmer footing. The strength of the local science base in the UK might also explain why British companies became the first movers in commercializing new pharmaceutical technology in Europe. By contrast, French and German producers were preoccupied with wartime demands and their aftermath (Henderson, Orsenigo, & Pisano, 1999).

**Scientific Specialization and International Openness**

We use bibliometric methods to generate qualified information related to the evolving patterns of scientific development efforts at the national level from 1976 to 2015. Most bibliometric analyses use Thomson Reuters' Web of Science (WoS) and Elsevier's Scopus as data sources to evaluate scientific research activities. Each of these sources have limitations well known in the literature. We therefore restricted our search to retrieve articles indexed in Scopus, which has a larger journal coverage difference than WoS (Mongeon & Paul-Hus, 2016), to generate the explanatory effect on locational technological specialization, and to allow for a meaningful statistical analysis of the distributions of complete and advanced research around the world.

For each country, data was collected from Scopus, the largest abstract and citation multidisciplinary database of peer-reviewed literature, on their publications in the scientific literature over the period, 1976 and 2015. To investigate the emergence and growth of specialization in the relevant sciences in various countries, we developed and used the revealed scientific advantage (RSA) index, a proxy for scientific specialization on an equivalent basis for the RTAs. The RSA index is therefore defined as a country's share of publications in the relevant scientific field divided by the country's share in all publications in the science and engineering fields as follows, where i=country, f=field, t=period:

$$\mathrm{RSA_{ijt}} = \left(\frac{\mathrm{S_{ift}}}{\Sigma_{\mathrm{i}}\mathrm{S_{ift}}}\right)/\left(\frac{\Sigma_{\mathrm{j}}\mathrm{S_{ift}}}{\Sigma_{\mathrm{ij}}\mathrm{S_{ift}}}\right)$$

We identified three related scientific disciplines in the life sciences plus chemistry from the physical sciences. We then developed four revealed scientific advantage (RSA) indices for biochemistry, genetics, and molecular biology (RSA_13), chemistry (RSA_16), immunology and microbiology (RSA_24), and pharmacology, toxicology, and pharmaceutics (RSA_30). The data was organized by country and sorted into eight adjacent time periods (broken into 5-year intervals) between 1976 and 2015. We then used number of publications, classified by the country and scientific field, to capture disciplinary specialization and give an account of the scientific specialization of publicly-funded research in each country relative to the world as a whole.

To capture the quality and openness of scientific developments over time, we take into account the change in the percentage share of internationally co-authored articles.

**University-Industry Linkages**

Though patents are more likely to reflect technological activities than scientific activities, the extent to which national systems differ in their commitment to university science is reflected in the number of university patents in the pharmaceutical field invented in that country. We therefore calculated the share of university patents in the pharmaceutical technology field, a proxy for university-industry knowledge spillovers. However, because we are interested in the change in these linkages over time, we then calculated the shifts between periods, over time.

University-industry interactions also involve knowledge flows that are difficult to measure due to their tacit nature. These interactions would include industry access to conferences that disperse information, informal contacts with university researchers who can readily share their research findings, university consulting arrangements provided for industry, and publications and the movement of highly skilled students and faculty from universities to industry and vice versa. From an evolutionary perspective, investment in physical and human capital are only part of the story. Here, public researchers and the institutions in which they belong, which focus on long term efforts that may open possibilities for future technological directions, are the social technologies (Nelson & Sampat, 2001)—i.e. which allows for the intellectual bridge between the sources [technological advance] of economic progress and institutions—is key to the success of the industry.

Moreover, and though the success of these linkages depends on the effectiveness of the IP system, the scope and efficacy of patent protection has varied over time and across countries. We therefore utilize Ginarte and Park index to control for the function of national IPR systems.

Table 2 below summarizes the explanatory variables used in the study.

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Insert Table 2 about here

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**Econometric Model**

This study develops a dynamic cross-section econometric analysis to examine the changing nature of the interrelationship between the technological and scientific specialization of countries, and the historical shifts between periods and over time. In this way, having controlled for the established level of specialization, we want to test whether (period by period and over time) the countries that, for example, increased their technological specialization the most were also those that increased in specializing in the relevant sciences the most, relative to other countries. Thus, a significantly positive slope coefficient implies an association with a change rather than in the level of the dependent variable.

The models considered consist of the following set of equations:

$$\Delta \mathrm{RTA}_{ijt} = \mathrm{a}_0 + \beta_1 \mathrm{RSA\_13}_{\mathrm{ijt}} + \beta_2 \mathrm{RSA\_16}_{\mathrm{ijt}} + \beta_3 \mathrm{RSA\_24}_{\mathrm{ijt}} + \beta_4 \mathrm{RSA\_30}_{\mathrm{ijt}} + \beta_5 \Delta \mathrm{IntOpen}_{\mathrm{ijt}} + \beta_6 \Delta \mathrm{UniPat}_{\mathrm{ijt}} + \beta_7 \mathrm{IPR}_{\mathrm{ijt}}$$

$$\Delta \mathrm{RTA}_{ijt} = \mathrm{a}_0 + \beta_1 \mathrm{RSA\_13}_{\mathrm{ijt}} + \beta_2 \mathrm{RSA\_16}_{\mathrm{ijt}} + \beta_3 \mathrm{RSA\_24}_{\mathrm{ijt}} + \beta_4 \mathrm{RSA\_30}_{\mathrm{ijt}} + \beta_5 \Delta \mathrm{IntOpen}_{\mathrm{ijt}} + \beta_6 \left( RSA\_13_{\mathrm{ijt}} * \Delta \mathrm{IntOpen}_{\mathrm{ijt}} \right) + \beta_7 \left( \mathrm{RSA\_16}_{\mathrm{ijt}} * \Delta \mathrm{IntOpen}_{\mathrm{ijt}} \right) + \beta_8 \left( \mathrm{RSA\_24}_{\mathrm{ijt}} * \Delta \mathrm{IntOpen}_{\mathrm{ijt}} \right) + \beta_9 \left( \mathrm{RSA\_30}_{\mathrm{ijt}} * \Delta \mathrm{IntOpen}_{\mathrm{ijt}} \right) + \beta_{10} \Delta \mathrm{UniPat}_{\mathrm{ijt}} + \beta_{11} \mathrm{IPR}_{\mathrm{ijt}}$$

## EMPIRICAL FINDINGS

The descriptive statistics and correlations of the variables included in the analysis are presented in Table 3.

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Insert Table 3 about here

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We now turn to the testing of the hypotheses. The first hypotheses predicted that, as the primary sources of growth in the pharmaceutical industry have shifted towards the life sciences, and away from chemistry, locations that are more specialized in the life sciences is likely to attract pharmaceutical research and to increase technological specialization in the pharmaceutical field. The second hypothesis predicted that greater industry-university interactions is likely to attract pharmaceutical research and to increase technological specialization in the pharmaceutical field.

The third hypotheses predicted the interaction between the scientific specialization in the relevant sciences and international openness to research in the life sciences is likely to attract pharmaceutical research and to increase technological specialization in the pharmaceutical field. The results of tests of these hypotheses are shown in Table 4. In model 1, the main effects of the scientific specialization in biochemistry, genetics, and molecular biology (RSA_13), chemistry (RSA_16), immunology and microbiology (RSA_24), and pharmacology, toxicology, and pharmaceutics (RSA_30), the change in university-industry linkages (UniPat), the openness and quality of research (IntOpen), along with a control for intellectual property were entered. In model 2, the multiplicative interactions of scientific specializations and international openness were entered.

Our predictions are broadly consistent with much of the prior research that found the ability to exploit university science, and make use of boundary-spanning relations, was correlated with technological productivity. Results from the first model suggest a shift in focus on chemicals to life science; i.e. that the levels of scientific specialization in the life sciences is likely to attract pharmaceutical research and to increase technological specialization in the pharmaceutical field. In particular, the level in the RSA index in biochemistry, genetics, and molecular biology (RSA_13) appears to negatively impact the change in the RTAs between periods. The level in the RSA index in pharmacology, toxicology, and pharmaceutics (RSA_30) also appears to negatively impact the change in the RTAs. The level in the RSA index in chemistry (RSA_16) seems to have no significant impact on the change in the RTAs over time. The level in the RSA index in immunology and microbiology (RSA_24) seems to positively impact the change in the RTAs. In other words, the increase in the specialization in biochemistry, genetics, and molecular biology, as well as pharmacology, toxicology, and pharmaceutics, seem to decrease the absolute change in the RTAs over time, whereas the increase in the specialization in immunology and microbiology increases the absolute change in the RTAs. These results support our first hypotheses, and discriminate between the effects of the relevant sciences on the change in technological specialization.

The change in the share of university patents in the pharmaceutical technology field seems to negatively impact the change in the RTAs. In other words, the increase in the change in university-industry linkages seems to decrease the absolute change in the RTAs over time. So, while we find significance in university-industry relationship using this measure, we find a limitation in our data. We measure university involvement technologically, short of business outreach in science, and the benefit from university networks.

The second model shows that the interaction between the scientific specialization in biochemistry, genetics, and molecular biology (RSA_13) and international openness to research in the life sciences is likely to attract pharmaceutical research and to increase technological specialization in the pharmaceutical field, supporting hypothesis 3a. However, we did not find support for this interaction with specialization in immunology and microbiology (RSA_24) or pharmacology, toxicology, and pharmaceutics (RSA_30) as predicted.

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Insert Table 4 about here

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## CONCLUSIONS AND DIRECTIONS FOR FURTHER RESEARCH

This paper empirically supports the proposition that as the primary sources of growth in the pharmaceutical industry shifts towards sciences in which a given country happens to be specialized in, that country benefits from the shift, and gains technological specialization in the international innovation network, and mixed support for international openness on research in the relevant sciences. We also found support for the effect of university-industry linkages on the change of technological specialization in the pharmaceutical field. However, we capture university involvement in technology and need to pay attention in future research in business involvement in science. In addition to gathering more data to test university and business involvement in the context of this research, this study has triggered our interest in answering a subsidiary question. It seems reasonable to assume that related classes in a technological field tend to move together in a given country, so that a rise in one would be associated with a rise in the other where resources are complementary. The reverse could also be the case, that a rise in one class would be associated with the fall in the other where resources might have shifted. We could therefore further the research program to examine the diffusion of new techniques and pharmaceutical innovations at a more detailed level of analysis.

To know more about the changes in the composition of technological position of each country, in future research we plan to examine the effects of location specific interaction between university science and technological efforts of the largest international pharmaceutical firms. In the context of the recent evolution of the international pharmaceutical industry, the technological specialization of firms in pharmaceutical activities have also shifted across countries, and individual firms remain highly uneven and differentiated. The emergence of a firm's technological specialization may be influenced by its capacity to effectively integrate knowledge across a network of scientifically proficient organizations, which encapsulate universities and public research institutions. Specifically, we will investigate whether a firm's technological specialization in the pharmaceutical field requires the coming together of other complementary elements: the firm's degree of internationalizing pharmaceutical activity, the interaction between the firm's research agenda and universities, and locational specialization in the life sciences for background knowledge and training. Where the combination of these conditions does not occur to the same extent, the firm's technological specialization in pharmaceuticals may develop with a lag and less effectively. In further research, we will proceed to apply techniques from network analysis to innovation networks to examine the geographical dispersion of pharmaceutical activities in large firms, as well as the locus of sites from which innovation emanates.

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# TABLES

Table 1. RTA Index of Locational Specialization Over Time

| *Country Code* | **Country** | **Period 1 to 2** | **Period 2 to 3** | **Period 3 to 4** | **Period 4 to 5** | **Period 5 to 6** | **Period 6 to 7** | **Period 7 to 8** |
|---|---|---|---|---|---|---|---|---|
| *AT* | **Austria** | -0.075 | 0.399 | -0.016 | 0.241 | -0.405 | 0.420 | 0.125 |
| *AU* | **Australia** | -0.187 | -0.051 | 0.730 | 0.285 | -0.271 | -0.223 | 0.464 |
| *BE* | **Belgium** | -0.081 | -0.174 | -0.075 | 0.008 | 0.041 | 0.697 | -0.175 |
| *CA* | **Canada** | 0.009 | -0.044 | 0.219 | 0.377 | 0.029 | 0.048 | -0.229 |
| *CH* | **Switzerland** | -0.194 | -0.238 | 0.011 | -0.219 | 0.072 | 0.516 | 0.011 |
| *CN* | **China** | 0.000 | 1.122 | 0.040 | 0.386 | -0.342 | -0.491 | -0.120 |
| *DE* | **Germany** | -0.268 | -0.037 | -0.044 | -0.111 | -0.029 | 0.175 | -0.015 |
| *DK* | **Denmark** | 0.795 | 0.561 | 1.384 | -0.203 | -0.403 | 0.196 | -0.295 |
| *ES* | **Spain** | -0.714 | 0.678 | -0.094 | -0.368 | 0.100 | 1.015 | -0.271 |
| *FR* | **France** | -0.382 | -0.132 | 0.166 | 0.223 | -0.002 | 0.003 | -0.046 |
| *IL* | **Israel** | -0.391 | 0.414 | -0.181 | -0.235 | -0.348 | 0.044 | -0.063 |
| *IN* | **India** | -2.304 | 1.085 | 0.550 | -1.415 | 0.034 | -1.539 | -0.964 |
| *IT* | **Italy** | 0.640 | -0.586 | -0.071 | -0.452 | -0.217 | 0.494 | 0.143 |
| *JP* | **Japan** | 0.044 | -0.206 | -0.061 | -0.199 | -0.085 | 0.040 | 0.025 |
| *KR* | **South Korea** | 0.472 | -0.907 | 0.008 | -0.082 | 0.055 | -0.016 | 0.054 |
| *NL* | **Netherlands** | -0.065 | -0.142 | 0.321 | 0.260 | 0.006 | 0.147 | 0.221 |
| *SE* | **Sweden** | 0.241 | 0.083 | 0.211 | 0.128 | -0.009 | 0.466 | -0.545 |
| *UK* | **United Kingdom** | 0.983 | -0.214 | 0.199 | -0.104 | -0.120 | 0.136 | -0.364 |
| *US* | **United States** | 0.042 | 0.134 | 0.043 | -0.137 | 0.337 | -0.033 | 0.004 |

**Table 1. RTA Index of Locational Specialization Over Time**

*Table 2. Explanatory variables used in the econometric analysis*

| **Variable** | **Description** |
|---|---|
| **RSA_13** | RSA in biochemistry, genetics, and molecular biology |
| **RSA_16** | RSA in chemistry |
| **RSA_24** | RSA in immunology and microbiology |
| **RSA_30** | RSA in pharmacology, toxicology, and pharmaceutics |
| **IntOpen** | Change in the share of coauthored articles |
| **UniPat** | Change in the share of university patents in the pharmaceutical field |
| **IPR** | Genarte and Park IPR Index |

**Table 2. Explanatory variables used in the econometric analysis**

*Table 3. Descriptive Statistics*

| **Variables** | Mean | St. Dev. | Min | Max | **RTA** | **RSA_13** | **RSA_16** | **RSA_24** | **RSA_30** | **IntOpen** | **UniPat** | **IPR** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **RTA** | -0.011 | 0.446 | -2.304 | 1.384 | 1.000 | -0.161 | -0.172 | 0.298 | -0.197 | 0.045 | -0.245 | 0.175 |
| **RSA_13** | 1.232 | 0.435 | 0.342 | 3.44 | -0.161 | 1.000 | 0.165 | 0.015 | -0.198 | -0.116 | 0.020 | -0.054 |
| **RSA_16** | 1.328 | 0.557 | 0.586 | 2.989 | -0.172 | 0.165 | 1.000 | -0.399 | 0.291 | 0.018 | 0.105 | -0.560 |
| **RSA_24** | 1.473 | 0.985 | 0.187 | 6.502 | 0.298 | 0.015 | -0.399 | 1.000 | 0.043 | 0.000 | 0.018 | 0.158 |
| **RSA_30** | 1.233 | 0.852 | 0.138 | 5.31 | -0.197 | -0.198 | 0.291 | 0.043 | 1.000 | 0.003 | -0.015 | -0.266 |
| **IntOpen** | 0.057 | 6.524 | -19.554 | 19.723 | 0.045 | -0.116 | 0.018 | 0.000 | 0.003 | 1.000 | 0.036 | -0.010 |
| **UniPat** | 0.787 | 3.217 | -8.404 | 16.817 | -0.245 | 0.020 | 0.105 | 0.018 | -0.015 | 0.036 | 1.000 | -0.136 |
| **IPR** | 4.158 | 0.657 | 1.23 | 4.88 | 0.175 | -0.054 | -0.560 | 0.158 | -0.266 | -0.010 | -0.136 | 1.000 |

**Table 3. Descriptive Statistics**

| | *Dependent variable:* | |
|---|---|---|
| | `Change in the RTA Index` | |
| | (1) | (2) |
| RSA_13 | -0.248*** | -0.289*** |
| | (0.086) | (0.088) |
| RSA_16 | 0.146* | 0.135 |
| | (0.087) | (0.087) |
| RSA_24 | 0.170*** | 0.172*** |
| | (0.040) | (0.040) |
| RSA_30 | -0.154*** | -0.168*** |
| | (0.046) | (0.046) |
| IntOpen | 0.002 | -0.017 |
| | (0.005) | (0.058) |
| `RSA_13* IntOpen` | | 0.070** |
| | | (0.035) |
| `RSA_16* IntOpen` | | -0.033 |
| | | (0.028) |
| `RSA_24* IntOpen` | | -0.009 |
| | | (0.016) |
| `RSA_30* IntOpen` | | -0.012 |
| | | (0.025) |
| UniPat | -0.036*** | -0.035*** |
| | (0.011) | (0.011) |
| IPR | 0.062 | 0.063 |
| | (0.065) | (0.065) |
| Constant | -0.191 | -0.087 |
| | (0.369) | (0.371) |
| Observations | 129 | 129 |
| $R^2$ | 0.258 | 0.290 |
| Adjusted $R^2$ | 0.216 | 0.223 |
| Residual Std. Error | 0.395 (df = 121) | 0.393 (df = 117) |
| F Statistic | 6.024*** (df = 7; 121) | 4.339*** (df = 11; 117) |
| *Note:* | | *p<0.1; **p<0.05; ***p<0.01 |

**Table 4. Regression output for changes in the RTA index**