Calibrating an Agent-Based Model: The case of the Vienna Biotech Innovation System

Manuela Korber

Contact

manuela.korber@ait.ac.at

AIT Austrian Institute of Technology GmbH
Foresight & Policy Development Department - Research, Technology & Innovation Policy
Donau-City-Straße 1 | 1220 Vienna | Austria

Vienna University of Economics and Business
Department of Socioeconomics - Institute for Economic Geography and GIScience
Nordbergstr. 15/3/D - UZA 4 | 1090 Vienna | Austria

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Abstract. This paper aims at calibrating an agent-based model of the Vienna biotech system, created to analyze the dynamic effects of public RTI funding (Research, Technology and Innovation) on its innovative performance. The model comprises heterogeneous agents representing universities, companies and research organizations that are linked through various forms of R&D (Research and Development) collaboration. The agents have different knowledge endowments which are the basis for knowledge creation in the system. In the biotech innovation system, knowledge exchange occurs among the agents and with extra-regional sources, and is triggered by direct, indirect and institutional government funds. The innovation output is measured in terms of patents and publications at the agent-level, while agents also contribute to the number of high-tech jobs in the region, a system-level performance indicator. The model is intended as a tool for policy makers to elaborate different public RTI funding mixes and allows testing concrete funding alternatives. The fine-grained empirical calibration is intended to improve the credibility of the model in this application context. Thus, this model expands existing agent-based models of innovation in the biotech sector that focus primarily on qualitative aspects of agent behaviour.

1 Introduction

The biotech innovation system in the Vienna region shares the characteristics of a complex social system, i.e. numerous organizations are linked by nontrivial and nonlinear interactions. Feedback loops between the different organizations influence the system behaviour in an unpredictable way. Due to self-organization and the organizations' adaption processes to a changing environment, emergence occurs in the system. Policy makers that wish to steer dynamics in complex systems face difficulties in predicting processes of system change after interventions, which cannot be captured by conventional methods, but in agent-based models.

Agent-based modelling (ABM) techniques are used to analyze systems with a large number of interacting agents and emergent system properties that cannot be deduced by aggregating the agents' properties (Axelrod and Tesfatsion 2006, pp. 74-75). Concerning the use of agent-based models in the context of innovation and innovation policy, however, their predictive power matters. Here we face a trade-off between closeness-to-reality and analytic clarity. Credibility of the model is crucial and is guaranteed only if policy makers recognize the economic structure in detailed models and find them more reliable than a general overview obtained by abstract mathematical models characterized by consistency requirements of rationality and equilibrium (Fagiolo and Dawid 2008, pp. 351-352). Thus, the empirical calibration and validation of agent-based models become an issue.

In a previous paper (Korber et al. 2009) an agent-based model of the biotech[1] innovation system[2] was conceptualized. This paper presents the first implementation of the conceptual model involving data on the Vienna biotech (biotechnological) sector for calibrating parameter values at setup. The agent-based model serves as a tool for policy makers to evaluate ex ante different combinations of public RTI (Research, Technology and Innovation) funding and specific funding alternatives. After its calibration and validation, this agent-based model allows capturing the effects of these interventions on the innovative performance of the biotech system and its agents.

Inspired by the SKIN model ("Simulating Knowledge Dynamics in Innovation Networks", (Ahrweiler et al. 2004; Pyka and Saviotti 2002; Gilbert et al. 2001), the agent-based model presented here includes additional agent types comprising public and private research organizations, universities and universities of applied sciences. Further agent heterogeneity is assured by introducing new agent attributes, such as R&D (Research and Development) infrastructure or application orientation. For the first time, the kene concept (Gilbert 1997) is extended by the use of capabilities and core competencies with empirically calibrated meaning, thus allowing for the calculation of thematic proximity with measures based on co-occurrences in the agent population (e.g. the Jaccard index).

Notwithstanding its increasing popularity for interdisciplinary research, ABM leaves plenty of room for methodological improvement. The literature highlights the need for advancing the transparency, replicability and comparability of findings produced by agent-based models in order to achieve an accepted methodological standard for social sciences (e.g. Hamill 2010; Squazzoni 2010; Brenner and Werker 2007; Richiardi et al. 2006; Tesfatsion 2006; Boero and Squazzoni 2005).

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1 Biotechnology involves the "*the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or nonliving materials for the production of knowledge, goods and services*" (OECD 2009).

2 Biotech in Vienna is regarded as a sectoral innovation system (Malerba 2002) that consists of organizations involved in the creation, development and utilization of the sector's technologies and products. Processes of interaction and cooperation in technology development, competition and selection in innovative and market activities form the relations within the system (Breschi and Malerba 1997, p. 131).

The creation of an agent-based model for policy makers requires sound empirical calibration and validation in order to improve the credibility and usability of simulation findings. Therefore, a more descriptive view according to the KIDS[3] principle is taken which involves empirical embeddedness throughout the modelling process. The empirical foothold for agent-based models, i.e. their empirical calibration and validation, is essential to develop the standing and usability of ABM for scientific research in social sciences and economics (Brenner and Werker 2007, p. 238). This paper concentrates on these issues while referring to the case of the Vienna biotech sector.

Empirical validation of simulation results is the process of testing data produced by the simulation through the comparison of these outputs to empirical data. Due to the fact that ABM is an iterative process which comprises design, programming and simulation, refining empirical calibration may be necessary in the case empirical validation fails (e.g. Fagiolo et al. 2007a, pp. 190-191; Boero and Squazzoni 2005).

The paper is organized as follows: The model of the Vienna biotech innovation system and the main stylized facts affecting its simulation input and output are introduced in Section 2. Section 3 gives an overview of the main strategies for the empirical calibration of agent-based models. Then the methodology of the empirical calibration of our model at the micro-level is provided in Section 4. Section 5 focuses on the macro-foundation of agent behaviour, interactions and regularities. The paper closes with a short discussion of the preliminary findings and an outlook on further research.

2 Model specification

This section briefly summarizes the conceptual model (Korber et al. 2009). So far viewed as a black box, the Vienna biotech innovation system[4] in this simulation exercise is represented by organizations modelled as interdependent agents, comprising public and private research organizations, universities, small and medium-sized enterprises, start-up and spin-off companies, as well as multinational companies. Agents perform own R&D and are linked through collaborative R&D projects resulting in co-patents and co-publications.

The final goal of this simulation project is to analyze the influence of government funds. Knowledge exchange and cooperation are triggered by government through direct funding comprising projects initiated bottom-up by the organization or top-down by government, as well as by indirect measures such as tax allowances and the deduction of R&D expenses from tax. The model accounts for regional as well as extra-regional cooperation of agents that perform R&D in national and international collaboration projects. Universities and public research organization agents benefit from institutional funding. Another more institutionalized form of promoting science-industry cooperation is the creation of competence centres. The system is analyzed with a focus on the funding portfolio which is extracted and considered as an *input* into the black box (Figure 1). Further possible resources for an agent to finance its research activities are venture capital, market revenues or bank loans.

[3] KIDS – ***K**eep **I**t **D**escriptive, **S**tupid* (Hassan et al. 2008; Edmonds and Moss 2005)
[4] Life Science Austria Vienna Region (LISA VR) cluster (Life Science Austria Vienna Region 2007)

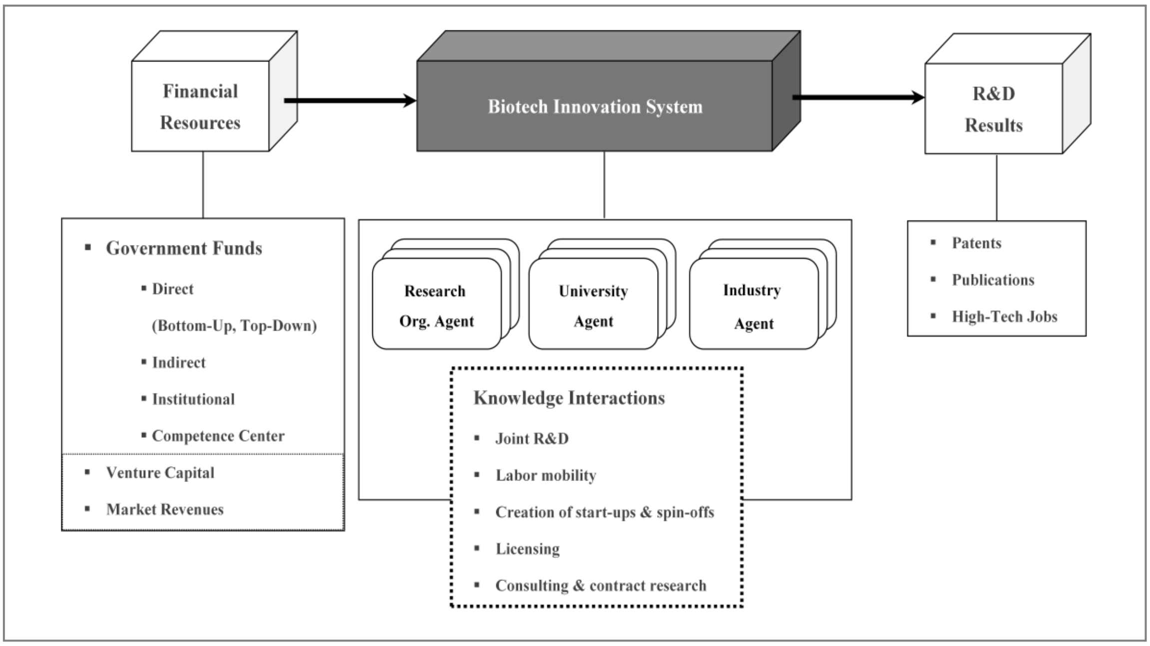

Figure 1: Conceptualizing the agent-based model

Innovation performance is measured in terms of patents and publications at the agent-level and the creation of high-tech jobs reflects the development at the system-level. As indicated in Figure 1, these are viewed as the *output* from the model. Consequently, political interventions in the form of public RTI funding become quantifiable, thus being captured during the simulation. The effects of different types and combinations of RTI funds can be analyzed in the model. The input and output boxes are extracted from the biotech innovation system and serve as empirical anchor points for validating the model ex post.

This paper concentrates on the *biotech innovation system*, depicted as a black box in Figure 1, and the agent-level interactions therein (see Figure 2 below). Three types of core agents, namely university agents, research organization agents and industry agents cooperate during contract research, consulting, licensing contracts or benefit from labour mobility of researchers. These non-linear interactions between the various agent types create either information or money flows, or even both. In addition, adjunct faculty creates information flows from research organization agents and industry agents to university agents because students benefit from tacit knowledge[5] and experience passed on by researchers giving lectures (Schartinger et al. 2002, p. 305). The formation of spin-offs is a further empirical phenomenon that is reflected in the agent-based model, as university members often become entrepreneurs, thus, creating an industry agent.

[5] In contrast to codified knowledge, tacit knowledge is the "knowledge of techniques, methods, and designs … that work in certain ways and with certain consequences" (Rosenberg 1982, p. 143) and often one is not fully aware of this knowledge and finds it difficult or even impossible to share it (Nelson and Winter 1982, p. 73).

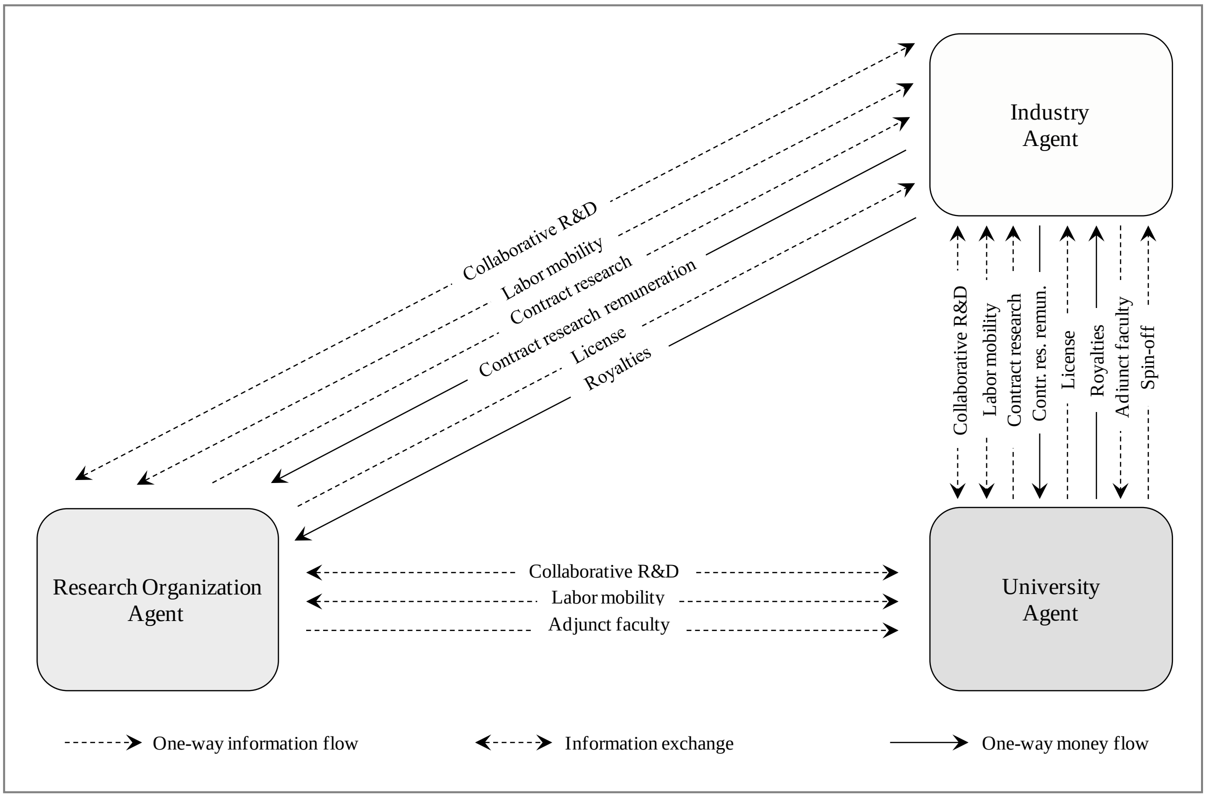

Figure 2: Agent types and their relations

Bearing the above in mind, we now move from the relation- to the agent-level. According to the literature on innovating organizations the following parameters influence invention behavior. These are necessary in order to allow emergence in the model of the biotech innovation system. Every agent is characterized by particular knowledge endowments and other attributes that influence its behavior in the system. The specific knowledge endowment is represented by a set of kenes (see Table 1). This kene is a triple of variables that consists of *capabilities* (Cs), *core competencies* (As) and of the respective *expertise level* (E). During the simulation the kene set of an agent is subject to transformations and expansions provoked by R&D activities or cutbacks through inactivity. While the capabilities (Cs) of an agent refer to a scientific or technological field or a particular business domain, core competencies (As) relate to particular competencies within the specific C. The expertise level of each triple reflects the experience and know-how gathered in the certain C and A.

Table 1: The knowledge endowment of an agent

Kene element	**Scale type**	**Possible values**	**Parameter initialization**	**Variability during simulation**
Capability	Categorical	1, …, 36	Individual calibration according to	Variable
Core competency	Categorical	1, …, 7	Austrian Life Sciences Directory (2011)	Variable
Expertise level	Ordinal	1, …, 10	Random allocation	Variable

Agent behavior is not only driven by its knowledge endowment but also by other attributes as provided in Table 2. Whether an agent's *application orientation* is basic or applied determines the agent's behavior during own and collaborative R&D. The *R&D strategy* of an agent decides, if an agent performs only own research or if it heads for cooperation. An agent's search for project partners is influenced by its conservative or progressive *partner search strategy*. An agent's *collaboration strategy* is either imitative, i.e. an agent performs only collaborative R&D or collective involving own and cooperative R&D. During collaborative research an agent's *absorptive capacity* influences the ability of integrating external knowledge from project partners. *Financial stock* and *R&D infrastructure* are further determinants of an agent's possibilities during the R&D loop (see Figure 3). An agent's *research attitude* affects the choice of new capabilities during learning and R&D processes.

Table 2: Further parameters of an agent

Attribute name	**Scale type**	**Possible values**	**Parameter initialization**	**Variability during simulation**
Organization type	Categorical	Industry agent, University agent, Research org. Agent	Individual calibration according to Austrian Life Sciences Directory (2011)	Fixed
Application orientation	Trichotomous	Basic research, Applied research, No research	According to agent type; Research organization agent acc. to actual research or finance structure	Fixed
Partner search strategy	Dichotomous	Conservative, Progressive	Derived from own empirical investigations	Fixed
Collaboration strategy	Dichotomous	Imitative, Collective	Derived from own empirical investigations	Fixed
R&D strategy	Dichotomous	Go-it-alone, Cooperative	Derived from own empirical investigations	Fixed
Research attitude	Dichotomous	Incremental, Radical	Derived from own empirical investigations	Fixed
Absorptive capacity	Ordinal	1, …, 10	Derived from own empirical investigations	Variable
Financial stock	Ratio		According to agent type and agent size	Variable
R&D infrastructure	Ordinal	1, …, 10	According to agent type and agent size	Variable

Figure 3 below shows the main procedures an agent has to go through during an R&D loop. At decision points, decisions of an agent are influenced by its particular strategy that is defined through its kenes and attributes (Table 1 and Table 2). Agents try to create R&D concepts after each time-step they performed R&D, these R&D concepts are then evaluated through a fitness function. Depending on the result of this evaluation phase a certain status is attributed to each R&D concept.

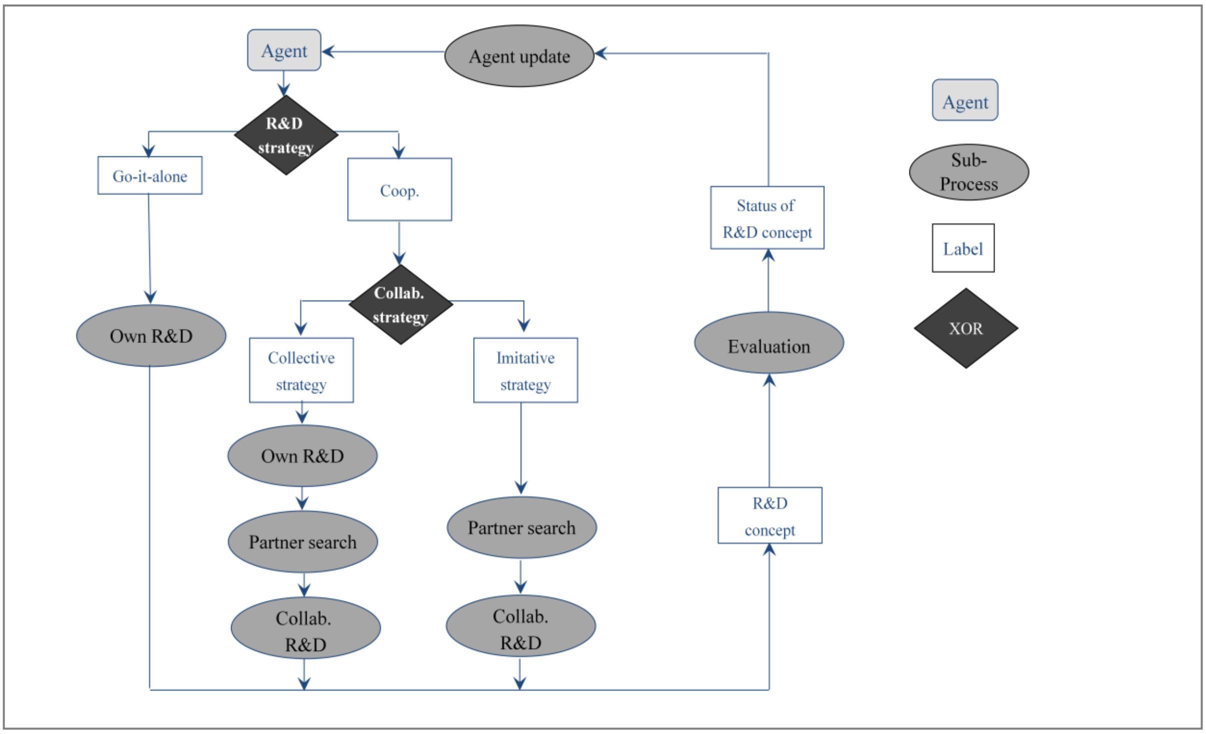

Figure 3: Main procedures for an agent during one time-step

For model dynamics the meaning of time plays an important role. This will be a core aspect of the macro-foundation discussed in Section 5. Existing models foresee new combinations of kenes four times each year an R&D project is running (Pyka and Scholz 2008, p. 21).

3 Strategies for empirical calibration

According to the heterogeneity of existent approaches to ABM, there is no single state-of-the-art how to do empirical calibration and validation (Fagiolo et al. 2007a, p. 191). We find three principal and most common approaches to empirical calibration in the recent ABM literature: the *indirect calibration*, the *Werker-Brenner* approach and the *history-friendly* view.

Indirect calibration starts with the validation of model outputs, the parameters consistent with the validation are then used to indirectly calibrate the model. First, stylized facts are identified and the model is designed according to empirics about micro-economic behaviour and interactions. Then, the empirical evidence on stylized facts is used to restrict the parameter space and the initial conditions in case the model becomes non-ergodic.[6] The major drawback concerning this approach stems from potential problems in matching theoretical underpinning and empirical observations.[7] The main problem roots in the fact that the parameters are potentially characterized by path dependence (Fagiolo et al. 2007b, pp. 208-210).

The *Werker-Brenner* approach starts with the empirical calibration of the initial conditions and the parameter ranges. If there is a lack of empirical detail regarding certain parameters, these take wide ranges and the model remains rather general. The output of each model

[6] After long-term evolution, an ergodic system is not able to recall its initial state (Morone and Taylor 2010, p. 124). It is important for the modeler to be aware, whether a system is ergodic or not, a discussion on this issue is provided by Fagiolo et al. (2007b, p. 210).

[7] For examples of agent-based models with indirect calibration and validation, refer to Fagiolo and Dosi (2003), Fagiolo et al. (2004) or Dosi et al. (2005).

specification is empirically validated by relying on Bayesian inference procedures[8], consequently further reducing the set of dimensions within the initial dimension space through the generalization of particular events. Whereas the first two steps are similar to indirect calibration, the third step differs substantially and involves further calibration of the remaining dimensions by including expertise, if necessary (Werker and Brenner 2004, p. 13)[9].

Indirect calibration and the Werker-Brenner approach do not aim at constraining parameter ranges, but they rather detect sub-spaces in the possible parameter space by including empirical observations. Regarding these sub-spaces the agent-based model should produce similar statistical regularities or stylized facts as captured empirically beforehand (Windrum et al. 2007).

The *history-friendly* approach coined by Malerba et al. (2001, 1999) is especially useful for analyzing the processes of industry evolution. An early model in the line of history-friendly modelling was the approach taken by Grabowksi and Vernon (1987) for their evolutionary model of the pharmaceutical industry. In these types of models, empirics about the history of a particular industry are integrated in the model, while limiting the number of parameters, interactions and decision rules (Fagiolo et al. 2007b, p. 206). A history-friendly model is definitely not a strict reproduction of an industry's history (Gilbert 2008, p. 43), but it rather allows the replication of main events characterizing the industry's history by choosing a parameter setting coherent to basic theoretical assumptions. Thus, qualitative theories about mechanisms and factors influencing industry evolution, technological progress and institutional change (e.g. the organization of an industry, its businesses and their respective strategies) are detected in a stylized manner (Malerba and Orsenigo 2002; Malerba et al. 2001, 1999). This approach is criticized for its focus on one specific case that leads to a lack of generalisability. As suggested by Brenner and Werker (2007, pp. 233-234) this drawback can be eliminated by carrying out sensitivity analyses of the results[10] which allow evaluating the results regarding their stability and their dependence on random effects. The specifications of agent behaviour, its decision rules and interactions, as well as the initial conditions and parameter values of key variables in history-friendly models are built relying on a comprehensive data set including empirical studies as well as anecdotal evidence on the industry evolution provided by experts. The same data collection is used for the validation of the simulation outputs of the model (Morone and Taylor 2010, p. 116).

Other taxonomies have been presented in the literature in connection with the empirical embeddedness of agent-based models (e.g. Brenner and Werker 2007). According to a taxonomy suggested by Boero and Squazzoni (2005), agent-based models are divided into "case-based models", "typifications" and "theoretical abstractions". The authors argue that the extent of integrating empirics in social simulation depends strongly on the target of the model. The integration of empirical knowledge requires careful adjustment of modelling strategies and methods along the process of model construction and validation.

Taking into account these approaches, the simulation of the Vienna biotech innovation system is chosen to be a case-based model in the line of history-friendly modelling, because agents and their interactions are founded on theoretical hypotheses. The objective is the investigation of empirical macro-properties which help to get an idea about the micro-macro generative

[8] In Bayesian simulations knowledge about the parameters is inferred from empirical data about the system's dynamics (Brenner and Werker 2007, p. 231). In this connection, the likelihood for the acceptance of each model specification is defined. Model specifications which are contradictory to empirical data are excluded (Fagiolo et al. 2007b, p. 211).

[9] Applications of the Werker-Brenner approach are found e.g. in Brenner and Murmann (2003) and Brenner (2004).

[10] For an example of successfully overcoming the case-specific dilemma in history-friendly models by performing sensitivity analyses, please refer to Eliasson and Taymaz (2000).

mechanism that might lead to scenarios for policy implications (Boero and Squazzoni 2005). Later, sensitivity analyses will be carried out in order to avoid the simulation results being too case-specific.

4 Micro-foundation of agents

A strategy that supports the credibility of the model in the policy context has to account for a high degree of empirical detail. For this model, the empirical foothold is provided by comprehensive organization-level time series data on R&D, innovation output and performance of biotech agents in Vienna's life sciences cluster from 1999 to 2009. In this paper the term *empirical calibration* will be used for the micro-validation of the model, while the expression *empirical validation* refers to its macro-validation. Empirical calibration is the use of empirical detail as the basis for model design and parameter initialization. This involves selecting model assumptions and components, their respective values as well as the formulation of stylized facts and the adequate level of detail regarding the micro-foundation and -specification of the agent-based model (e.g. Fagiolo et al. 2007a, p. 190-191; Boero and Squazzoni 2005). Following Gilbert (2008, p. 30 and p. 80) stylized facts rely on empirical observations and describe phenomena in a simplified way. Although stylized facts usually refer to the macro-level of an agent-based model, they can also reflect cross-sectional regularities (Fagiolo et al. 2007b, p. 208).

4.1 Some empirics on the Vienna biotech innovation system

In the mid-1980s, the foundation of a joint venture of Boehringer Ingelheim and Genentech (IMP 2011) sparked off new dynamic activities in biotechnology which have gained momentum since then. In 1999, an Austrian biotech program was introduced which led to the setup of the LISA VR cluster initiative in 2001 which serves as a coordination and information platform for the *biotech innovation system in the Vienna region* (Life Science Austria Vienna Region 2007, p. 7). Since 2003, the focus of Vienna's research policy lies on biotechnology and specific calls for projects in this field are offered on a regular basis (WWTF 2011).

By 2007, 170 biotech companies were located in the Vienna region and engaged around 11,000 employees. In addition, 4,300 academic researchers were active in the field of life sciences (Life Science Austria Vienna Region 2007, p. 7). Today, the region around Vienna is leading in oncology, immunology and neurobiology, three quarters of the total amount of agents operate in red biotechnology[11] (Jörg et al. 2006, p. 8) and a large part of the organizations is active in analytical methods and services, diagnostics and diagnostic technologies, microbiology or pharmaceuticals (see Figure 4).

[11] Red biotechnology is the definition for research and application in medical and pharmaceutical science and includes the whole range from diagnostics to therapy (OECD 2006, p. 88).

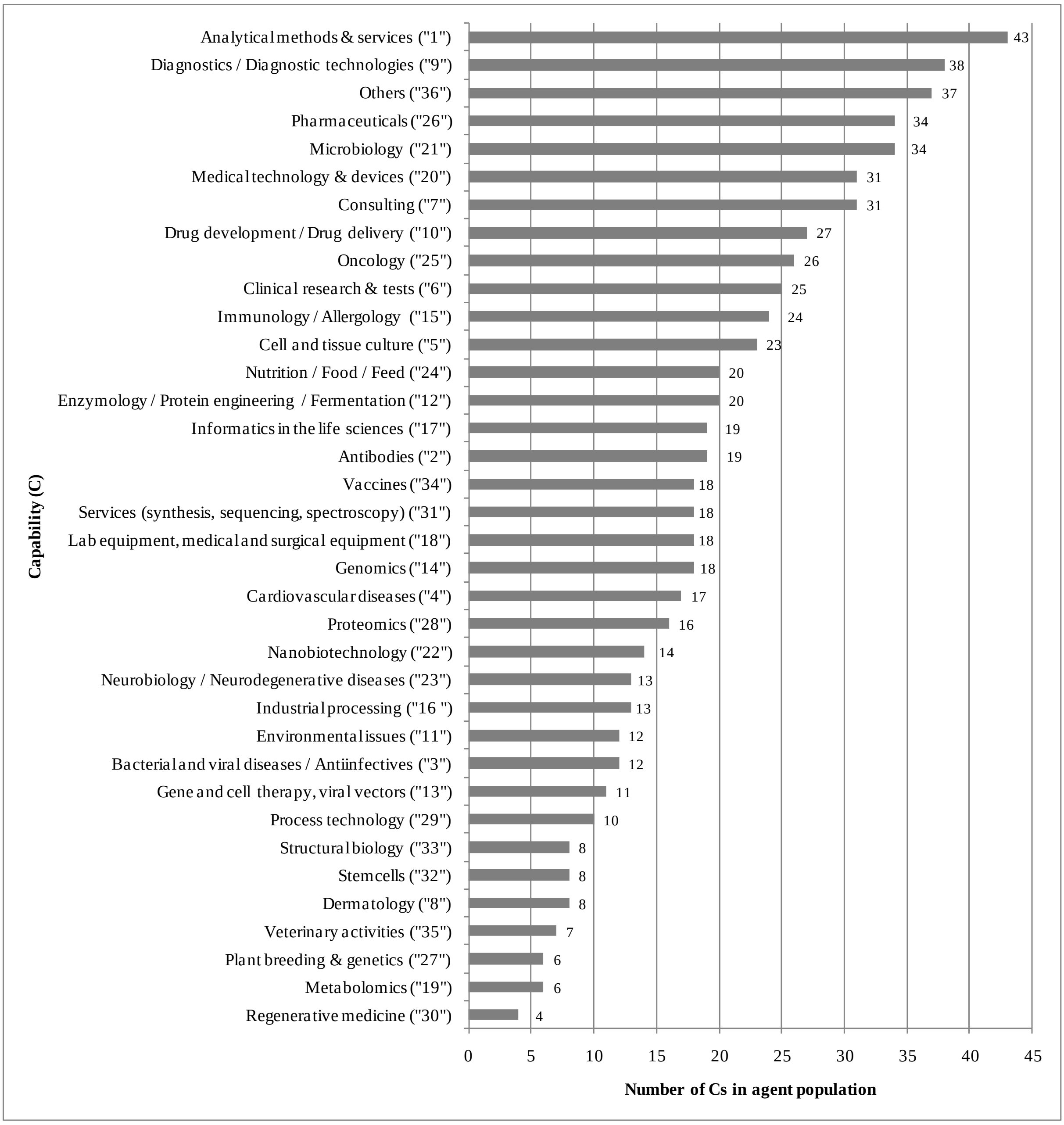

Figure 4: Self-reported capabilities of biotech organizations in the Vienna Region
Source: Data adapted from Austrian Life Sciences Directory (2009)

Generally, Vienna's reputation as a science think tank is fairly better than its effective ability to exploit and commercialize R&D results (Reiss et al. 2003; Senker et al. 2000, p. 605). These findings are in line with our data (Figure 5), which shows virtually all organizations stating "R&D" as a core competence, while "Sales" is reported as a core competency by less than 40% of the organizations.

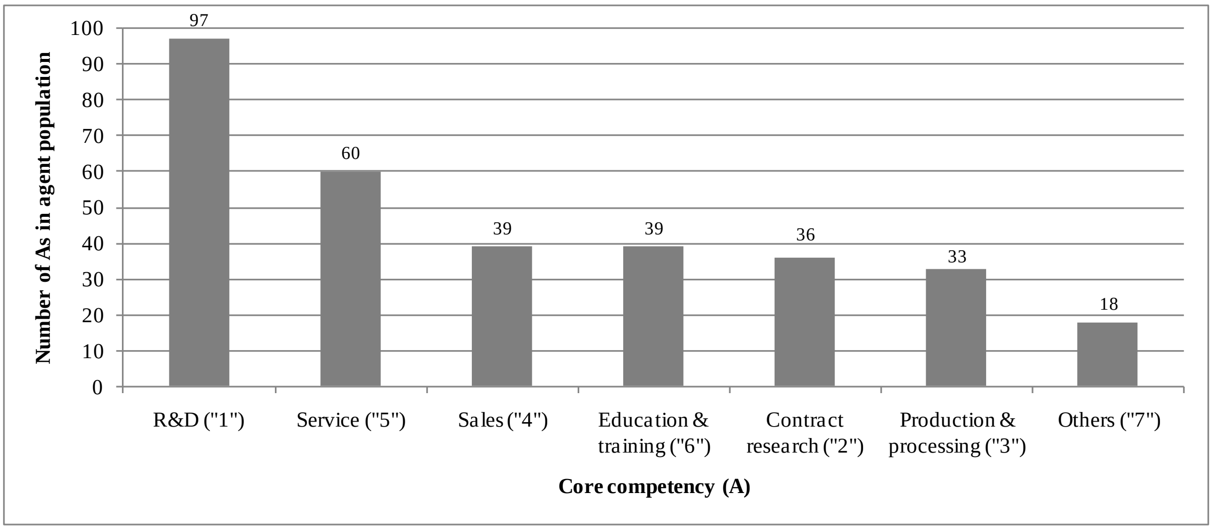

Figure 5: Self-reported core competencies in the Vienna Region
Source: Data adapted from Austrian Life Sciences Directory (2009)

The long tradition in Vienna's biomedical research attracted worldwide renowned research organizations and multinational pharmaceutical companies that settled down their facilities in Vienna. As indicated in Figure 6, start-up and spin-off companies were founded resulting from the dynamics caused by knowledge transfer in complex networks.

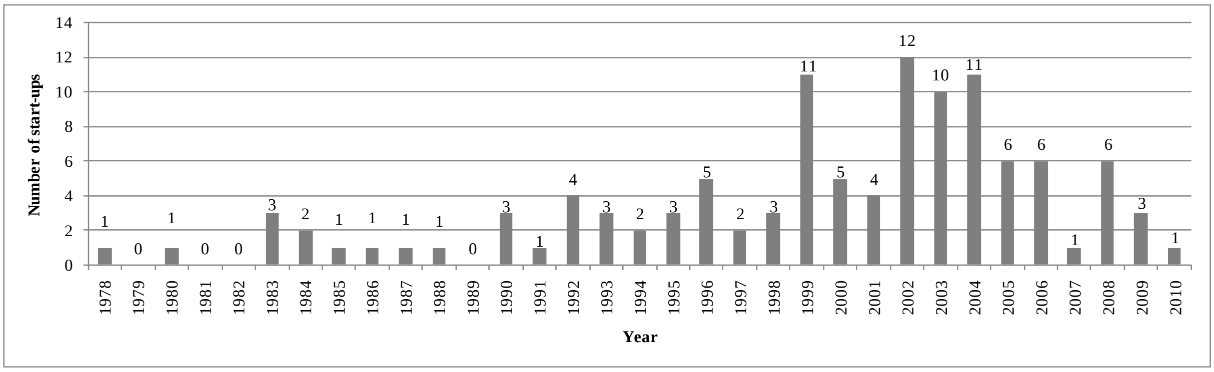

Figure 6: Start-up dynamics in the Vienna Region
Source: Data adapted from Austrian Life Sciences Directory (2009)

In the Vienna biotech innovation system cooperative R&D plays an important role and biotech companies rely heavily on knowledge that originates from universities, research organizations and public laboratories. Therefore, a company's absorptive capacity and its ability to evaluate external knowledge are crucial to success (Liebeskind et al. 1996; Cohen and Levinthal 1990, p. 128). Research regarding the influence of absorptive capacity in the R&D process of pharmaceutical and biotech companies revealed that industry agents that cooperate with university agents and do basic research are likely to invent faster with a superior quality (Fabrizio 2009). Concerning internal capabilities and competencies of biotech companies, additional research should reveal how knowledge transfers from universities to the industry could be enhanced (McMillan et al. 2000, pp. 1-8). In this regard, successful industrial exploitation of R&D is not only driven by public expenditure but also by associated policies that promote technology transfer (Senker et al. 2000).

In the following, some insights regarding the *input* to the Vienna biotech innovation system are given. Although being part of the system as such, for the purpose of this simulation government funds are extracted from the black box for validation reasons. In the early 1990s, political activities relevant to Austrian biotechnology were rather underdeveloped and their effects very weak. In 2004, more than five percent of the Austrian public R&D budget was invested in biotechnology, covering all parts of the innovation system with a combination of generic and biotech-specific instruments and a focus on education, research and fiscal policy[12] (Reiss et al. 2005, pp. 74-75). This is the particular period of interest for this simulation exercise. Regarding RTI policy in Austria, considerable weight has been put on indirect funding, i.e. tax incentives for R&D, in the last few years. Despite a fundamental reform of the university sector, institutional funding by the government is to a large extent absorbed by universities, while the non-profit research sector is small in international comparison. Direct funding, i.e. government programs, exists on national as well as on regional levels, and includes measures supporting R&D collaboration and also a more institutionalized form of collaboration between science and industry, so-called competence centres which are relevant for the life sciences sector in Vienna.

Since life sciences cluster promotion in Vienna does not exist as long as in other international biotechnology clusters, it is still in its development and the lack of venture capital and knowledge regarding commercialization of research results harm the success of the biotech cluster (Cooke et al. 2007, p. 250). In addition, the relatively low number of really successful companies (Tödtling and Trippl 2007, pp. 351-357) and the missing global pharmaceutical player with Austrian roots are constraints for the rosy progress of the biotechnology cluster Vienna region. The lacking credibility after failures[13] and the fact that Austrian scientists have not yet reached a certain reputation lead to difficulties in attracting venture capital. Pre-financing from universities is required and public funding inflows are conducted much later. Moreover, there are no risk funds which fulfil the specific requirements to finance R&D in biotechnology, e.g. the long developmental periods for pharmaceutics.

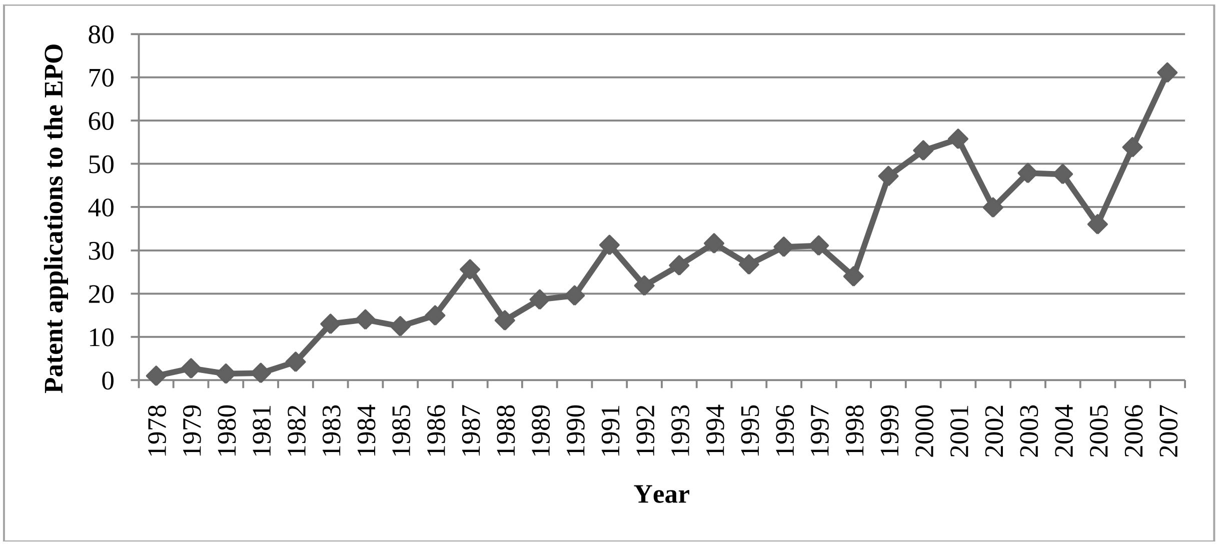

Figure 7: Patenting in the Vienna Region
Source: Data adapted from OECD (2011) OECD.Stat, Biotechnology,
Dataset: Patents by regions, EPO_A Patent applications to the EPO, Inventor(s)'s country(ies) of residence, Vienna, Lower Austria, Burgenland, rounded to the nearest integer, data extracted on 30 January 2011

12 Reiss et al. (2005, pp. 74-75) used historical data (1994-2002) on policy activities and national performance in biotechnology for the validation of the historical analysis and benchmarked data regarding biotech policies in the year 2004.

13 Bankruptcy proceedings against the formerly well-performing Austrianova were instituted on May 9th 2008 (KSV 2008).

On the *output* side, the number of high-tech jobs, publications and patents serve as a performance indicator of the system. Preliminary results regarding the patenting activity in the Vienna region show a considerable increase after RTI policy started to focus on the biotech sector (see Figure 7). In the next step publication data retrieved from the Social Sciences Citation Index (Web of Knowledge) (2011) will be analyzed to see the development in the scientific field and in its particular capabilities.

4.2 Parameter initialisation

As the prime data source, we use the Austrian Life Sciences Directory (2011) which is a regional promotion and coordination platform of the LISA VR cluster initiative and offers information on participating organizations over the Internet. For the purpose of this project, 136 relevant organizations have been identified that operate in the Vienna region, including Austria's capital city Vienna and the two provinces Lower Austria and Burgenland. Referring to expert advice, this set of organizations represents a comprehensive empirical population relevant for the calibration of the agent-based model. Where organization data was missing, complementary information from the company database Aurelia (Bureau van Dijk 2010) as well as the specific web pages of the companies filled the gaps.

The empirical data are collected and formatted in an *empirical input file* for parameter initialisation of the model. In the following, due to space constraints, we focus on specific aspects of parameter initialisation.

According to the shares of agent types in the empirical population, the agent population in the model is constituted by 62.50% industry agents, 20.59% university agents and 16.91% research organization agents. Industry agents are further divided, following the EU definition for SMEs[14] into 45.6% small and medium-sized enterprises (SMEs) and 16.91% multi-national companies (MNCs). Some organizations did not find any of the provided main categories (*Industry*, *Research Organization*, *SME* or *University*) appropriate and chose the agent type *Other*. In a second review after deciding carefully for every single organization these other agents were attributed either to the SME or to the MNC category by relying on additional data research, resulting in the above mentioned initialization of the agent population in the model. Moreover, research organizations are separated in public or private research organization agents, and university agents specified according to whether they are universities or universities of applied sciences[15].

In addition to information on the location, R&D personnel and foundation year, every organization chooses from thirty-six keywords and seven core competencies (see Figure 5) that describe themselves best. The keywords reflect the specialization of an agent and are used as its particular capabilities for the model (see Figure 4).

The empirical input file contains the data obtained from the Austrian Life Sciences Directory (2011) which is based on the particular organization's data set. So far, one data set consists of a specific organization ID number, the agent type and a list of its capabilities as well as its core competencies, its foundation year and its application orientation (e.g. [128 "ROR" [6 9 11 36] [2 1 5 6]] "2007" "Basic research"). At a later stage further data will be read in from the empirical data base.

In the setup procedure the *kene set* is formed following a simple principle: Every capability is combined with every core competency and the expertise level is randomly assigned (therefore

[14] According to the EU definition, an SME has fewer than 250 employees, an annual turnover not exceeding 50 million euro, and/or an annual balance-sheet total not exceeding 43 million euro. Furthermore, an SME must not be owned by 25% or more by a company which is not an SME (European Commission 2011).

[15] Universities of applied sciences: *Fachhochschulen*

in italics, see (1)). Thus, for the research organization agent with the ID number 128 in the example above with the capabilities [6 9 11 36] and the core competencies [2 1 5 6] the following kene set at time step *t* is formed:

Kene set at time step *t*:

$$\left\{ \begin{pmatrix} 6 \\ 2 \\ \mathit{1} \end{pmatrix} \begin{pmatrix} 9 \\ 2 \\ \mathit{2} \end{pmatrix} \begin{pmatrix} 11 \\ 2 \\ \mathit{1} \end{pmatrix} \begin{pmatrix} 36 \\ 2 \\ \mathit{9} \end{pmatrix} \begin{pmatrix} 6 \\ 1 \\ \mathit{8} \end{pmatrix} \begin{pmatrix} 9 \\ 1 \\ \mathit{7} \end{pmatrix} \begin{pmatrix} 11 \\ 1 \\ \mathit{6} \end{pmatrix} \begin{pmatrix} 36 \\ 1 \\ \mathit{5} \end{pmatrix} \begin{pmatrix} 6 \\ 5 \\ \mathit{3} \end{pmatrix} \begin{pmatrix} 9 \\ 5 \\ \mathit{3} \end{pmatrix} \begin{pmatrix} 11 \\ 5 \\ \mathit{8} \end{pmatrix} \begin{pmatrix} 36 \\ 5 \\ \mathit{6} \end{pmatrix} \begin{pmatrix} 6 \\ 6 \\ \mathit{3} \end{pmatrix} \begin{pmatrix} 9 \\ 6 \\ \mathit{2} \end{pmatrix} \begin{pmatrix} 11 \\ 6 \\ \mathit{4} \end{pmatrix} \begin{pmatrix} 36 \\ 6 \\ \mathit{8} \end{pmatrix} \right\} \qquad (1)$$

In a first attempt, in order to avoid fuzziness and too long kene sets, it was intended to combine Cs and As of a particular agent only where empirical proof was found in additional in-depth analyses that the agent uses the particular C and A together for its operations. But then this approach was discarded in favour of this rather basic kene-formation procedure due to the following reasons. The argument that kene sets become too long is undermined by the fact that more than half of the agent population holds only one or two core competencies and almost 75% hold one, two or three core competencies. Furthermore, if an organization has a core competency, it is probable that this in-house expertise is used for all the different capabilities held by this agent. These considerations make the effort for supplementary data research so far obsolete.

An agent's *application orientation* is calibrated according to its particular agent type. It is assumed that university agents concentrate on basic research, while industry agents focus on applied research. Research organizations were analyzed agent-specific. First, it was decided based on information regarding its R&D activities. If this information was not available on the Internet or in annual reports, the ownership structure (private or state-owned) and finance structure of every single agent was taken as a basis of decision-making. Approximately 5% of the total amount of agents does not perform R&D, these are only industry agents and most of them are occupied with consulting or services related to biotech. The remaining industry agents (57% of the total amount of agents) focus on application-oriented research. After the second empirical analysis around 6% of the research organizations work in basic research, while 11% perform applied research.

The attributes absorptive capacity, financial stock and R&D infrastructure are rather difficult to calibrate as data is not easily available. Therefore, proxy variables need to be defined for these parameters which are discussed below.

As mentioned above, the value of *R&D infrastructure* is attributed according to the agent type and agent size. While industry agents might take a value from 1 to 7, university and research organization agents' values range from 4 to 10. Industry agents which are MNCs take a higher value than SMEs do and smaller scientific agents have a lower value than large agents have, this is to account for given budget constraints.

The *absorptive capacity*[16] of agents is also an important driver in R&D of biotech organizations (Traore 2004) and is therefore considered as an agent attribute in the model. The transfer of tacit knowledge requires not only direct interactions but also a sufficient level of absorptive capacity which is necessary to effectively recombine the acquired external knowledge in the cognitive framework of the recipient agent (Morone and Taylor 2010, p. 152). An agent's absorptive capacity refers to its ability to integrate pieces of external knowledge into its own knowledge stock during collaborative R&D (Fischer 2003), p. 344). Following a fieldwork study on wine clusters by Giuliani and Bell (2005) the absorptive capacity of an agent in the model is influenced by the *share of R&D personnel* working for

[16] Absorptive capacity is here defined as the knowledge stock accumulated within an agent, embodied in the skills of (R&D) personnel and increased by in-house learning efforts (Morone and Taylor 2010, p. 102).

the agent and by the agent's *expertise level*. Furthermore, the type and intensity of R&D performed by the agent which in the model is reflected by its *research attitude*, its *application orientation*, its *partner search strategy* and its *R&D strategy* determines an agent's absorptive capacity (Morone and Taylor 2010, pp. 92-93). While Giuliani and Bell (2005) study the individual employee's level, so far, for this simulation a more aggregate view is taken referring to an agent as the employer of R&D personnel, leaving the possibility for future expansion of the model. For the further improvement of model calibration it is aimed to take a more detailed individual view, exploring the knowledge that rests in the minds of the respective employees.

5 Macro-foundation of agent behaviour, interactions and regularities

The agent-based model presented here is programmed in the software environment NetLogo (Wilensky 1999). NetLogo is given preference over several other software toolkits for agent-based modelling due to various reasons: Beside its free availability, the current modelling exercise refers to prior models (Pyka et al. 2002) written in NetLogo. Moreover, it is rather easy to use and, thus, practicable for interdisciplinary work (Robertson 2005, pp. 526-527). The topology of the model's world in NetLogo has no significance in the current version but might be included at a later stage as a technology space showing R&D trends and the evolution of the agents' capabilities and core competencies. While referring to the structure of the sub-processes shown in Figure 3, the following sections explain the challenges that have to be overcome during model calibration.

During (*own* or *collaborative*) *research* agents learn, i.e. agents acquire new capabilities, whereby incremental innovation is associated with the acquisition of rather "similar" capabilities, and radical innovation with more "dissimilar" capabilities. Previous research (e.g. Ahrweiler et al. 2004; Pyka et al. 2002) treats capabilities formally as integer numbers, thus the dissimilarity (distance) between two capabilities $c_i = k$ and $c_j = l$ can be described simply by their algebraic difference $|k - l|$. In contrast, our model of the Vienna biotech innovation system employs agents' capabilities that are empirically based, and are therefore represented not by a numeric but by a nominal variable. These capabilities are adopted from the activity domains of the Austrian Life Sciences Directory (Austrian Life Sciences Directory 2011).

An important part of the model calibration is to imprint a metric, i.e. a proximity measure on this set of n = 36 capabilities. A plausible approach is to assume that two capabilities are similar, if they are both held by relatively many agents. This is reached by taking the number of co-occurrences y_{ij} of two respective capabilities i and j in the agent population and calculating the Jaccard index (Leydesdorff 2008) as a measure of thematic proximity of the capabilities.

$$J_{ij} = \left(y_{i\bullet} + y_{\bullet j} - y_{ij}\right)^{-1} y_{ij} \qquad i, j = 1, \ldots, n \tag{2}$$

$$\text{with} \quad y_{i\bullet} = \sum_{\substack{j=1 \\ j \neq i}}^{n} y_{ij}\,, \; y_{\bullet j} = \sum_{\substack{i=1 \\ i \neq j}}^{n} y_{ij}$$

and y_{ij} is the number of co-occurrences of capabilities in organizations. The Jaccard index belongs to the set-theoretic similarity measures that concentrate on the relative overlap of two data sets. As Van Eck and Waltman (2009, p. 1648) point out, co-occurrence data is better analyzed with *probabilistic* similarity measures, such as the use of the association strength, and not with *set-theoretic* similarity measures because they lack an appropriate correction for size effects. At a later stage of this project the results for the association strength will be compared to the results obtained from the Jaccard index, whether this is the case for the Vienna biotech dataset.

According to the research attitude of each agent, those acting according to the *incremental* research attitude choose the new capability with the highest proximity to the nearest C of the agent, while those with a *radical* research attitude take the capability with the lowest proximity to the nearest C of the agent[17].

Regarding *partner search* for *collaborative R&D*, the following findings are taken as a basis for the simulation. Research on the partner choice for R&D projects within the EU framework programmes revealed that collaboration choices are primarily determined by prior cooperation, thematic and geographical proximity (Paier and Scherngell 2011). Due to the fact that 87% of the organizations in the Vienna life sciences sector participate in European projects, these reasons influencing partner choice need to be accounted for (Heller-Schuh and Paier 2009, p. 162).

In our model, the attractiveness of a potential partner depends on past experience. Previous partners and network members, suppliers and customers are preferred to all other agents. The attractiveness of a potential cooperation partner is measured by the number of Cs their last R&D concepts have in common. This is to account for the fact that the integration of external knowledge is more difficult and bears risks. Moreover, cooperation experience (past success or failure of cooperative R&D concepts) is memorized as it serves as a basis for future partner search (Gilbert et al. 2007; Pyka et al. 2002). International cooperation partners are modeled as one collective agent, e.g. European project partners are calibrated according to data retrieved from the EUPRO database[18].

[17] In order to give an example and to test this for an agent, the Trimed Biotech GmbH is chosen. It possesses the following capabilities: “Clinical research & tests”; “Drug development / Drug delivery”; “Immunology / Allergology”; “Oncology”; “Vaccines”. According to the procedure of acquiring a new capability described above, if this industry agent follows the *incremental research* attitude it chooses “Cardiovascular diseases”. In contrast, it chooses “Process technology”, if its research attitude is *radical research*.

[18] The EUPRO database is maintained by the AIT Austrian Institute of Technology GmbH, Foresight & Policy Development Department. It includes all projects and participants of the European Framework Programmes (FP1-FP7) from CORDIS (www.cordis.lu) and is updated on a regular basis. The data has been further processed in order to identify unique organization names, to break down large organizations into meaningful sub-entities, and to include geographical attributes. For detailed information on the EUPRO database, see Barber et al. (2006).

During R&D each agent or project team creates an *R&D concept*[19] (see Figure 8) which is then evaluated according to a scientific and a technological fitness function. For the creation of the R&D concept three kenes are chosen randomly out of the kene set at time step t (as was shown above in (1)).

$$\left\{\begin{pmatrix}6\\2\\\mathit{1}\end{pmatrix}\begin{pmatrix}9\\2\\\mathit{2}\end{pmatrix}\begin{pmatrix}11\\2\\\mathit{1}\end{pmatrix}\begin{pmatrix}36\\2\\\mathit{9}\end{pmatrix}\begin{pmatrix}6\\1\\\mathit{8}\end{pmatrix}\begin{pmatrix}9\\1\\\mathit{7}\end{pmatrix}\begin{pmatrix}11\\1\\\mathit{6}\end{pmatrix}\begin{pmatrix}36\\1\\\mathit{5}\end{pmatrix}\begin{pmatrix}6\\5\\\mathit{3}\end{pmatrix}\begin{pmatrix}9\\5\\\mathit{3}\end{pmatrix}\begin{pmatrix}11\\5\\\mathit{8}\end{pmatrix}\begin{pmatrix}36\\5\\\mathit{6}\end{pmatrix}\begin{pmatrix}6\\6\\\mathit{3}\end{pmatrix}\begin{pmatrix}9\\6\\\mathit{2}\end{pmatrix}\begin{pmatrix}11\\6\\\mathit{4}\end{pmatrix}\begin{pmatrix}36\\6\\\mathit{8}\end{pmatrix}\right\}$$

R&D concept
created after own R&D
at time step t + 1

$$\left\{\begin{pmatrix}11\\2\\\mathit{1}\end{pmatrix}\begin{pmatrix}9\\1\\\mathit{7}\end{pmatrix}\begin{pmatrix}36\\5\\\mathit{6}\end{pmatrix}\right\}$$

subject to evaluation
through a
fitness function

Figure 8: Creation of an R&D concept by random choice of three kenes from the kene set

R&D concepts have to undergo an *evaluation* procedure before they can obtain the status of an R&D output. Hereby, an R&D concept is assigned a scientific value S and a technological value T. In some more detail, the scientific value S of an R&D concept is defined as the sum of the "scientific values" s_j of its three kenes, times a function f of the cumulative distance of the three capabilities involved. It is given by

$$S = f(d_{123})(s_1 + s_2 + s_3), \tag{3a}$$

where d_{123} is the cumulative distance of the three capabilities in the capability space, and the scientific value s_j of kene j is defined as

$$s_j = s_j(C_j, A_j, E_j) = E_j v_S(C_j) \qquad \text{if } A_j \in \{1,2,6\} \qquad j = 1,2,3 \tag{3b}$$

and

$$s_j = s_j(C_j, A_j, E_j) = 0 \qquad \text{if } A_j \in \{3,4,5\} \qquad j = 1,2,3 \tag{3c}$$

whereby $v_S(C_j) \geq 0$ denotes the relative publication intensity within capability C_j, obtained from the empirical data, and E_j is the expertise level of kene j. This definition takes into account that scientific value can only be generated with the core competencies $A_j \in \{1,2,6\}$, i.e., "R&D", "Contract research" and "Education & training", while "Production & processing", "Sales" and "Services" do not contribute to scientific value. It is also important to note that the function $f(d_{123})$ is of "inverted u-shape", so that a medium overall distance between the capabilities C_j creates the maximal scientific value.

[19] This is similar to the innovation hypothesis coined by Gilbert et al. (2001).

Likewise, the technological fitness T of an R&D concept is defined as the sum of the "technological values" t_j of its three kenes, times a function g of the cumulative distance of the three capabilities involved. Thus, T is defined as

$$T = g(d_{123})(t_1 + t_2 + t_3) \tag{4a}$$

where d_{123} is the cumulative distance of the three capabilities in the capability space, and the technological value t_j of kene j is defined as

$$t_j = t_j(C_j, A_j, E_j) = E_j v_T(C_j) \qquad \text{if } A_j \in \{1,2,3\} \qquad j = 1,2,3 \tag{4b}$$

and

$$t_j = t_j(C_j, A_j, E_j) = 0 \qquad \text{if } A_j \in \{4,5,6\} \qquad j = 1,2,3 \tag{4c}$$

whereby $v_T(C_j) \geq 0$ denotes the relative patenting intensity within capability C_j, obtained from the empirical data, and E_j is the expertise level of kene j. This definition takes into account that "technological value" can only be generated with the core competences $A_j \in \{1,2,3\}$, i.e., "R&D", "Contract research", and "Production & processing", while, "Sales", "Education & training", and "Services" do not contribute to technological value. Again, the function $g(d_{123})$ is of "inverted u-shape", so that a medium overall distance between the capabilities C_j creates the maximal technological value.

As the final step of the evaluation, the *R&D concept* is attributed the status of an *R&D output*, either a "scientific publication" or a "patent application" (or both), if its scientific value S or technological value T exceeds a threshold value S_{success} or T_{success}, respectively. This constitutes agent-level as well as system-level outputs.

The successful generation of output feeds positively back on the agents: By increasing the expertise levels E_j of the kenes of a successful R&D concept and incorporating these updated kenes into the kene sets of the involved agents, the agents cumulatively increase their expertise levels. The scientific evaluation is used not only for the assessment of the scientific value of R&D concepts after research, but it is also necessary to evaluate whether a project proposal of an agent or project group is granted public funding.

A similar procedure is applied to the kenes if the technological value T is greater than the threshold value T_{success}. Thus, in the case of a patent application, the expertise levels of the agent (or in cooperative projects, of the project partners) increase. Moreover, the technological evaluation is used in the assessment for venture capitalists and banks to decide in the case agents apply for venture capital or a bank loan.

6 Conclusions and outlook

This paper highlights the necessity for improving agent-based simulation models by several aspects. The most important issue is the integration of more empirical detail. It is argued that by focusing on empirical calibration and validation the methodological standing of ABM is advanced and the credibility of findings is improved. By taking up the suggestions presented in this paper, models calibrated with a sound empirical basis can become an important tool for policy makers to test the effects of public RTI funding on a system level.

The focus of this paper is the empirical calibration of an agent-based model. As has been pointed out, this is an important step, both for a future application in the policy context in particular, and for the development of the standing and usability of ABM for scientific research in social sciences in general (Brenner and Werker 2007, p. 238). The agent-based model presented here complements existing agent-based modelling approaches that focus on network formation and innovation processes in the biotech sector in general but disregard the complexity of a specific innovation system (Triulzi et al. 2009; Pyka and Saviotti 2002; Gilbert et al. 2001). Therefore, the model contributes to ABM platforms like SKIN (http://cress.soc.surrey.ac.uk/SKIN) or OpenABM (http://www.openabm.org) by following the state-of-the-art guidelines on transparency, comparability and replicability. Our model advances from former models in several aspects. It uses empirically calibrated kenes that are changed and recombined through joint R&D. The results may become patents or scientific publications depending on the evaluation process with corresponding fitness functions. The elaborate calibration of the model is expected to improve the credibility of the model, especially in the policy context.

The next steps include further empirical data collection so as to ensure sound calibration and validation. Cooperation behaviour and government intervention still need to be implemented. At a later stage of the project, different RTI funding regimes and instruments will be tested in various policy experiments and in the creation of scenarios in order to evaluate their influence on the innovative performance and interactions of agents and on the performance of the system. Finally, the conceptual model will be validated by comparing artificial data produced by the simulation with empirically observed data. Future research might include a more detailed view on labour mobility and the generalization to other sectors.

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