Chapter 5
Science Policy of Systems Biology

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Abstract In this chapter, we examine the science policy of systems biology and perspectives thereof. Based on interviews with actors from different fields such as science, politics, media, and economy, we contrast the scientists' conceptualization and assessment of systems biology and their perception of science policy with that of societal actors on what systems biology is and how it should be governed.

Discussions in these different fields are interconnected. We therefore highlight interdependences and shared topics where the separate discourses influence and interact with each other. Aspects addressed touch upon the identity of systems biology as a new science, and the effect of further specialization, the similarity of the scientific and public images of what systems biology is, and the sustainability of funding. While participation and inclusion of the general public is seen as an important achievement in politics, media, and public interest groups, it is less important in the scientific perspective. This raises the question of whether it is ascribed an appropriate role.

Keywords Systems biology • Science policy • Science and society • Scientists • Societal actors • Interdependencies

5.1 Systems Biology as a Topic of Science Policy

Systems biology is commonly understood as an emerging interdisciplinary approach in the life sciences. As such, it depends massively on research funding as does any other scientific development. Budgets for systems biology derive to a large part not from universities or research institutions, but—especially regarding personnel cost—from third-party funding. In Germany, those funds are mainly governmental-driven and, as such, are subject to corresponding science policy. In this chapter, we analyze and discuss the social and scientific dynamic interdependencies that result

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M. Döring et al., *Contextualizing Systems Biology*,
DOI 10.1007/978-3-319-17106-7_5

from this kind of research funding and development. Furthermore, we wanted to know how the discourse on science policy of systems biology is characterized by representatives of science, the media, industry, and public interest groups, and from research funding and science policy.

5.1.1 Systems Biology and the Dynamics of Science Policy

Topics of new approaches in science are not only discussed in science itself, but also in politics and by the public. Questions regarding a science's funding, its expected value for science and society, its applications, implications, and possibly necessary regulations relate to the corresponding science's policy. The latter is usually examined by scientific as well as by societal actors. Relevant societal actors are, for instance, research funding bodies and representatives from science policy and administration, but also by industry, nongovernmental organizations, and public interest groups, as well as the media (comp. Fig. 5.1). The positions of such actors often vary widely, not only regarding the perspective, but also regarding the selection of topics seen as relevant, such as content, research funding, application, chances, and risks of the scientific development.

The discourse on the future direction and funding of science was not always shared between that many actors, as it used to be more one-dimensional: in the past, public opinion mainly placed its trust in the self-regulatory mechanisms of science,

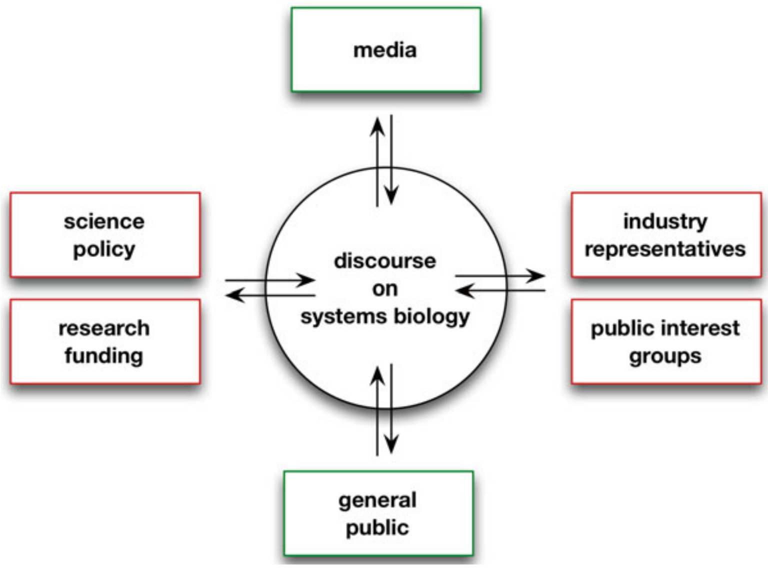

Fig. 5.1 Discourse on systems biology: societal actors

because "[s]cience and technology [were] for the most part removed from attempts to make them topics of public discussion and objects of political regulation"[1] (Bogner 2012, 380). Since then, the relationship between science and the public has been subject to fundamental change: the relationship between scientific practice and public opinion has shifted to a degree that today a "closer coupling"[2] can be found that surfaces in various connections between the two systems (Weingart 2001, 175; see also Dunwoody and Ryan 1985; Sturgis and Allum 2004). Scientific development, for example, make an impact on the daily life of the public, through applications and the public tries to influence the direction of science. In this context, networks of actors in finance, politics, industry, business, and civil society groups interact within the realm of research governance (Peters and Weingart 2009), often by means of the media. Furthermore, Peters et al. (2009) describe the transfer of the direction of science to the political sphere. They discuss that the media play a critical role: the medialization of science is driven by a medialization of politics. Media are increasingly instrumentalized by science to hold priority conflicts and to mobilize public support (Weingart 2001, 244). On the other hand, science is more and more oriented towards political or economic objectives and thus interested in its public image and hence, its perception by the public and the media. This interest has reached a degree that the question arose whether the direction of scientific development is determined by the media (Weingart 2005, 168ff).

As a consequence, the public is not only a passive observer of science, but influences partly (e.g. via the media) its content and directions. Hence, laypersons enter into scientific relationships (compare further, for example, Bogner 2012). In this sense, science, the public, media, politics, the law, industry, and interest groups are not discrete and independent systems but have to be considered as linked and interconnected. The discourse on scientific progress and the orientation of research is thus not determined by science alone but has become subject to the influence of the public and politics, albeit science conceived as a system remains autonomous (cf. Rödder 2009, 33ff).

This is different, however, with regard to its societal legitimization. Here, science does not possess exclusive interpretive authority as the public and politics discuss scientific topics and their worth and merit for society. This is especially true when systems biology is understood as a "technoscience," (Nordmann 2005). Technoscience is characterized by the fact that basic research, technology development, and application are inextricably linked. Inherent in this understanding is that the different subsystems described above are involved in the development of a technoscience (cf. Brüninghaus 2012). As systems biology is seen as at least partly established and increasingly accepted from the perspective of research funding, it is necessary to examine the perceptions and opinions of other relevant actors in order to make statements on its current and possible further development and impacts. In order to put such statements on a sound basis we chose an empirical approach

[1] Original quote: "Wissenschaft und Technik [waren] öffentlicher Problematisierung und politischen Steuerungsversuchen weitgehend entzogen".

[2] Original quote: "engere Kopplung"

that allowed us to include different levels of the discourse on systems biology, as well as important actors and focus on the influence of the different discourses (cf. Bora 2012, 345ff).

In essence, this chapter aims at answering questions regarding science policy of systems biology. We focus on the discourse of science policy in science, media, industry, nongovernmental organizations and public interest groups, research funding, and science policy referring to

- systems biology's funding mechanisms and constraints,
- reactions to its funding,
- its value for scientists, the public, and research funding representatives,
- its application,
- its implications and possibly regulations.

5.1.2 Science Policy and Research Funding of Systems Biology

In Germany, public research funding is mainly driven by the Federal Ministry of Education and Research (BMBF), the German Research Foundation (DFG), and the Helmholtz Association. The BMBF started its first program of systems biology funding in 2001 with a line of funding titled "Systems of Life—Systems Biology" (Systeme des Lebens—Systembiologie). Since then, systems biology was supported financially continuously, for example, in a large collaborative research project on liver cells that started 2004 (HepatoSys); in a project targeting the development of systems biology infrastructure since 2008 (FORSYS); with a focus on medical applications in the 2009 line Medical Systems Biology (Medizinische Systembiologie); in another large collaborative research project that started in 2009 centering around aging processes (GerontoSys), and since 2009 in one that concentrates on new methodologies (SysTec). The BMBF also funds interdisciplinary collaborative projects through a program called ERASysBio (2006–2011). Its primary aim is the development of personalized medicine, and pharmaceutical advances, of treatments for multifactorial diseases, and measurements to increase life expectancy (Rahmenprogramm Gesundheitsforschung 2010).[3]

What follows is a short description of the main funding agencies and instruments in order to provide a background for the better understanding of the statements and claims of the interviewed actors and our interpretations thereof.

The German Research Association (Deutsche Forschungsgemeinschaft; DFG) has no documented guidelines regarding the funding of systems biology due to its nature as a bottom-up organization. It is funding about 80 projects in the area of systems biology.

[3] https://www.erasysbio.net/. Accessed November 15, 2014.

The Helmholtz Association (Helmholtz-Gemeinschaft) has a focus program for systems biology (Helmholtz-Allianz Systembiologie). It aims to "contribute to clarifying the underlying mechanisms in the emergence of complex diseases."[4] Examples are the development of computational mathematical models for cellular processes connected to cancer or heart diseases that are based on data generated by previous experiments and enable a better holistic understanding of processes in human cells. This also includes the "possibility to predict opportunities for targeted intervention when diseases emerge".[5] The funding program includes six research centers within the Helmholtz Association, as well as other universities and research institutes.

The reconstruction of the funding of systems biology by programs of the European Commission is somewhat more complicated. Such programs were started in 1984; first they ran for five, and since 2007 for 7 years. The first seven funding periods were called Framework Programs for Research and Technological Development, abbreviated FP1 through FP7, whereas the current program is named Horizon 2020. The specific objectives and actions vary between funding periods. In FP6 and FP7 the focus was still on technological research, in Horizon 2020 the focus is on innovation-driven research (including support for research infrastructures), developing technologies that support European industries and connecting research results to market, and, finally, benefits to the citizens including research on health, demographic change, food security, energy, and climate as well as secure societies. In FP6 and FP7 (2002–2013) the most important funding instrument was the "Collaborative Research" composed of a minimum of three partners coming from three different EU countries with a typical duration of 3–5 years. The research projects could address basic or applied research. In the context of the "Virtual Physiological Human (VPH)" initiative, more than 30 research projects were funded by the European Union. One of these projects listed is our case study Advanced Clinical-Genomic Trials on Cancer[6] (see Chap. 4) and its various follow-up projects such as p-medicine, INTEGRATE, or VPH Share. Another instrument of FP6 and FP7 were networks of excellence. Such networks were set up to strengthen scientific (and technological) communities in a particular research area through sustainable integration of the research capacities of the participants. As described in Sect. 5.3.2, the "Virtual Physiological Human Network of Excellence" was funded in FP7 to connect the various VPH research projects and to foster the development of educational, training, and career structures in the communities related to VPH and systems biology.[7]

For Horizon 2020 (2014–2020) the funding type terminology has changed according to the general orientation toward innovational research and market-ready

[4] Original quote: "einen Beitrag zur Aufklärung der zugrunde liegenden Mechanismen bei der Entstehung von komplexen Erkrankungen zu leisten"

[5] Original quote: "Möglichkeit zur Vorhersage von Möglichkeiten für eine gezielte Intervention bei der Entstehung von Krankheiten."

[6] http://vph-portal.eu/projects. Accessed January 26, 2015.

[7] http://vph-portal.eu/vph-noe-home. Accessed January 26, 2015.

products: (1) “Research and Innovation Action Projects” (RIA) may get 100% funding because they are not close to market. (2) “Innovation Action Projects” (IA) only get 70% funding; they are close to market and especially target small and medium-sized enterprises (SME). (3) “Coordination and Support Action Projects” (CSA) are studies, networking, and distribution of results getting up to 100% funding (but not meant for research). In addition, there are other new funding instruments such as prizes and pre-commercial procurements.[8]

In Horizon 2020, life science research is addressed in the third funding priority of societal changes, in particular in the programs of health and food security, but also in the second funding priority (e.g., biotechnology programs) and in the first pillar (e.g., research infrastructure programs). According to the EU office of the German Federal Ministry of Education and Research (BMBF),[9] the total funding budget for the life sciences has increased from 8 billion euros in FP 7 to 13 billion euros in Horizon 2020.

5.1.3 Method

The empirical material and evidence used in this chapter consists of transcribed interviews with actors from different groups that are described below in more detail. In order to capture the different perspectives on science policy, a wide range of actors involved in the discourse were invited for interviews. Included were representatives from science, media, industry, and nongovernmental organizations, public interest groups, research funding, and science policy. The interview method was adapted to the individual interviewee and the actor group to whom he or she belonged.

5.1.3.1 Scientific Actors

The empirical material used in Sect. 5.2 is based on 23 interviews that were conducted with scientists working in systems biology in Germany. The scientists were identified by the following search procedure. First, a literature review was undertaken which used the *PubMed PubReMiner* to locate all scientific reviews available of 10 leading authors. PDF-files of the reviews were downloaded and studied as outlined in Grounded Theory (Glaser and Strauss 1967). The categories brought about by this analysis revolved around the conceptual history of systems biology, explanations of what systems biology is, the assessment of current research undertaken, possible areas of application, basic theoretical concepts applied or defined, and the outline of important future research tasks to be addressed. Results were

[8] http://ec.europa.eu/research/participants/data/ref/h2020/grants_manual/amga/h2020-amga_en.pdf. Accessed January 26, 2015.

[9] http://www.nks-lebenswissenschaften.de/de/1075.php. Accessed January 26, 2015.

gathered and correlated to tackle thematic overlaps and divergences. This research was supported and extended by a close reading of edited volumes and introductions to systems biology. Once this conceptual overview was generated, a second round of research started in which the *PubMed PubReMiner* was used to find publications of German scientists: 23 German authors found in the database were located and contacted via e-mail. The sample consisted of heads of institutes, group leaders, and post docs to cover the full range of professional experience and views on systems biology available.

In the meantime, a semi-structured questionnaire was developed based on the literature research undertaken. Five topics were addressed in the interviews: (1) the nature of systems biology (2) the history of systems biology, (3) basic concepts applied in systems biology, (4) national and international differences in doing systems biology, and (5) assessment of possible futures of systems biology as seen through scientists' eyes. Data were taped with a tape recorder, fully transcribed, and analyzed by applying a linguistically (Wetherell et al. 2002, 2003) informed grounded approach (Charmaz 2006; Clarke 2005). This methodological combination was chosen because it productively places emphasis on the deductive development of analytical categories from data and is easy to combine with the analysis of linguistic structures. Once main themes or topics emerged during the process of analyzing data, segments of transcripts were grouped under emergent headings, and significant linguistic structures were analyzed that substantiated ad hoc categories. In doing so, an underlying and saturated semantic network of categories permeating the different topics addressed in the interviews became available. These were then systematized and analyzed from an interpretative point of view.

The second series of interviews is part of our case study of the EU-funded project "Advancing Clinico-Genomic Trials on Cancer: Open Grid Services for Improving Medical Knowledge Discovery (ACGT)" presented in Chap. 4. Here, we refer to 18 interviews conducted with consortium members. Structured questionnaires were used for the interviews. The questionnaire regarding the ACGT research project consisted of four sections addressing the following topics: (1) experiences of scientific and practical cooperation in the project collaboration (in particular interdisciplinary negotiations), (2) experiences regarding the realization of the ACGT infrastructure, (3) judgments regarding the project outcome and science policy, (4) judgments regarding the anticipated profit of ACGT for cancer research and systems biology.

To select the 18 interview partners according to their visibility in the ACGT project, we conducted a bibliometric analysis of the collaborations for internal publications (deliverables) and external publications (peer-reviewed articles, books, conference proceedings). Additionally, we drew on their designated tasks within the project (e.g., work package leadership, project management, quality control). The interviews were digitally recorded, anonymized, and literally transcribed. The empirical results are based on qualitative content analysis by using the software MAXQDA 11. Below, the interview citations are characterized by the professional background of the interviewee.

5.1.3.2 Societal Actors

The governance and policy analyses presented in Sect. 5.3 draw from interviews with German experts. In addition, written documents were analyzed that were deemed relevant to the establishment or evaluation of systems biology. The criteria for selecting of both the interviewees and the documents was their belonging to or close affiliation with the media, industry, public interest groups, research funding, science policy bodies, or administration. For the interviews, actors were identified who possess "technical, processual, and terminological knowledge that relates to [...] [a] specific or professional field of action" (Bogner and Menz 2005, 46). Thus, they can be considered as informants who "possess knowledge that is not available from other sources" (Littig 2008, paragraph 12) and command the power to enforce or champion their own orientations and conceptions within their profession (cf. Bogner and Menz 2005, 46). We thus selected interviewees who do not only have their own informed and specific perspective on the field but who bear, to some degree, an impact on the establishment of systems biology and thus have subtle power (Stehr and Grundmann 2010, 57).

Selection of the interviewees was initially based on a theoretical sampling (Flick 2000, 58). Basis for sampling was a comprehensive media analysis of the German press coverage that enabled us to gather first hints with regard to major players in the field. Other clues came from an analysis of central policy documents and from a formal analysis of persons responsible for science policy in political parties. In selecting interview partners from these fields, we paid attention to maintain political balance in order to avoid bias. Actors from research funding, the science policy, and administrative area were selected on the basis of existing research programs and chosen in order to maintain a balance between the main funding institutions. A similar approach was followed for actors from industry and public interest groups. To represent the media, such authors were contacted who have consistently written about systems biology and/or are known to have a good overview of the life sciences. In selecting the interviewees, we included the results of the document analysis to complete the sample. In total, we interviewed 10 actors from the different fields in Germany.[10]

For the interviews, a semi-structured questionnaire was developed. It consisted of an actor-specific and a general part. The specific section of questions differed depending on the actor area. We asked, for example, for the understanding of systems biology, its state of establishment, research funding, application, its implications, and the role of the general public in science development and governance.

The analysis of the interviews was carried out according to Meuser and Nagel (1991): First, the interviews were fully transcribed and anonymized. As a next step, we paraphrased and sequenced the individual transcripts and created headings

[10] As part of the THCL research project, we also conducted and analyzed interviews with Austrian representatives of media, industry, and public interest groups, research funding, science policy bodies, and administration. These outcomes and a comparison between Germany and Austria will be published elsewhere.

(categories) for individual statements. We then compiled topically similar statements and provided a corresponding main heading for each topic.

In the following three sections we discuss the social and scientific dynamics that result from this kind of research funding and development. Furthermore, we look into how the discourse on science policy of systems biology can be characterized looking at representatives from science, media, industry, and public interest groups, and from research funding and science policy. Thus, Sect. 5.2 discusses science policy from the scientist's view, Sect. 5.3 from the public's perspective, and Sect. 5.4 discusses the interdependencies between scientific actors and the public.

5.2 Scientific Actors' Perceptions of Science Policy

Scientists are an important target group of science policy. Research and development (R&D) programs usually address researchers working at universities whereas some specific programs explicitly include research departments of companies or research organizations as well (e.g., Fraunhofer Organization). The main aim of R&D programs is to ensure the marketability of research and to bring science and industry together. Hence, scientists are requested to contribute to applied research and to establish contacts to industry if they want to participate in such funds. Furthermore, because successful university careers nowadays depend more and more on successfully raising external funds, competition on claiming funds from national and EU R&D funding agencies for doing research is high. To this effect, the landscape of research is changing in terms of research goals. In addition, researchers have to define and to manage their research activities according to funding strategies.

The following section analyzes how—from the scientists' perspective—funding programs are structured and how scientists assess and strategically cope with funding mechanisms. The final section summarizes the findings of both sections, combines them, and reflects on the interdependency of trends in funding and developments in research. The research question we address is threefold. How do funding mechanisms exert an impact on the research landscape in terms of exploitation of research results and development of research fields? What is their impact on establishing research agendas? In what way do these mechanisms contribute to doing research and developing academic careers?

5.2.1 Funding Mechanisms

Let us now turn to the first section in which the reflections of our scientific interview partners are analyzed with regard to funding mechanisms. This is important in order to find out, in which way research activities related to systems biology are or have been established and maintained.

5.2.1.1 Contents of Funding

In the interviews, emphasis is put on R&D programs such as Horizon 2020[11] run by the European Commission (see Sect. 5.1.2). The interviewees stress that the primary focus of R&D funding is research with the future goal of application, but not development of technology, a point that became apparent in the interviews with scientists having worked in the ACGT project on the development of a sustainable ICT infrastructure (see Chap. 4). From a more general perspective, the interviewees refer to research done in the context of such R&D programs in the sense of raising new research questions, defining research objectives, evaluating alternatives, and coming up with innovative solutions to address and answer the research questions and agendas set up by the research agencies.

With regard to new fields of research, one of the key questions is how such fields and targets of research are being selected and defined. This is usually done by national and international funding agencies and programs which in large define topics and substance of such programs via the themes addressed in their calls. Looking at the calls in a research field such as the life sciences from a chronological perspective, they represent common trends in funding domains. As the following quotation shows, these trends exert an impact on current trends and future developments in research. Using the example of the priority of funding research on simulation in systems biology, one member of the ACGT consortium explained who in his view is responsible for this trend in research, which was funded by a series of different funding initiatives of the European Commission (FP6,[12] FP7,[13] Horizon 2020):

> I think, if somebody has to look for reasons, I think, these have to do with the way they are running the procedures in the selection of projects and the design of the research policy. In that sense, I would mainly consider the EU director somewhat responsible for this kind of research. So, if you have a closer look to the genealogy, let's say, to the succession of projects, they tend to have certain lineages with most of the same people being in the same lineages. That means that they do not implement a really open approach in the selection and I suppose this reflects somehow their political agendas. But this of course isn't fair. But at the same time it also reflects some of the procedures in the selection of the projects. In that sense, I can be a bit more specific. There are particular lines of research especially in this particular area we are talking about, systems biology, that tend to do with simulation of particular systems and it appears that they have been pulling money in that kind of research activities, practically paying again and again for the same kind of hypothetical applied research. That is an exercise that is not going to yield significant results. So I would expect this kind of decisive bodies to be more careful with the kind of selection and spending of public or common funds. (I6, BioMed)

Apparently, the interviewee holds the opinion that the funding system is a more or less private and possibly a closed circle. This is indicated by the metaphors used from kinship terminology ("genealogy," "lineage"). A succession of projects related to the respective trend is usually funded. At the same time, scientists who were able

[11] Horizon 2020, ec.europa.eu/programmes/horizon2020/. Accessed January 26, 2015.

[12] FP6, ec.europa.eu/research/fp6/index_en.cfm. Accessed January 26, 2015.

[13] FP7, ec.europa.eu/research/fp7/index_en.cfm. Accessed January 26, 2015.

to integrate themselves in the funding lineage are usually able to receive funding for successive projects in the trend domain. These participating researchers build social networks to apply to and to receive funding together in certain research areas. In particular the ACGT consortium stressed that they were able to build a stable community which succeeded in receiving funding for continuing research together after ACGT had ended. Scientists already participating in one of the funding lineages also support science policy organizations in seeking new trends for funding strategies at the same time. One of the ACGT consortium members provided personal insights of how science policy representatives interact with scientists in the research domain of ICT in the life sciences:

> These so called experts [science policy representatives] are talking to people trying to get their antenna on what is the next big thing, and who the cools are, and who should I speak to in order to draw my next new program? So there is very much dependency on whom you talk to and who will paint the best picture. I will never forget, for example, a statement once by an EU functionary, whose role at the time was to contribute to the work program. I think, this was work program five and they were tasked with writing the ten pages that we receive for the part of ICT in the life sciences. So these poor guys are talking to people like you or me or whoever saying 'Come on guys, help me to write the paper. I've got to write ten pages that will then become the policy booklet of the commission'. And it has to be slightly different from what they wrote four years ago, because otherwise the politicians will say,we have paid for this four years ago!' So they have to come up with new buzzwords. You know, for me this is very silly. I don't know, but it is inevitable. For example, in ACGT we were talking about the Grid. Tell me about the Grid. Now it is about the Cloud. We haven't even solved the problems of the Grid and now it's the Cloud. Why? Because now the Cloud is the next big thing. It is essentially, if you look at it, the same concepts with different clothes. And there is this issue as well. It is like the engine, you know, life goes on, therefore, it has to go on. It has to go, it has to go on. So how do we keep it going on? It is easier to come up with a new dress than to say 'I'm losing my hair or my body is fat. I need to lose weight.' This is more difficult than if I go and buy some fancy clothes and look nice. (I4, IT)

To receive continuing funding for their research, scientists are willing to deliver and follow new buzzwords or, according to the interviewee's metaphor, to present "the same concepts with different clothes." At the same time, the quotation illustrates that the interaction between scientists and science policy representatives leads to scientists contributing or even initiating their own funding programs by delivering new buzzwords for continuous research.

However, scientists sometimes want to give their research a push into a new and different direction. Then they have to find new options of how to receive funding for their upcoming research interests in addition to the established tracks. If the research area is not on the funding agenda yet, one possibility is to try to attract the attention of science policy organizations to set up a new program. However, this is only possible if the respective scientists play a prominent role in the organization. Such individuals may be labeled as science managers exerting political influence to initiate shifts and redeployments in the distribution of funding. To this effect, one interviewee of the systems biology community in Germany described the role of an individual systems biologist in the science policy initiatives of the German Federal Ministry of Education and Research and the European Union to establish systems biology.

> I think it started with these activities that he [the scientist] did for the BMBF [German Federal Ministry of Education and Research] and that then positioned and supported him there. Um, that he acted like a mover and shaker who said, ‘we have to press forward with this’. At the time, I was much too naïve, for example […]. I was the kind of person who, if there was a program, then I applied to take part in it. But I would never have had the idea to go to Brussels and tell them that there should be this kind of program that I would like to have. (I19)[14]

Scientists who proactively approached the science policy organizations in Berlin and Brussels in the view of the interviewee played a crucial role in setting systems biology on the funding agenda. However, science policy representatives of the funding organizations are the necessary teammates to let the funding initiative become real, as the interviewee carried on.

> […] The BMBF played practically the biggest role. Because I already said I assume that the role that he [the scientist] played in the beginning, that that was also decisively linked to the activities of the BMBF. And this impression that the funding organizations like the BMBF and the EU were actively, that is, not reactively, but actively trying to establish this field. So, the BMBF then said, ‘okay, we’ll do [it], we’ll set up a program. But we’ll try to do it not just in Germany, but push for it in parallel at the EU level’, and then bringing this conference to Germany and all that. And it isn’t … it wasn’t the scientists who were knocking down the doors, it was individual people in the ministries who are really proactive and also incredibly motivating. (I19)[15]

To sum up, the cited quotations show that science policy organizations are positioned in between the political and the scientific spheres. They have to be accountable to the political representatives and have to address the scientific community at the same time. The interviews also illuminate that functional interrelations are deeply interwoven with personal relationships. To receive funding or to make a career in research, scientists align with others to develop stable social networks in order to apply and receive funding. Once they have become part of one of the funding lineages, they may stand a good chance to receiving continuous funding.

[14] Original quote: “Ich glaube, das ging los mit diesen Aktivitäten, die er [der Wissenschaftler] fürs BMBF[Bundesministerium für Bildung und Forschung] gemacht hat und die ihn dann dort auch positioniert haben und ihn unterstützt haben. Äh, dass er aufgetreten ist als ein Macher, der gesagt hat, wir müssen das vorantreiben. Da war ich zu dem Zeitpunkt zum Beispiel auch viel zu naiv […]. Ich war so jemand, der, wenn ’s da ’n Programm gibt, dann hab ich mich da beworben. Aber auf die Idee zu kommen nach Brüssel zu fahren und denen zu sagen, dass es so ’n Programm geben sollte, das ich gerne hätte, wär ich damals nicht gekommen.” (I19)

[15] Original quote: “[…] Das BMBF hatte fast die größte Rolle. Weil ich ja eben schon gesagt hab, ich vermute, die Rolle, die er [der Wissenschaftler] gespielt hat am Anfang, auch maßgeblich mit den Aktivitäten des BMBF verbunden waren. Und das hat sich, dieser Eindruck, dass die Geldgeber wie BMBF und EU, aktiv, also nicht reaktiv, sondern aktiv darum bemüht [waren], ein Gebiet zu etablieren. Also das BMBF hat dann gesagt ‘okay, wir machen [das], wir setzen ‘n Programm auf. Aber parallel versuchen wir das nicht nur in Deutschland zu machen, sondern auch auf EU-Ebene voranzutreiben’, und dann eben diese Konferenzen nach Deutschland zu holen und so. Und das ist nicht … das waren nicht die Wissenschaftler, die die Türen eingerannt haben, sondern das sind einzelne Personen in den Ministerien, die wirklich proaktiv sind und auch unheimlich motivierend.” (I19)

Beyond that, a few scientists, the so-called science managers and makers, hold a prominent role because they know the network and the structure of the interrelated spheres which to a large part they established themselves. They proactively approach the science policy representatives to have direct influence on funding policy. Social networks between science policy representatives and scientists emerge because they jointly tackle upcoming trends in science and lobby for funding. These successful scientists usually become prominent in scientific networks and in the emerging branch albeit so-called funding lineages clearly display self-referential features.

5.2.1.2 Structure of Funding

National and EU-funding programs mainly support research projects that are expected to be accomplished within a limited budget and timeframe. Generally speaking, a project is defined as a joint enterprise that is carefully planned to achieve a particular aim.[16] Consequently, especially EU-funded projects are structured in multiple tasks that are assigned to different work packages. Such packages are designed to achieve specific goals and they are handled by teams of scientists coming from one or more research sites to deal with the assigned tasks. The work packages are the smallest components of the project and the time schedules, the workflows, and the budgeting of the project are allocated to them.

Many calls for proposals define applied research topics. As such calls target predetermined objectives, the project structure outlined above is particularly suited for applied research. Therefore, the funding structure especially pushes problem-oriented approaches within research domains. This might include specific methodological approaches as well, as one of the German systems biologists explained with regard to funding programs in systems biology:

> […] nowadays a systems biology project, that is, a proposal with systems biology in the title, requires certain ingredients. You have to use certain high-throughput methods in order to see what's happening. You have to use mathematical models. That's an absolute must today. Without mathematical modeling, it's practically impossible to get funding for a proposal. (I21)[17]

To prioritize research proposals using a specific method or approach is regarded as a necessary requirement to establish new approaches within established research areas. The integrative role of mathematical modeling for systems biology is often brought up in the interviews. The interviewees refer to mathematic modeling as a

[16] See Oxford English Dictionary, www.oed.com/view/Entry/152265?rskey=8tUCpe&result=1#eid. Accessed September 3, 2014.

[17] Original quote: "[…] heutzutage [gehört] zu einer systembiologischen Projektstudie, also zu einem Antrag, der überschrieben ist mit Systembiologie, dass bestimmte Ingredienzien drin sind. Man muss bestimmte Hochdurchsatzmethoden benutzen, damit man ganzheitlich sehen kann, was passiert. Man muss mathematische Modelle verwenden. Das ist heute auch ein absolutes Muss. Ohne mathematische Modellierung können Sie kaum noch 'n Antrag durchkriegen." (I21)

method for integrating knowledge and as a tool for verifying knowledge with regard to consistency.

In systems biology, mathematical modeling is usually used in order to tackle research questions related to medical or biotechnological applications of biological knowledge. This problem-oriented approach is characterized by its interdisciplinary nature. However, crossing disciplinary boundaries in interdisciplinary teams is always challenging (see Sect. 4.1.2); this may be the reason why interdisciplinary research units are seldom found at universities but in larger research institutions that are especially equipped for this type of research, such as the Helmholtz Association. Compared to other countries, it is often stressed in the interviews that the institutionalization of systems biology is relatively poor in Germany. Departments of systems biology where mathematicians, physicists, chemists, and biologists are working under a single roof are strongly requested by the interviewees to establish the systems approach in biology permanently, but they do not exist yet.

One of the essential preconditions to receive funding for establishing systems biology and conducting systems-oriented biomedical research is collaborating in interdisciplinary research projects. Joint projects are usually the first link between the involved disciplines.

> That wouldn't have been possible in the past. All of a sudden, you're directly connected to clinical research, with the people who are basically operating on the ground—that's great! That's, well, I think that's something very important. Scientists are coming together who would certainly never have come together in the past, when systems biology didn't exist as a roof, as a funding roof, well, who wouldn't have been forced to integrate with each other. (I23)[18]

As the quotation shows, the funding structure and its strategies to supporting systems biology—metaphorically described as a roof—coordinate and establish systems biology as an interdisciplinary approach. However, another German systems biologist expressed in the interview that the interests of scientists in interdisciplinary working collaborations are in general limited. In most cases, it is only the higher likelihood to receive funding for their own research that lets scientists get involved with other disciplines. Our interviewee described that he wrote enquiry letters to his colleagues asking for interdisciplinary collaboration before the funding programs for systems biology came up.

> Zero interest. And then, when these programs came up, all of a sudden it worked. That means, you have to give the funding organizations credit for that. (I6)[19]

Another scientist of this interview series goes one step further and wants to turn the scientific culture of biology towards a culture of interdisciplinarity.

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[18] Original quote: "Das wär früher nicht möglich gewesen. Auf einmal ist man mit der klinischen Forschung direkt verbunden, mit den Leuten, die sozusagen vor Ort das operieren—toll! Das ist, also das halte ich für was ganz Wichtiges. Wissenschaftler kommen zusammen, die früher mit Sicherheit, wenn es das Dach Systembiologie auch als Förderdach nicht gäbe, äh die nicht gezwungen gewesen wären sich zu integrieren, die wären nie zusammengekommen." (I23)

[19] Original quote: "Null Interesse. Und als dann diese Programme auftauchten, auf einmal funktionierte das. Das heißt, das muss man den Geldgebern anrechnen." (I6)

> A culture of large projects [has yet to] develop in biology. People usually respond to that by saying, 'But they do exist! That Human Genome Project.' But that's of a completely different nature. All you had to do in that project was to sequence. In other words, set up devices here and there. And all of them were independent of one another. So, although that's an example of a large international project in biology, it isn't what I described, where the partners in the various countries with various technologies and various research questions are dependent on each other. (I24)[20]

From this it follows that interdisciplinarity can only develop and prosper in a scientific culture in which disciplinary research is integrated not only in terms of methods but also in terms of common research questions and goals. Interdisciplinary work, using different methods and technology to investigate different research questions, is dependent on a collaborative environment and a common roof. It can be said that the project structure outlined above as a frame for collaboration is a constitutive part of the vision to widen the scientific culture of molecular biology towards interdisciplinary systems biology. However, the last quotation refers to structural aspects of integration only; conceptual integration of research results, for instance, is not addressed. But conceptual integration is needed to pave systems biology's way toward the formation of an independent epistemic culture.[21]

Interdisciplinarity offers not only new prospects, but also points to new challenges. Let us now turn to the constraints and obstacles posed to systems-biological projects and their funding mechanism in general.

5.2.1.3 Constraints by Funding Mechanisms

As described in the previous section, research projects are basically structured in work packages in which consortium partners work together on specific research questions and tasks. The pieces of work have to be aligned and bound together and to be interrelated with other work of the research project and with its objectives. In the interviews it is often stressed that the integration into the whole, the entirety of the overall project, is the most challenging task. It is therefore usually coordinated and supervised by the project management being responsible for the progression of the project and its coherence. However, one of the ACGT consortium members pointed out that most partners do not work enough on what he metaphorically called "the glue".

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[20] Original quote: "[I]n der Biologie [muss sich] eine Kultur für Großprojekte entwickeln. Darauf sagen die meistens immer: 'Gibt's doch! Dieses Human Genome Project.' Aber das hat 'ne ganz andere Natur, und zwar hat man dort nur sequenzieren müssen. Das heißt, Geräte sich hierhin gestellt und dahin gestellt. Und alle waren voneinander unabhängig. Also das ist zwar ein Beispiel für ein internationales Großprojekt in der Biologie, aber es ist nicht das, was ich beschrieben hab, wo die Partner in den unterschiedlichen Ländern mit unterschiedlichen Technologien an unterschiedlichen Fragestellungen voneinander abhängig sind." (I24)

[21] Epistemic culture is a prominent concept in Science and Technology Studies referring to the practices and beliefs that constitute a culture's attitude toward knowledge and its way of justifying knowledge claims. Based on this concept, various settings of knowledge production have been identified and distinguished by stressing their contextual aspects (Knorr-Cretina 1999).

> [T]he glue is the work that every partner needs to do on top of what they do, on top of their daily business, to make their work stick with the work of the others to have the integrated whole. And in my experience,—I have a lot of experience with EU projects, many years with EU projects—this is a very weak point of EU projects. And the bigger the consortium, the bigger the problem. Because everybody tends to do their own little bit. We tend to scramble together before the reviews to do the general thing and then there is not a lot of thought going into the whole. So generally speaking, I think collaboration is suboptimal I would say. (I4, IT)

Whether an interdisciplinary collaboration in a research project functions, depends on many different factors. In the quote cited above the size of the project is mentioned. Another factor is, again, how experienced the project partners are in interdisciplinary work and how heterogeneous in terms of disciplines the consortium is. The more heterogeneity, the more time the group needs to become acquainted, to get to know each other's strengths, to overcome disciplinary mindsets, and to agree on shared concepts and terminology (see Sect. 4.1.2). In addition, project partners may join the consortium for very different reasons and interests. They also have to be aligned in order to be able to reach the objectives of the project.

> I think it is a case of alignment from the project proposal stage on. So usually, if you have had this experience, there are one or two people who have the big idea and then they are scrambling to find partners for the different parts. Now these partners might buy in or they might join the project just because it is good money. And not a lot of thought is put in after the project is accepted for funding. So that is one. I think there are diverging agendas or interests. Not done on purpose, but just because that is the way it is. And the incentive is not enough from the project itself. […] The universities are pressured to get funding not only by the state. So you need to do competitive bidding. So that means that there is a lot of…, you know, you accept to become a member of a project just for the money rather than the absolute interest. Then there is, I think, also this divergent on the technical level whereby there is not a very close match, or the match is imposed from the top, let's say, from the project structure and you do what you have to do. (I4, IT)

To ensure that the project partners share the project's objectives, or—according to the interviewee's wording—to assure that the glue is working, the project management needs to stick to the project's aim and to communicate the project's goals to the partners. According to the interviewed ACGT consortium members, this is often a problem in EU projects. In particular, uncertainties about the target exploitation of the research project were addressed. Many of the interviewees said that they had no clear expectations in the beginning of the ACGT project regarding its prospective outcomes. Some interviewees would have been satisfied with a research prototype of the developed ICT infrastructure as a final result of the ACGT project and very few expected an implemented infrastructure by the end of the project, which was, according to the project proposal, in fact the explicit target of the ACGT project (see Sect. 4.1.1). One of the ACGT consortium members pointed out that R&D projects need, at least at the EU level, a broader understanding of what exploitation might mean in its specific context:

> Because every time you start an R&D project, the first question that they [the European Commission] ask you is 'how are you going to exploit the results?' Of course, you expect

> the results, which could be patented, could be prototype of systems, etc. But there is a need to understand that it is a different… and there are a lot of exploitations that are taken place, of exploiting your individual outcome. Whether it is a technology outcome or whether it is knowledge or expertise, etc. And it is a different issue as I have already said, to try to exploit an infrastructure. An infrastructure should be seen as a service to a community and I think the Commission is now […] realizing that yes, you need on the European level a much more longer termination and dedicated groups who are not only focusing on addressing research questions, but also focusing on making quality production systems and infrastructures that can then be utilized by the wider community. (I7, IT)

The quotation reflects on the definition of exploitation in R&D projects, asking what could be understood as an exploitable result. Another issue, which was raised even more often in the interviews, was the appropriate timeframe necessary to get beyond results and succeed in exploiting them in a different context. As the national and EU funding programs usually limit the duration of a research project to three, four, or sometimes five years, the timeframe was often regarded as too restrictive and too inflexible. In particular, it was criticized that the time allocated by the budget may not match with the project's objectives and that such a mismatch is usually charged to the debit of the project's exploitation. Many of the ACGT members described such a dilemma concerning the expected and realized exploitations of their project. One of them said:

> I see an intrinsic problem in the way European projects are being defined. Because they ask you to focus specifically on research while building a production system. This requires much more effort exactly for implementation, that they wouldn't like to fund anyways, because it would not be research. It would be implementation. So as long as the funding is for research, at the end you end up with a research prototype and then you really need to find ways to turn that into a production system. (I2, IT)

At least in the case of the ACGT project, it seemed very difficult to fulfill the targeted expectations. "We hope that we move closer to a better exploitation through the follow-up projects," the interviewee cited above continued. However, the funding stops after termination and the partners of a current project usually do not know if they will be able to continue their collaborative work. This means that exploiting results is usually something researchers must do outside the time frame of the project. Sometimes follow-up proposals are prepared during the runtime of a project depending on the upcoming calls. But decisions on proposals take time and a smooth transition from project to project is more than unlikely.

> It's difficult for any European project to come out with something as a whole, because it's simply not built for it; the funding mechanism. The only thing that they do is they give you three, four or five years of time to build something and there is no follow-up. The funding stops and it is done. So there is no incentive to actually build something that can last. (I11, IT)

Hence, the ACGT consortium was not successful in building up a lasting infrastructure at the time when the original funding stopped, even though the ACGT consortium was very successful in applying for follow-up funding. The ACGT consortium was able to become part of the funding lineage on ICT in health and many consortium members have therefore been able to continue the collaborations initiated during the lifespan of ACGT still working together on ICT infrastructures, mainly in the domain of systems research in oncology. Nevertheless, in the interviewees' view, not follow-up projects but an extension of the ACGT project would have been the best solution with regard to exploitation.

> The duration of the project was simply too short. It just can't be done in four years. And I think it would actually have been much more practical if the ACGT project had run for eight years. So if people had continued to work in the group, like in the follow-on project p-medicine, that is, entirely new partners, entirely new constellation, entirely new goal. Actually, a lot was thrown away from ACGT. (I15, IT)[22]

> Continuing it in p-medicine, that meant a disruption again. It's true that individual components were used again, but in principle, if people had really wanted a stable environment, then they would have had to say, 'Okay, everyone with any significant involvement will get time and money again to develop precisely the same thing further.' A new system is being created yet again in p-medicine. Based on a slightly different technology. That means that whole procedure is beginning all over again, the definition of the architecture and then agreeing on standards, and so on. That means, another entire loop, and that raises the question again how far you'll get in the end. (I12, IT)[23]

Inspecting the broader picture of EU funding in the field of ICT applied to biomedical questions and problems, several research projects with very similar intentions and goals can be found that have been or are funded simultaneously or consecutively. As the example of ACGT follow-ups illustrate, they may be part of one of the funding lineages we discussed above. However, they may also be part of different funding lineages. In health-oriented programs, for example, medical projects with ICT components are funded, and in programs focused on ICT, technological projects with clinical components are supported. Altogether, conceptual integration of research developments seems necessary to prevent double funding. However, as long as the funding structure is based on timely restricted research projects with no option of extension or integration respectively, double funding will be an intrinsic part of the funding system.

[22] Original quote:"Die Projektlaufzeit war einfach zu kurz. In vier Jahren kriegt man das halt nicht hin. Und ich meine, eigentlich wäre es viel praktischer gewesen, wenn das ACGT Projekt acht Jahre gelaufen wäre. Also man dann halt in der Gruppe weiter gearbeitet hätte als wie jetzt das Anschlussprojekt p-medicine, also noch mal komplett neue Partner, komplett neue Zusammenstellung, komplett neue Zielsetzung. Also aus ACGT ist eigentlich sehr viel weggeschmissen worden." (I15, IT)

[23] Original quote: "Die Fortsetzung in p-medicine ist schon ein Schnitt gewesen wieder. Einzelne Komponenten wurden zwar genommen, aber im Prinzip hätte es ja so sein müssen, wenn man wirklich eine stabile Umgebung haben will, dann hätte man sagen müssen, 'So, alle die wesentlich daran beteiligt waren, kriegen jetzt noch mal Zeit und Geld, um genau dieses jetzt weiterzuentwickeln.' In p-medicine entsteht auch wieder ein neues System. Basiert ja auch auf einer leicht anderen Technologie. Das heißt, diese gesamte Prozedur fängt wieder von neuem an, die Definition der Architektur und dann die Einigung auf Standards und so weiter. Das heißt, wieder eine komplette Schleife, wo dann eben auch die Frage ist, wie weit man am Ende kommt." (I12, IT)

5.2.2 Scientists' Reactions to Funding Mechanisms

After having discussed the basics of funding mechanisms in interdisciplinary, systems-oriented research in the life sciences along with constraints exerted by these mechanisms and its consequences we now look at how the scientists react to it.

University careers today depend to a considerable extent on the success of raising external funds. As a rule, applicants for scientific appointments have to prove that they are capable of participating in the competition of receiving funding from national and international funding agencies and programs. The funding either pays one's own job or the one of PhD students and post-docs within one's working group. Hence, successful work and careers of young researchers mostly depend on external funding. Private companies, institutes, and research associations are applying for public funding as well. As discussed in Sect. 4.3.1, they are primarily seeking to be involved in academic research. For them, social networking with academia is important to be at the front line of research, to understand future trends and take them up early, and to be directly involved in innovative developments.

These different groups and interests align together to social networks that apply collectively for money. As illustrated in Chap. 4, the network originated in the ACGT project concentrates, for example, on EU funding to continue its research and established working collaborations. The network has established itself in the funding lineage of ICT for health. "Over time you see the groups that are good keep getting the projects. So I think over time, there is a congregation of the good," said one ACGT consortium member (I4, IT). To be successful in receiving the funding therefore is synonymous with, first, to be good in evaluating trends in science policy and, second, in detecting innovative trends in research that match with the trends in science policy. Using the development of the oncosimulator as an example (see Sect. 4.2), one of the interviewees explained that having a good sense for trends has a lot to do with the right intuition or, in other words, with tacit knowledge (Polanyi 1958).

> But … and I don't really know why we introduced… I mean in ACGT we introduced knowingly a specific work package through the work of the group of Georgios Stamatakos and other individuals who even then were for years working on a more systemic approach to cancer modeling trying to model and understand cancer evolution as a system, as a phenomenon that evolves rather than simply trying to either define gene signatures or selected elements of information that could be used to predict or validate specific hypothesis. And I think that it was anticipation and of course one does that because, as I said, you have information, you understand or you make a prediction of how things will evolve in the research domain and sometimes you are right, sometimes you are wrong. It seems that we were correct in predicting these dynamics of the field, which gradually through the evolution during the course of ACGT and afterwards… I mean more and more the emphasis both in the ICT domain through the VPH type of projects, but also in the health program, the emphasis is more and more trying to understand living systems as systems. Therefore, systems biology and modeling at various levels of biological complexity, etc. They became very important and as a result, I think, we were we as a group, as a large community of people involved originally in ACGT, we've been very successful after ACGT in various subsequent efforts. (I7, IT)

In silico medicine is one of the prominent targets of the current EU funding program Horizon 2020. It is integrated in different funding domains, such as ICT, health, or emerging technologies. The development of the oncosimulator is therefore placed in a strong funding lineage that was started in FP6 in some of the research projects of the VPH-initiative and has accumulated many grants. As presented in Sect. 4.2.2, the former ACGT consortium member developing the oncosimulator—the In Silico Oncology Group at the Institute of Communication and Computer Systems, National Technical University of Athens—is now participating in numerous projects funded in the EU programs FP7 and Horizon 2020. One of the interviewees explained the success of the In Silico Oncology Group in receiving EU funding by the alignment of research interests with the vision of the future use of systems biology held by the European commission.

> The commission itself has realized that such an approach, the integrity of the systems biology approach, can use in various terms in order to describe the same or almost the same vision. So the vision of the European Commission is absolutely in line with the vision concerning the oncosimulator. And what differentiates the Virtual Physiological Human with in silico medicine is the emphasis to be put on the clinical adaptation and validation of complex biological models dealing with disease primarily. (I8, IT)

From the perspective of the individual scientist, the social networks in the funding lineages are the basis for his or her orientation. What projects are successful in receiving grants and who is successful in submitting proposals? Accordingly, for scientists seeking grants, it is necessary to be acknowledged in the social networks that are established in strong funding lineages.

> A lot of these choices are dictated by who your buddies are and who gets in early on the project consortium as it is forming. And again this ties in… I think this is important. It is very much buddy driven. And social network driven. And why no and why neither and how do I bring somebody in… who do I bring in… so I need to address a specific concern of the call. So when the European Commission is drawing its work programs it is saying, you know, 'I think we should put money in this area.' So then they say, 'Okay, for this area I need to have this and this and that.' So it is kind of like a menu. For me as a proposal writer, I have to fit in. So in order to get my high marks, if I don't have someone who is convincing on exploitation then I've got to bring, let's say, BIOVISTA in. They will write a good one pager on exploitation and I will get good points. You know things like this. (I4, IT)

In particular, those teams are successful in the funding lineages that fulfill the interdisciplinary requirement that is usually part of the calls. One of the strength of the ACGT consortium was, for example, to overcome interdisciplinary problems and to merge into an interdisciplinary team. However, with regard to promoting university careers, the interdisciplinary focus of the social networks is not conducive. Academic careers at universities have to fit into the disciplinary profiles and standards and the national culture of the universities. Hence, instead of international interdisciplinary activities, disciplinary networking in the home country is a crucial factor for successful applications and appointments. One of the interviewees stated that the disciplinary-oriented tenures are an obstacle for interdisciplinary approaches in general.

> At the moment, the situation is that the disciplines and, the impact factor matters and that kind of thing, career concerns, work against such [interdisciplinary] approaches. Well, it isn't motivating for people to work in this field, and that's why it has to be promoted. (I23)[24]

As a result, the individual scientists are somewhat trapped. They are forced to raise as much grant money as possible in order to have a good starting point for a career in science. However, to succeed at least in the EU R&D funding system, they need to be part of and active in interdisciplinary networks. If one tries to make an academic career and to get tenure, this is often counterproductive because in this case one has to be part of national disciplinary social networks.

5.2.3 Concluding Remarks

The final section is dedicated to summarize the findings of the last two sections and to reflect on the interdependency of funding and science. What effects do funding mechanisms have on doing research and making an academic career? According to Norma Morris and Arie Rip (2006), it is undisputed that during the last two decades science policy has increasingly taken over the steering of scientific activities by allocating and distributing funds. The chronological succession of the calls for proposals illustrates scientific trends in funding initiatives. In the interviews, the trends in funding were associated with funding lineages in which certain groups or researchers received their funding. According to the analyses of scholars from the Science and Technology Studies, the biggest impact of science policy is in fact the trendsetting in research areas and the coordination of scientific networking (Reiß et al. 2013, 33). The interviews further illuminated that the scientists are basically willing to accept such trendsetting by funding organizations. Creating new buzzwords was one example of how trendsetting in science policy works and how scientists adapt to it by renaming their concepts, or metaphorically speaking, by dressing the same concepts with new clothes to receive continuous funding.[25]

Concerning the trendsetting, one of the interviewees assigned the responsibility for trends in research solely to the funding organizations, whereas other interviewees underlined the interaction between science policy representatives and scientific actors involved in policy making. Given the example of setting up systems biology programs, it was argued that individual scientists have had the political influence to initiate new trends in science policy and to initiate shifts and reallocations in the distribution of budgets. Ongoing interactions between these politically involved scientists and science policy representatives finally lead to social networks in which

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[24] Original quote: "Im Moment ist das so, dass die Disziplinen und die Impactfaktoren-Geschichten und solche Sachen, Karrieresachen, gegen solche [interdisziplinären] Ansätze arbeiten. Also es ist nicht motivierend für Leute in diesem Gebiet zu arbeiten, und deswegen muss man es fördern." (I23)

[25] See also Morris and Rip (2006, 256).

upcoming trends in funding and research are aligned and the distribution of the budget is negotiated.

In the interviews, the decisive framework conditions for receiving funding and, thus, doing research were not negatively evaluated. The interviewees explained that, to support or even establish new approaches or methodologies within a scientific domain such as mathematical modeling, it is necessary to prioritize certain proposals. However, the example also illustrates that the preconditions set by funding organizations definitely restrict the innovative potential of science and corroborate mainstream trends in research.

Currently, applied approaches of systems-oriented research in medicine is one of the most prominent trends on the research funding agenda in the life sciences (see Sect. 5.1.2). Michael Gibbons and his colleagues characterize problem-focused research carried out in a context of application as a new mode of knowledge production. The so-called Mode 2 knowledge is directly generated in its context of application in which the scientific problem arises, methodologies are developed, and outcomes are disseminated and used (Nowotny et al. 2001, 2003; see Sect. 5.3.2). From this it follows that Mode2 knowledge can only be achieved in interdisciplinary teams that work together for certain periods of time on specific problems (Gibbons et al. 1994, 4). Hence, the problem-focused funding agenda is complemented by certain funding mechanisms. First, grants for problem-oriented research are usually not given to support institutions or persons, but to finance time- and budget-limited projects. Second, projects, defined as collaborative undertakings to achieve specific objectives, are a very suitable structure for interdisciplinary research. As interdisciplinary research units are still rare, at least at German universities, grants from funding organizations are the best chance to work on interdisciplinary approaches. To this effect, the funding organizations have a leading role in coordinating and structuring interdisciplinary approaches. At the same time, the funding organizations frame the requirements of interdisciplinary research. Many interviewees stressed that interdisciplinary research needs funding mechanisms adapted to the challenges and conditions of interdisciplinarity. They also made clear that successful interdisciplinary collaboration cannot be achieved in the same time as established disciplinary research.

However, project funding as one of the basic funding instruments for interdisciplinary research was often criticized in the interviews. It seems difficult to ensure that all project partners share the project's vision and objectives, and direct their work toward the common goal. In particular, very heterogeneous interdisciplinary research consortia need more time than groups coming from the same disciplinary background to understand each other's concepts and mindsets. If the time frame of a project is too restrictive, the complexity of these processes often results in dissatisfaction and a lack of exploitation. To extend funding of ongoing research, scientists have only the opportunity to apply for follow-up research projects. Scientists' strategies are to adapt not only to trendsetting in science policy but also to funding instruments, for example, by dressing research they are working on with new clothes in follow-up research proposals.

Even if there are often up-coming calls in the same funding lineage, the discontinuity in funding has a negative impact on the established working collaborations. As a consequence, the scientists have to put a lot of effort into social networking to be continuously present and acknowledged in certain funding lineages. This is a dilemma for the individual scientist who is planning an academic career. He or she is forced to receiving as many grants as possible to get visible in the scientific community and to promote younger fellows. On the other hand, the scientist has to establish herself in social and local networks at the university. At university, the disciplinary orientation, for example, publishing activities in disciplinary high-impact journals, is an important career strategy. Therefore, research in the disciplinary established mainstream is usually given preference over interdisciplinary, risky, or long-lasting research (Reiß et al. 2013, 22). Hence, young scientists find themselves in a double-bind: they are institutionalized in a more or less monodisciplinary, local, and administrative structure, but have to fulfill at the same time the international and interdisciplinary funding requirements. Instead of doing research, becoming a scientist at a university seems to incorporate more and more management skills shaping the actual work context. In conclusion, funding mechanisms, in particular the prioritized funding of projects, have a complex impact on doing research and making an academic career. Generally speaking, time-limited funding programs are suitable to hook up with and give support to new emerging trends in research. However, for individual scientists, following funding lineages such as the ones generated to foster the establishment of systems biology and related approaches is risky, because their influence on important parameters is limited: on their future membership in the network of a funding lineage, on the sustained funding of the lineage, and on the relevance of the research in a funding lineage for their career.

5.3 Societal Actors' Perceptions of Science Policy

In this chapter, we explore the perception and the conceptualizations of systems biology by societal actors. Societal actors are linked to the discourse on systems biology and its science policy, yet without themselves being scientists in the conventional meaning. As representatives of the media, of industry, public interest groups, research funding organizations, administration, and of science policy, they both influence the direction of scientific research, and are affected by science policy.

The discussion on science policy that we analyze in the following sections draws upon themes such as establishment of systems biology, its medical application, and possible implications for science and society. How do different societal actors discuss questions regarding science policy of systems biology and related fields of interest? In their understanding is systems biology already established, or do they perceive it as an approach just emerging? And if so, why? How do they assess the application of systems biology? Which implications and regulations do they deem relevant?

In order to clarify some of the differences that exist with regard to the discourse among scientists, we start with a short section on the conceptualization of systems biology by societal actors in Germany (Sect. 5.3.1). The following sections deal with the establishment of systems biology (Sect. 5.3.2), its application potential (Sect. 5.3.3), and its possible societal implications and eventual regulation (Sect. 5.3.4). These sections are structured according to different actor groups and their perspective on systems biology. The grouping of the individual interview findings is done according to the interviewees' proximity to science policy decisions. Media, industry, and public interest group representatives form the first cluster, research funding and science policy the second (comp. Sect. 5.1 regarding method).

5.3.1 Societal Actors' Understanding of Systems Biology

In the public discussion, there is no predominant understanding or definition of systems biology. This is the result of a first assessment of the discourse on the terminology of systems biology; in this, it resembles the scientific discourse (comp. Sect. 2.1). Thus, the topic of the discourse itself is not clearly defined. However, compared to the scientific actors, industry, media, and public interest group representatives leave even more room for interpretation as they use the term systems biology less specifically. This was made explicit in our interviews as there is, according to one interviewee, "no generally valid definition, as far as I'm aware, but many, many different ones. But in the end, systems biology is mathematical modeling of biological processes on the basis of quantitative biological process—in other words, data. Actually, that's relatively simple"[26] (industry representative).

Other actors try to connect systems biology to existing currents in science by stressing its systemic and integrative nature. "Well, I wouldn't really say a new form of research. I mean, its charm is more in the fact that it brings together the most varied branches of research streams, as it were, and integrates them, and it's precisely that that makes it possible to draw summarizing conclusions and gain new knowledge from them"[27] (industry representative). This interpretation is openly questioned by one representative of the media when he draws a comparison to systems science:

> [W]ell, that's a technical-mathematical description of what's supposedly going on in life processes, but it didn't really have all that much explanatory power, […] it's simply an attempt to find […] orientation and meaning in a flood of data […], well, so living organ-

[26] Original quote: "keine allgemeingültige Definition, soweit mir das bekannt ist, sondern viele, viele verschiedene. Aber die Systembiologie ist letztendlich die mathematische Modellierung biologischer Vorgänge auf Basis quantitativer biologischer Prozesse—also Daten. Das ist eigentlich relativ einfach."

[27] Original quote: "[A]lso eine neue Form der Forschung würde ich jetzt eigentlich nicht sagen. Ich meine, sie hat ja eher den Charme, dass sie die unterschiedlichsten Äste sozusagen von Forschungsströmungen zusammenführt und integriert und eben dann ermöglicht, daraus zusammenfassend Schlüsse und neue Erkenntnisse zu ziehen."

> isms are somehow biocybernetic systems that respond to their environment in some kind of feedback loops and then reach certain states, and those states change again, and so on. Well, more like a, well, science of the logic of wiring.[28] (media representative)

Still, for most industry representatives, systems biology also carries a certain amount of novelty beyond the connection to existing sciences. Exemplary is the statement that "you don't [have to] understand every little cog […] any more to arrive at biological understanding, but [you] […] [can] start to model things precisely because biology and computer science are coming together and then simply compare them with the reality that you observe in an experiment. And that's a pretty interesting way to approach biological systems, after people tried for a long time to simplify model systems to the extent that you could only observe isolated components"[29] (industry representative).

Systems biology is seen here as a discipline providing an example with a process that starts from modeling before going into analysis, an approach that is understood as a novel perspective that might help other areas of research. It may possibly be described as a top-down approach to biological systems.

For industry representatives, the coexistence of the continuity with pre-existing research on the one hand, and the novelty of the approach have pragmatic reasons: systems biology "complements the existing quite well. That is, what we can do quite well already"[30] (industry representative). We were told by one interviewee that one has learned in a variety of different projects that an interdisciplinary cooperation is promising or even indispensable:

> Well, experimenters don't like it if theorists make experimental designs for them. […] There are positive exceptions, too. Well, there are also working groups that have an almost 10-year history together, where theorists from one group and experimenters from the other were systematically paired off. And they've learned that they benefit from it.[31] (industry representative)

[28] Original quote: "das ist halt so eine technisch mathematische Beschreibung dessen, was da in Lebensvorgängen abgehen soll, hatte aber nicht so wirklich viel Erklärungskraft, […] das ist halt der Versuch, in einer Flut von Daten […] Orientierung und Sinn zu finden […], also dass praktisch Lebewesen irgendwie biokybernetische Systeme sind, die in irgendwelchen Feedbackschleifen auf die Umwelt reagieren und dann wieder bestimmte Zustände erreichen, die sich dann wieder ändern, und so weiter. Also eher so eine, ja, Verschaltungslogik-Wissenschaft."

[29] Original quote: "man […] nicht mehr jedes einzelne Rädchen verstehen [muss], um zum biologischen Verständnis zu kommen, sondern [dass man] […] auch gerade durch das Zusammenwachsen von Biologie und Computerwissenschaften eben Modellierung anfangen [kann] und die dann einfach mit der Realität, die man beobachtet, experimentell abgleichen. Und ist mal ein ganz interessanter Weg, sich biologischen Systemen anzunähern, nachdem man eben lange Zeit eben immer versucht hat, Modellsysteme soweit zu vereinfachen, dass man immer nur isolierte Komponenten eben betrachten konnte."

[30] Original quote: "ergänzt ganz gut das bereits Vorhandene. Also was man schon ganz gut kann."

[31] Original quote: "Also Experimentatoren mögen es nicht, wenn ihnen Theoretiker Versuchspläne machen. […] Es gibt auch positive Ausnahmen. Also es gibt auch Arbeitsgruppen, die jetzt also schon fast zehn Jahre Geschichte haben, eine gemeinsame, wo es also konsequent Pärchenbildung gibt zwischen Theoretikern von der einen Gruppe und Experimentatoren von der anderen. Und die haben gelernt, dass sie davon profitieren."

Here, the step towards interdisciplinary work is marked as a necessary one if systems biology is to catch up with other natural sciences. Among all, catching up with theory and theoretical reasoning plays an important role in this process. In contrast to (molecular) biology, systems biology contains "Modeling methods coming from mathematics, and that are the standard in physics and in other more technical, or at least non-biological disciplines […]. But first of all, I think it very clearly has to be organized from the theoretical side"[32] (industry representative).

In retrospect, the emergence of systems biology was interpreted by most actors as consequential, for example, as a "logical further development of what we learned from genome research, that a lot can be seen at the DNA level, but nothing can be understood […] [and that systems biology] is simply necessary to see how this whole new level of -omics, metabolomics and proteomics, all of them are also benefiting from the systems biology approach"[33] (public interest group representative).

Representatives of science policy in Germany seem to have a more specific definition of systems biology. One interviewee made this explicit as he compared the German understanding with the US-American:

> About looking across the Atlantic, for us, the question is//has always been, what do the Americans mean by systems biology? What do the Europeans mean by systems biology? After all, we in Europe defined the term. Of course, especially against the background, how do we want to assess projects and have reviewers evaluate them if we don't have a uniform definition of what [a] systems-biology research approach means? And if I compare that with America, then we see that there's a different concept especially between the US and Europe—what is systems biology? The Americans define systems biology very broadly. [...] That's why the figures for research funding are so impressive there, because they include a lot of things that we'd consider to be in other areas here.[34] (research funding/administration representative)

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[32] Original quote: "Modellbildungsmethoden, die also aus der Mathematik kommen, die in der Physik und in anderen eher technischen oder eben nicht biologischen Disziplinen Standard sind […]. Aber zunächst einmal muss das meiner Meinung nach ganz klar von der theoretischen Seite aufgezogen werden."

[33] Original quote: "logische Weiterentwicklung dessen, was wir aus der Genomforschung gelernt haben, dass einfach auf der Ebene der DNA vieles zu sehen ist, aber nichts verstanden werden kann […] [und Systembiologie] einfach nötig ist, um dann zu sehen, wie diese ganze Ebene der -omics, die da jetzt kommt, die Metabolomics und Proteomics, die alle profitieren ja auch vom Ansatz der Systembiologie."

[34] Original quote: "Was den Blick über den Teich betrifft, da ist//war für uns immer die Frage, was verstehen die Amerikaner unter Systembiologie? Was verstehen die Europäer unter Systembiologie? Wir haben ja in Europa diesen Begriff definiert. Insbesondere natürlich auch vor dem Hintergrund, wie wollen wir Projekte evaluieren und bewerten lassen von Gutachtern, wenn wir keine einheitliche Definition dessen haben, was [ein] systembiologischer Forschungsansatz bedeutet? Und wenn ich das mit Amerika vergleiche, dann haben wir festgestellt, dass es eine unterschiedliche Auffassung gibt zwischen insbesondere USA und Europa—was ist Systembiologie? Die Amerikaner definieren die Systembiologie sehr breit. Und deshalb sind auch die Forschungsförderungszahlen dort so beeindruckend, weil dort sehr vieles darunter gefasst wird, was wir hier anderen Bereichen zuordnen würden."

Our interviewees' reflection on the definition of systems biology thus seems to be at least partially driven by his awareness of an (apparently) higher funding level connected with this label in the United States. We also found that research funding representatives made a clear differentiation towards synthetic biology, something which was not mentioned in the interviews with members of other groups. Yet, the understanding of the subject matter of systems biology varies widely. We now take a closer look on how different actors discuss science policy regarding systems biology.

5.3.2 Establishment of Systems Biology and Need for Science Policy

The different societal actors did not only have divergent understandings and interpretations with regard to what systems biology is and what it comprises, as documented in the previous section, but also concerning its current state of establishment in science and industry. In fact, the experts do agree in a cautiously optimistic assessment of the scientific progress in systems biology: while they do not expect realization of the grand promises made for systems biology in the near future, such as modeling complete cells or even organs, they look forward to smaller albeit encouraging steps and successes.

5.3.2.1 Media, Industry, and Public Interest Groups

For example, industry representatives expect results from modeling smaller systems: "I'd tend to see [the] next 10 to 20 years more in the simple systems, it isn't all that simple to understand an entire human being"[35] (industry representative). For public interest group representatives, the larger aim plays a role as there is still great hope towards systems biology that leads to some fundamental change in our perspective on life and of the interrelationships between organisms and environment, and expectation for beneficial applications in medicine. One stakeholder put it this way:

> And in this respect, I expect that the possibilities of interfering in organisms and changing the cell metabolism, and producing materials or actually organisms that have new characteristics […]. And of course there will be new knowledge about how life is organized fundamentally, how interactions play out between the environment and the living organism, too.[36] (public interest group representative)

[35] Original quote: "[Die] nächsten 10 bis 20 Jahre würde ich eher also in den einfachen Systemen sehen, das ist ja nicht so ganz einfach, einen ganzen Menschen zu verstehen".

[36] Original quote: "Und insofern erwarte ich, dass da eben die Möglichkeiten in Organismen einzugreifen und den Zellstoffwechsel zu verändern, und Stoffe zu produzieren oder eben Organismen zu schaffen, die neue Eigenschaften haben […]. Und natürlich wird es darüber auch neue Erkenntnisse darüber geben, wie Leben grundsätzlich organisiert ist, wie Wechselwirkungen auch zwischen Umwelt und Lebewesen sich abspielen."

Regarding the expectations towards application of systems biology, industry representatives maintain a low profile. For most, systems biology is in the research stage but offers nevertheless interesting perspectives. For them, systems biology is "currently in the research phase […], but we can already tell that it will be important, an important development in biology, because unlike how it used to be, it enables a kind of holistic observation of cells and cell systems with high-throughput methods"[37] (industry representative). Here, the prevailing view is that some systems approaches in biology indeed begin to reap first recognition; a large-scale deployment, however, is still inconceivable. An industry representative states, "that to this day, systems biology in industry is mostly a hope or a promise. And depending on which company you're talking about, people tend to take these promises more or less seriously. […] That means especially that hardly any companies are using approaches that really work well to integrate systems biology fully into the company's research workflows that are used to develop pharmaceuticals. And in that way to develop products with which the companies can then recoup their money"[38] (industry representative). Thus, the attitude of industrial professional associations can be described as anticipatory:

> [F]rom the perspective of companies, I think there is relatively little initiative to say now, we'll support systems biology or we'll call for research programs in that area. What we're tending to see, just like in other areas, too, is that opportunities are emerging from basic research, from the classical way of gaining scientific knowledge, new technologies, new analytic platforms, where companies are feeling their way forward cautiously. I mean, it's always about feeling your way forward. It's rarely the case that a new technical perspective pops up on the horizon and then industry jumps on it right away and says: that's what we want.[39] (industry representative)

[37] Original quote: "derzeit im Forschungsstadium […], aber es zeichnet sich schon ab, dass es wichtig wird, eine wichtige Entwicklung in der Biologie wird, weil es eben anders als früher ermöglicht, durch so High-Throughput-Methoden so eine holistische Betrachtung auf Zellen und Zellsysteme ermöglicht."

[38] Original quote: "dass die Systembiologie bis heute in der Industrie im Wesentlichen eine Hoffnung oder ein Versprechen ist. Und in Abhängigkeit davon, über welche Firma man dann spricht, wird diesen Versprechen mehr oder weniger geglaubt. […] Das bedeutet insbesondere, dass es in kaum einer Firma bisher wirklich gut funktionierende Ansätze gibt, Systembiologie voll zu integrieren in die Forschungsworkflows der Firmen, die eingesetzt werden, um Arzneimittel zu entwickeln. Und damit halt auch Produkte zu entwickeln, mit denen die Firmen dann wieder ihr Geld einspielen können."

[39] Original quote: "auch aus Unternehmenssicht gibt es, glaube ich, relativ wenig Initiative jetzt zu sagen, wir fördern Systembiologie oder wir fordern Forschungsprogramme in dem Bereich. Wir sehen eher, so wie es in anderen Bereichen eben auch ist, dass aus der Grundlagenforschung, aus dem klassischen wissenschaftlichen Erkenntnisgewinn heraus eben Möglichkeiten entstehen, neue Technologien, neue analytische Plattformen, in die sich Unternehmen ja zunächst mal vortasten. Ich meine, das ist auch immer ein Vortasten. Es ist ja selten so, dass da eine neue technische Perspektive am Horizont auftaucht und dann sofort die Industrie drauf springt und sagt, das wollen wir."

Although the immediate application of systems biology currently seems out of reach, industry representatives paint an optimistic picture for the future:

> Well, for years systems biology has been an area that's received government funding, and by now, it has also achieved a certain significance at universities. And that's certainly something that is increasing at the moment and that will continue to become more important. And yes, it has a lot of open connections to other areas of biotechnology. And in that respect, I think it's an area that will still be relevant in the coming years, yes.[40] (industry representative)

We also found a strong agreement between representatives of professional associations and the industry: whereas the former state "a very high potential [. . .] in questions like that [. . .] concerning personalized medicine"[41] (public interest group representative), the latter describe: "It's also the case that more and more people are (1) recognizing that that might be the only opportunity the pharmaceutical industry still has to improve its research effectiveness or efficiency. And more and more people are also acknowledging that apparently, it can work, and in individual areas, it really has worked already. [. . .] So what I expect is that its use will increase massively. Really massively. I mean, by orders of magnitude, possibly by a factor of 10 or 100"[42] (industry representative). An example for the future application of systems biology could be the operation of research service agencies: "There is partly a very marked interest in, well, getting the best overview possible, trying out as much as possible, well, especially companies, big companies are not confining themselves to doing that with their own resources, but trying out research service providers that work in the area [. . .]. Well, things are happening there, that's clear"[43] (industry representative). Thus, our interviewees from the media agree with the interpretation of systems biology as an emerging approach in science: "Well, I do see that as a major trend, I'd say. So, centralization, coordination, access, networks, big science"[44] (media representative).

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[40] Original quote: "Systembiologie ist ja seit Jahren ein Zweig eben, der staatlich gefördert wird und auch an den Universitäten einen bestimmten Stellenwert inzwischen hat. Und das ist bestimmt etwas, was im Moment eben im Wachsen ist und auch in seiner Bedeutung eben noch zunehmen wird. Und ja, ganz viele offene Enden hat zu anderen Bereichen in der Biotechnologie. Und insofern denke ich, ist das ein Bereich, der also die nächsten Jahre noch relevant sein wird, ja."

[41] Original quote: "ein sehr hohes Potenzial [. . .] in so Fragestellungen [. . .], die die personalisierte Medizin betreffen"

[42] Original quote: "Es ist auch so, dass es mehr und mehr Leute gibt, die erstens erkennen, dass das vielleicht die einzige Chance ist, die die Pharmaindustrie noch hat, um ihre Forschungseffektivität oder—effizienz zu verbessern. Und es gibt mehr und mehr Leute, die also auch sehen, dass es scheinbar funktionieren kann und in einzelnen Feldern auch wirklich schon funktioniert hat. [. . .] Meine Erwartungshaltung ist schon die, dass also der Einsatz massiv zunehmen wird. Wirklich massiv. Also um Größenordnungen, Faktor 10/100 möglicherweise."

[43] Original quote: "Es gibt teilweise ein sehr ausgeprägtes Interesse daran, also einen möglichst guten Überblick zu bekommen, möglichst viel auszuprobieren, also gerade auch Firmen, große Firmen beschränken sich nicht darauf, das mit eigenen Ressourcen zu machen, sondern testen Forschungsdienstleister, die in dem Bereich aktiv sind [. . .]. Also da passiert was, ganz klar."

[44] Original quote: "Also das sehe ich schon als einen großen Trend, würde ich jetzt sagen. Also Zentralisierung, Koordinierung, Zugang, Netzwerke, Big Science."

5.3.2.2 Research Funding, Science Policy, and Administration

In the interviews with representatives from research funding agencies, science policy and administration, the experts agreed on one thing: systems biology is seen as an approach that has largely established itself in the research community. Not all promises that were given have already been fulfilled, but important steps have been made towards the initial vision of what systems biology can achieve. The big leap, however, is still to come. Nevertheless, in biological research, medicine, and similar areas, as well as in academic training, systems biology as an approach is perceived as being largely established.

This has created the preconditions for integrating research funding for systems biology in new programs:

> I think that this approach has become established, that it's become the routine. And we're seeing that biologists and physicians are simply integrating this approach […] in many applications for research funding, not only in systems biology, but also in other areas. And that's why I think that in the foreseeable future, it won't be necessary any more for us to promote this approach ourselves, but that we should reorient research funding toward other goals and consider the systems-biology approach to be an integral part of every forward-looking research project.[45] (research funding/administration representative)

Our interviewees underlined that this does not mean that research funding agencies seek to shift funding, but rather that systems biology as a discipline is embedded in different contexts as it is firmly established already as a research approach. It is assumed that the establishment of systems biology will follow the general dynamics of scientific disciplines and their common scheme of disciplinary evolution.

In our interviews, we also found some requirements and expectations with regard to systems biology as they are directed towards applications in medicine and the pharmaceutical industry: "[I] would think that naturally, medicine will benefit from it to an extraordinary degree. We're seeing that research, especially in the field of individualized medicine, has benefited a lot from the funding that we initiated in recent years and are still pushing forward"[46] (research funding/administration representative). Here again, the expectation is not that it will be possible to reach visionary goals such as the modeling of complex biological systems in the near future; it is rather agreed upon that the development of models that will be necessary for medical applications

[45] Original quote: "Ich glaube, dass sich dieser Ansatz etabliert hat, dass er zur Routine geworden ist. Und wir beobachten, dass Biologen und Mediziner […] in vielen Anträgen zur Forschungsförderung nicht nur in der Systembiologie, sondern auch auf anderen Gebieten diesen Ansatz einfach integrieren. Und deshalb denke ich, dass in absehbarer Zukunft es nicht mehr erforderlich sein wird, diesen Ansatz selbst zu fördern, sondern die Forschungsförderung auf andere Ziele auszurichten und den Ansatz der Systembiologie als einen integralen Bestandteil jedes zukunftsweisenden Forschungsprojektes zu betrachten."

[46] Original quote: "[I]ch würde denken, dass die Medizin davon natürlich außerordentlich profitieren wird. Wir beobachten, dass die Forschung insbesondere im Bereich der individualisierten Medizin davon sehr profitiert hat, von der Förderung, die wir in den letzten Jahren angeschoben haben und auch noch anschieben."

still needs a great deal of work, even as "individual compartments are already successful"[47] (research funding/administration representative).

To summarize our findings: the different societal actors perceive systems biology as a discipline that is still on its way towards becoming an established approach or discipline. But there are quite diverging views if one compares the different actors: those related to research funding argue that systems biology is established insofar as it does not need special funding anymore, and that it can be supported by conventional research funding, however, other actors emphasize goals that are not yet reached but also the potential of systems biology to achieve them. Interviewees from all fields agree that the future will see systems biology as an established approach in scientific practice and commercial and medical application and they underline that research for the application of systems biology is still funded and will be funded.

5.3.3 The Application of Systems Biology

Research-funding initiatives are often justified with the scientific and technological potential of the emerging scientific field and the theoretical and practical goals to be reached; an important role is also played by the promises and hopes associated with future applications resulting from research. How are aspects of the application of systems biology described in public discourse? How do societal groups assess the importance of systems biology applications in science, medicine, and industry? In seeking answers to theses questions, we also take up considerations on possible paths towards commercialization and aspects of intellectual property.

5.3.3.1 Media, Industry, and Public Interest Group Representatives

For the interviewed members from different societal groups, the value of systems biology surfaces in three areas: basic scientific research, industry, and medical applications. For industry representatives, systems biology is proving its value not "primarily in medicine," but rather "in the laboratory market" or in the "production of resources". By now, the economic impact is determined to be sizable and understood as a "striking business argument"[48]. The use of results from systems research in medicine is likewise a stated goal in the public discourse. Here, the discovery of new drugs and early assessments of their potential play a big role: "And that offers opportunities and risks, it naturally also offers individuals the opportunity to assess early on in the development of a pharmaceutical, what are all the things this active substance does that you wouldn't ordinarily be able to see. And also being able to

[47] Original quote: "Einzelkompatimente bereits erfolgreich sind."

[48] Original quote: "schlagendes wirtschaftliches Argument."

assess earlier on, what is its efficacy/side-effect profile? In other words, to assess opportunities and risks"[49] (industry representative).

This aspect is seen as critical by one representative of a public interest group: He sees a danger in commercialization because systems biology as a scientific approach should primarily be driven by the ambition to gain knowledge instead by an interest in turning it into commercial value. In support of this argument, he notes that possible applications and the development of products often stand in the foreground when systems biology is discussed. Criticism is also directed towards the current state of systems-biology research and its maturity regarding the application in medicine:

> Can I find a better therapy for it? Yes or no? For the patient sitting in front of me, I'd say the answer is: in very few cases yes, in most cases no, so far. Could that change in the future? I'd say we don't know that yet. That research question is still open. There's still hope. And the hope is: more data, better prediction. But whether the prediction comes true, I'd say, well, personally, as a journalist, I'm agnostic. So my opinion is, let's let the researchers figure that out.[50] (media representative)

5.3.3.2 Research Funding, Science Policy, and Administration

In our interviews, representatives from research-funding, science policy and administration described their aims in funding research related to the field of systems biology as a first round of funding was dedicated to the establishment of systems biology as it was perceived as truly new and possibly game-changing:

> It was in 2004 that the BMBF (the German Federal Ministry of Education and Research) started funding systems biology for the first time, that was the systems biology of liver cells. That was a pilot project, and I think that was the first time that a coordinated research and funding measure was initiated in this field in Germany. Of course, the intention behind it had to do with funding policy. For one thing, it was about making this truly new approach, this new methodological approach available to research, too, and to try to integrate this new approach in science, too, to introduce it and to see whether the scientists actually take up this research approach. And later on, the idea was of course to determine whether it was successful, whether research funding in the way we structured it at that time, whether it was actually successful, too. That was certainly the case, and a very large package of research funding emerged.[51] (research funding/administration representative)

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[49] Original quote: "Und das bietet Chancen und Risiken, das bietet auch für Einzelne natürlich die Chance frühzeitig abzuschätzen in so einer Arzneimittelentwicklung, was tut dieser Wirkstoff so alles, was man normalerweise nicht so ohne Weiteres sehen würde. Damit auch frühzeitiger abschätzen zu können, wie ist er denn in seinem Wirkungs-/Nebenwirkungsprofil? Also um Chancen und Risiken einzuschätzen."

[50] Original quote: "Kann ich dafür eine bessere Therapie finden? Ja oder nein? Für den Patienten, der vor mir sitzt, da würde ich sagen, lautet die Antwort: In ganz wenigen Fällen ja, in den meisten Fällen bisher nein. Könnte das zukünftig anders werden? Ich würde sagen, das wissen wir noch nicht. Die Forschungsfrage ist noch offen. Es gibt noch Hoffnung. Und die Hoffnung heißt mehr Daten, mehr Prognose. Aber ob die Prognose eintritt, würde ich sagen, da bin ich jetzt persönlich als Journalist agnostisch. Also das sage ich mal, lassen wir die Forscher klären"

[51] Original quote: "Es war im Jahr 2004, als die Förderung zur Systembiologie zum ersten Mal gestartet ist durchs BMBF, das war die Systembiologie der Leberzelle. Das war ein Pilotprojekt,

Most interviewees of this group think that funding of applied systems-biology research will yield good results, especially in medicine, within the next few years and look forward to it:

> I would think that naturally, medicine will benefit from it to an extraordinary degree. We're seeing that research, especially in the field of individualized medicine, has benefited a lot from the funding that we initiated in recent years and are still pushing forward. I think that we'll be seeing results in the next few years. I see that in the projects, since we're getting very good results, we will get good results, possibly even breakthroughs in a few small areas. The second area is of course the area of biotechnology, in other words, everything described by the term metabolic engineering, and naturally, systems-biology funding measures play a very decisive role here, too.[52] (research funding/administration representative)

This is similar to how industry representatives judge the situation; they, however, see a need for more funding in the near future. Whereas for other topics (such as the state of establishment) the perspectives of all interviewees were quite similar, with regard to the application potential of current systems biology clear differences between actors' opinions exist: industry representatives emphasize economic interests, and stakeholders of public interest groups point out potential conflicts of interest. The media representatives are skeptical about when systems-biology research can be applied and which projects actually hold commercial value; however, this is in contrast to the more optimistic view of the research-funding agencies. These differences in assessing the state of and potential for application generate a number of issues regarding societal challenges of systems biology, which are discussed in the next section.

5.3.4 Societal Implications and Regulation

Important societal actors from funding agencies, administration and industry, as well as many scientists stress the huge application potential of systems-biology research and the results thereof in medicine and biotechnology, as well as the

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und damit ist zum ersten Mal glaube ich in Deutschland eine koordinierte Forschungs- und Fördermaßnahme auf dem Gebiet gestartet. Die Intention war natürlich förderpolitischer Art. Einmal ging es darum, diesen wirklich neuen Ansatz, diesen neuen methodischen Ansatz auch für die Forschung verfügbar zu machen und zu versuchen, diesen neuen Ansatz auch in die Wissenschaft zu integrieren, hineinzubringen und zu schauen, ob sich die Wissenschaftler tatsächlich auch dieses Forschungsansatzes annehmen. Und im weiteren Verlauf natürlich war festzustellen, ob sich das bewährt, ob sich die Forschungsförderung so, wie wir sie aufgesetzt haben damals, auch tatsächlich dann bewährt. Das war sicher der Fall, und daraus hat sich dann ein sehr umfangreiches Paket der Forschungsförderung ergeben."

[52] Original quote: "Ich würde denken, dass die Medizin davon natürlich außerordentlich profitieren wird. Wir beobachten, dass die Forschung insbesondere im Bereich der individualisierten Medizin davon sehr profitiert hat, von der Förderung, die wir in den letzten Jahren angeschoben haben und auch noch anschieben. Ich denke, da wird es in den nächsten wenigen Jahren zu Ergebnissen kommen. Ich beobachte das in den Projekten, da wir sehr gute Ergebnisse kriegen, werden wir gute Ergebnisse bekommen, möglicherweise sogar Durchbrüche auf einzelnen kleinen Teilbereichen. Der zweite Bereich ist natürlich der Bereich der Biotechnologie, also alles das, was man so mit Metabolic Engineering umschreibt, da spielen natürlich systembiologische Fördermaßnahmen hier auch eine ganz entscheidende Rolle."

putative commercial value that could be generated from these applications. Nobody can really be sure today, whether and to which extent these expectations will come true. However, it is reasonable to assume, that at least some of the putative or anticipated benefits of applied systems biology will be realized and have societal implications. Therefore it may be important to find out what societal actors think about such implications of systems biology and what they expect. This could at least in principle enable policy makers to think about necessary interventions, inasmuch as early interventions "can help to avoid that technologies fail to embed in society and/or help that their positive and negative impacts are better governed and exploited at a much earlier stage" (von Schomberg 2012, 50). Consequently, we identified statements of our interview partners related to possible implications of systems biology and analyzed them with regard to existing societal challenges and controversies.

5.3.4.1 Media, Industry, and Public Interest Group Representatives

In the interviews, few hints are given that point directly towards societal implications: instead, often synthetic biology was brought into the picture when the interviews turned towards the role of technoscientific developments for society. When our interviewees mentioned societal implications, they usually were related to the topic of public access and fair distribution. One public interest group representative states that one does have "very often the impression […] that technologies are developed, products are developed that aren't actually, let's say, necessarily in the public interest"[53] (public interest group representative). On the one hand, research is understood as meaningful even though resulting inventions are not immediately applicable in practice, however, systems biology could seem to have negative implications for society when industrial and economic interest come into play instead of basic research or medical applications.

Real or perceived negative societal implications often provoke calls for regulation. Well-known examples include stem cell research and genetically engineered crops. In the area of systems biology, our interviewees were reluctant to discuss sensitive issues coming up in fields related to applied systems biology and medicine such as the necessary establishment of large biobanks and databases, eventually comprising personal data. In general, they were cautious to talk about societal implications and regulation. This reluctance, however, does not seem to be due to the sensitivity of the issue but rather stems from the lack of an immediate need to deal with such issues. There seems to be a broad consensus that for systems biology there are no new ethical or societal issues at stake. An exemplary statement from an industry representative argues that ethical concerns would only be relevant, "if it really becomes a topic of discussion in practice. So, if you really have to consider, say, from an entrepreneurial point of view, […] in case of doubt, it's also a risk in

[53] Original quote: "sehr oft den Eindruck […], es werden Technologien entwickelt, Produktentwicklung betrieben, die eigentlich nicht im Sinne des, sagen wir mal, des öffentlichen Interesses unbedingt stehen."

terms of an additional regulatory requirement that precisely doesn't result in additional safety, but in more time and effort"[54] (industry representative).

In our interviews, the subject of databases was always linked to the topic of data protection and privacy. However, we found no indication that societal actors were aware of a new quality or challenge introduced by big data storage and processing as it is, for instance, necessary in systems medicine and research related to it. As a business representative remarked, the question of the databases was primarily a technical challenge with the aim of "enabling all research groups to access these resources. Somehow in a way that also conforms to data protection"[55] (industry representative). In contrast, one public interest group representative discusses the lack of transparence that is a reality for patients:

> Well, it's also the case that as a matter of principle, patients are simply asked whether they consent to having the data used in research. But whether they are exploited commercially, […] whether personal genetic data are even patented, these questions aren't discussed with the patients. And I believe that there should simply be more transparency here. And the […] level of data storage and anonymization is important, too, of course. And of course, there should be rules about who has access to these data at all and for which purposes.[56] (public interest group representative)

Although it is true that currently, no real need is seen to take regulatory action, such measures are not categorically ruled out for the future: "And I think we will also see, to the extent that these technologies become broadly available, sooner or later they will also be the subject of guidelines and, say, they'll play a role in regulatory frameworks and underlying conditions. […] I actually don't think there's a need to regulate right now that would go beyond what we have anyway"[57] (industry representative). Again, we found that for systems biology, the consequences are (still) quite unclear and there is a strong feeling that existing regulations for genetic engineering, clinical trials, or data protection are sufficient, inasmuch as no new or

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[54] Original quote: "wenn es in der Praxis wirklich mal zu einem Thema wird. Also wenn man wirklich auch dann abwägen muss, sagen wir, aus unternehmerischer Sicht betrachtet, ist das […] im Zweifel auch ein Risiko im Sinne einer zusätzlichen Behördenauflage, die mir eben keine zusätzliche Sicherheit schafft, aber mehr Aufwand."

[55] Original quote: "den Zugriff aller Forschergruppen auf diese Ressourcen zu ermöglichen. In irgendwo einer Art, die dann eben auch datenschutzkonform ist."

[56] Original quote: "Es ist ja auch so, dass Patienten grundsätzlich einfach nur gefragt werden, ob sie damit einverstanden sind, dass die Daten in der Forschung verwendet werden. Ob das dann aber eine wirtschaftliche Verwertung ist, […] personenbezogene genetische Informationen sogar patentiert werden, diese Fragen werden ja nicht erörtert gegenüber den Patienten. Und ich glaube, da müsste einfach mehr Transparenz vorhanden sein. Und wichtig ist natürlich auch die […] Ebene der Datenspeicherung, die Anonymisierung. Und es sollte natürlich auch geregelt werden, wer überhaupt Zugriff auf diese Daten zu welchen Zwecken hat."

[57] Original quote: "Und wir werden, denke ich, auch sehen, in dem Maße, wie diese Technologien in der Breite zugänglich werden, werden sie früher oder später auch in Guidelines auftauchen und sagen wir, in regulatorischen Rahmennetzwerken und in Rahmenbedingungen eine Rolle spielen. […] an sich sehe ich eigentlich momentan keinen Regulierungsbedarf, der über das, was wir ohnehin haben, hinausgehen würde."

enhanced societal effects are expected from systems biology. In contrast to this, synthetic biology evokes much stronger images of possible negative consequences that seem relevant for everyday life:

> Well, I mean, sure there are aspects that extend into classical genetic engineering, but we have a comprehensive legal regulatory framework for that. We have questions concerning biosecurity. But in my opinion, we have a sufficient, at least a sufficient framework for that, too. […] One thing that will certainly play a role in the future, but that doesn't concern systems biology at its core, but more a different area, the topic of synthetic biology. […] Life from the lab, designer organisms, etc. etc., and that will raise the question again, where are the reasonable limits in terms of aspects of security, but also in terms of ethical aspects?[58] (industry representative)

Thus, methods or applications developed in the field of systems biology are deemed to be possible subjects of regulation, yet the discipline itself is free from such restrictions: "Methods that are used in systems biology just as in//well yes, I can image that, but not for systems biology itself, at first. I can certainly imagine applications that aren't in the interest of society"[59] (industry representative). Furthermore, systems biology is not associated with an impact on ethical values as is, for instance, stem cell research: "Likewise, I can naturally imagine systems biology resulting in some kind of abstruse excesses, and especially synthetic biology, too, but first of all, I'd think that that can be managed relatively well—in the area of systems biology as well as in the area of genetics. […] In contrast to, let's say, early stem cell research, systems biology doesn't have the problem that it believes it's dependent on research funding sources that are ethically questionable per se"[60] (industry representative). Again, our interviewees find it difficult to identify problems and concerns. This is most likely due to the difficulty of knowing today what possible implications might surface in the future. None of our interview partners was comfortable with providing concrete examples for negative implications without any further indication that such problems might indeed become reality. Thus, many hopes but few problems or fears are identifiable in the context of systems biology and medicine; the only issue that emerged and may be relevant for regulation was the handling and protection of sensitive data.

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[58] Original quote: "Also ich meine, klar, da haben wir Aspekte, die in die klassische Gentechnik reinreichen, aber dafür haben wir ja einen umfassenden gesetzlichen Regulierungsrahmen. Wir haben Fragen, die die Biosicherheit betreffen. Aber auch dafür haben wir einen hinreichenden, aus meiner Sicht zumindest einen hinreichenden Rahmen. […] Ein Punkt, der sicherlich für die Zukunft eine Rolle spielt, der aber die Systembiologie im Kern nicht betrifft, sondern eher einen anderen Bereich, das Thema synthetische Biologie. […] Leben aus dem Labor, Designerorganismen, etc. pp, und das wird wieder die Frage aufwerfen, wo sind sozusagen da die aus Sicherheitsaspekten, aber auch aus ethischen Aspekten heraus vertretbaren Grenzen?"

[59] Original quote: "Methoden, die in der Systembiologie eingesetzt werden genauso wie in//also ja, da kann ich mir das vorstellen, bei der Systembiologie selber zunächst einmal nicht. Ich kann mir auch durchaus Anwendungen vorstellen, die nicht mehr im Interesse der Gesellschaft sind."

[60] Original quote: "Genauso kann ich mir natürlich auch bei Systembiologie irgendwelche abstrusen Auswüchse, also gerade bei der synthetischen Biologie sowieso vorstellen, aber ich würde zunächst einmal denken, dass das—also im Bereich Systembiologie genauso wie im Bereich Genetik—relativ gut handhabbar ist. […] Systembiologie hat im Gegensatz zu der—ich sage mal—frühen Stammzellforschung nicht das Problem, dass sie glaubt, angewiesen zu sein auf Quellen oder auf Mittel für ihre Forschung, die per se ethisch bedenklich sind."

In this context, the concept of anticipatory regulation (regulation of future fields of research) surfaces: "That's why I'd see that less in relation to systems biology or synthetic biology, instead, I'd argue strongly for establishing control mechanisms that establish responsible handling of certain research, of sensitive research areas, for example pathogen research and so on. So, similar to medical guidelines"[61] (industry representative). One public interest group representative expresses similar thoughts regarding anticipatory regulation:

> And all these questions and also especially in relation to possible environmental impacts haven't really been discussed so far and should be taken up by the legislature, and they should try first of all to map everything that's actually happening, what's new, and to what extent the current legal provisions are actually sufficient.[62] (public interest group representative)

No immediate measures are called for, but there remains a certain awareness of the fact that should negative implications from systems biology become reality, it would have been better to have taken preventive measures. The guidelines mentioned above are not exactly the strictest option available, and the call for legislative action is brought forward with little urgency. Thus far, the outlooks of the interviewees do not address imminent threats, and not even indirect threats such as possible negative impacts on public opinion. Hence, they do not see a need for proactive or anticipatory regulation.

Furthermore, one stakeholder poses the question of who could develop schemes for dealing with such uncertainty and lack of knowledge:

> Interdisciplinary working groups including civil society should be put in a position to deal with the question, which questions are new, which questions have come up recently, what is the need for regulation? I do think that that is a process that can't really go to the Bundestag (parliament) immediately, where you could say, well, the Bundestag or the government will simply put forward a proposal for a new Genetic Engineering Law, and then it's just about the details. I think that it's actually about a survey, and also about the attempt to take an interdisciplinary look at how to develop reasonable legal provisions here in terms of future developments.[63] (public interest group).

[61] Original quote: "Von daher würde ich das weniger auf die Systembiologie oder synthetische Biologie bezogen sehen, sondern ich würde stark dafür plädieren, dass Kontrollmechanismen etabliert werden, die einen verantwortungsvollen Umgang mit bestimmten Forschungs-, sensiblen Forschungsbereichen, wie zum Beispiel Pathogenforschung und so weiter etablieren. Also ähnlich ärztlichen Leitlinien."

[62] Original quote: "Und all diese Fragestellungen und auch in Bezug eben auf mögliche Umweltauswirkungen sind eigentlich bisher nicht wirklich diskutiert worden und sollten vom Gesetzgeber aufgegriffen werden und sollten also versuchen, hier erst mal abzubilden, was eigentlich alles passiert, was Neues hinzu gekommen ist und inwieweit hier eben auch tatsächlich die derzeitigen gesetzlichen Vorgaben ausreichend sind."

[63] Original quote: "Es müssten interdisziplinäre Arbeitsgruppen auch unter Beteiligung der Zivilgesellschaft dazu in die Lage versetzt werden, sich damit zu befassen, welche Fragestellungen sind neu, welche sind neu dazu gekommen, welchen Regulierungsbedarf gibt es. Ich glaube schon, dass das ein Prozess ist, der nicht jetzt irgendwie sofort in den Bundestag gehen kann, wo man sagen kann, also der Bundestag oder die Bundesregierung macht jetzt einfach einen Vorschlag für ein neues Gentechnikgesetz und dann geht es nur noch um die Details. Ich glaube, hier geht es tatsächlich schon noch mal um eine Bestandsaufnahme und auch den Versuch, interdisziplinär einfach mal zu gucken, wie man auch in Bezug auf die zukünftigen Entwicklungen hier vernünftige gesetzliche Regelungen entwickeln kann."

Today, it is no longer sufficient to assess implications post hoc, but it is understand that new approaches and sciences and their applications require constant assessment.

5.3.4.2 Research Funding, Science Policy, and Administration

Research-funding agencies and science policy, as well as industry emphasize the benefits and possible positive outcomes of systems-biology research and its applications. The possible benefit of systems biology is projected on three areas: basic scientific research, and industrial and medical applications. A research funding representative summarizes this as follows.

> In the end, the benefit lies in advances in knowledge, on the one hand, in other words, the systems-biology research approaches, I'd say, of course have resulted in a very big step in advancing knowledge. And on the other hand, the benefit of systems biology lies in its prospects for innovation, of course, in particular for medicine, and for the chemical industry, too, for the food industry, for the relevant sectors of the economy.[64] (research funding/administration representative)

At the present time, the economical importance is estimated to be substantial and thus seen as a "striking business argument"[65] (research funding representative). This explains the fact that every "business of even only minor significance [...] has systems biology in its portfolio as a research approach[66] (research funding/administration representative).

For systems biology, there is broad consensus that the field does not create outcomes or impacts that would have to come along with ethical concerns. An exemplary quote from an interview with a German industry representative is that ethical concerns would only become relevant "if it really becomes a topic of discussion in practice. So, if you really have to consider, say, from an entrepreneurial point of view, [...] in case of doubt, it's also a risk in terms of an additional regulatory requirement that precisely doesn't result in additional safety, but in more time and effort"[67] (industry representative). Similarly, we found in the interviews with research-funding agencies it is unanimously stressed that "the moment for civil commotion is limited as the research takes place in cell cultures and in a containment

[64] Original quote: "Der Nutzen liegt schlussendlich im Erkenntnisfortschritt einerseits, also die systembiologischen Forschungsansätze, ich sage es mal so, haben natürlich zu einem Sprung im Erkenntnisfortschritt geführt. Und andererseits liegt der Nutzen der Systembiologie natürlich in ihren Innovationsperspektiven, für die Medizin insbesondere, und eben auch für die chemische Industrie, für die Ernährungsindustrie, für die einschlägigen Wirtschaftsbranchen."

[65] Original quote: "schlagendes wirtschaftliches Argument."

[66] Original quote: "Unternehmen von auch nur kleinerer Bedeutung [...] Systembiologie als Forschungsansatz in seinem Portfolio hat."

[67] Original quote: "wenn es in der Praxis wirklich mal zu einem Thema wird. Also wenn man wirklich auch dann abwägen muss, sagen wir, aus unternehmerischer Sicht betrachtet, ist das [...] im Zweifel auch ein Risiko im Sinne einer zusätzlichen Behördenauflage, die mir eben keine zusätzliche Sicherheit schafft, aber mehr Aufwand."

environment. Concerns are therefore raised"[68] (research funding/administration representative). Furthermore, it was stated that "I'm not concerned here because of course, I also know that all the actors in the field are well aware of the legal, ethical, and other implications that are relevant. And that is of course routinely part of the reason that research projects in this area are called into question. So I think that's established, and so far I don't know of anything that resulted in major//well, society calling this field of research into question"[69] (research funding/administration representative).

In summary, in the eyes of our interviewees coming from different societal groups, few negative societal implications of system biology are visible at present. Correspondingly there seems to be no acute need for action. In this evaluation of systems biology, no difference between the actors could be found. It is pointed out that a broad discourse involving the public would be helpful to start an anticipatory discussion of advantages and disadvantages, possible consequences, funding strategies, and the handling of the data generated in medical systems research. Desired positive impact and hope draws mainly on medical application. However, although there is wide agreement that an involvement of the public and relevant societal groups in a comprehensive debate would be beneficial, it is stated at the same time that the topic of systems biology is not well known or even accessible to a wider audience. This contradiction is not solved, but the issue is given further attention in the next section.

5.3.5 Concluding Remarks

Perceptions and statements of experts from industry, and public interest groups, media, research-funding, administration, and science policy are—regarding systems biology's science policy—relatively homogeneous with the exception of three aspects:

- First, there is no shared interpretation of what systems biology comprises between the different actor groups. The interpretation seems to be rather subjective as we found many diverging variations and no underlying pattern. This is quite similar to our results from examining the scientific discourse, where interpretations range from understanding systems biology as an applied method (comp. Lee et al. 2006) to a focus on mathematic models (comp. Williamson

[68] Original quote: "das Aufruhrpotential begrenzt sei, weil die Arbeit in Zellkulturen und im Containment stattfinde. Bedenken würden deshalb geweckt."

[69] Original quote: "Ich habe da keine Bedenken, weil ich natürlich auch weiß, dass alle Akteure auf diesem Feld die rechtlichen, ethischen und sonstigen Implikationen, die dort relevant sind, sehr im Auge haben. Und das natürlich regelmäßig auch Bestandteil der Hinterfragung von Forschungsprojekten auf diesem Gebiet ist. Also das ist glaube ich eingeführt, und bisher ist mir nichts bekannt, was zu größeren//ja, gesellschaftlichen Hinterfragungen dieses Forschungsfelds geführt hätte."

2005) to a highly integrative, interdisciplinary field of research (Bruggeman and Westerhoff 2007, Kitano 2002). The interviewees seem to accept the obvious inaccuracy of available definitions. This might be a result of the unclear state of establishment of systems biology in Germany, and it can also indicate a lack of a clear and unified understanding of the core of systems biology in science.
- Second, there were clear differences between actors regarding the application of systems biology when it came to questions of a fair distribution of investment and access to knowledge and technology: some raised the point that both funding and access were spread unequally; others didn't seem to share this perspective.
- Third, the establishment of systems biology is partially different: fewer governmentally oriented stakeholders (industry, public interest groups, media) do not understand systems biology as completely established, yet funding stakeholders draw more upon the advanced (but yet not finished) state of establishment. This refers to the very different perspectives on an emerging approach in science.

The interviewed experts are very cautious when it comes to the application of scientific results, the societal implications of systems biology, and its regulation: There is agreement on the importance of the application of scientific results. It is a valid argument for funding basic research. Results from research in systems biology are seen to be relevant for both industrial and medical applications. With regard to industrial application, it was felt that real value is already measurable. Concerning the promise of systems or individualized medicine, applications were not perceived yet and systems biology was understood as not yet (fully) established. It was not expected that systems biology could deliver in the near future grand visions such as modeling complete cells or organs, but many shared a rather positive anticipation of smaller, stepwise successes. Here, the extent of expectations seems to be influenced by the interpretation of systems biology as a science, approach, or applied method.

Societal implications are deemed to be few and immaterial. Thus, the societal actors' perception is scarcely influenced by questions regarding regulation or the necessity of regulation. When it comes to consequences of systems biology for society, topics such as data security and privacy govern the discussion. But we also found that after raising the issue of societal implications, the discussion often turned to synthetic biology, which was, in the context of regulation, often chosen as the example for the application of systems biology. There is an obvious difference in how the discourse is shaped in the two different fields: in the debate on synthetic biology, research results and the handling of the results are a prominent part of discourse, to a degree that stakeholders involved in scientific and technological development such as the J. Craig Venter Institute have started to work on possible strategies for governance (comp. Garfinkel et al. 2007). There is no evidence for similar strategies in systems biology. Following Bogner et al. (2010), we understand that in the framing of the discourse on systems biology, there is no visible role for either risk assessment or ethics. This seems to be somehow in contradiction to the fact that involvement of the public in the discourse is deemed to be necessary by the experts. However, at the same time, the experts express ambivalence towards laypersons taking an active role in discussing research funding, because the topic is highly complex and difficult to grasp. Furthermore, inasmuch as there is no concrete application, there also is no immediate interest for the public. This is quite different when one compares this with the discourse on biobanks (comp. Gottweis and Zatloukal 2007) or on stem cells (Gottweis 2008).

What is not surprising is that actors from the different areas do not disagree with regard to the assessment of application and with regard to the possible societal implications and corresponding need for regulation. Although the actors' perspectives are obviously quite different, they all share the assumption that an application of systems biology is inevitable and desirable, and no implications are currently to be feared. Still, it seems advisable to establish a common ground in an open discussion with all stakeholders in order to make transparent the ongoing development of systems biology.

It is only partly possible to attribute the broad scope of interpretations of the term "systems biology" to the variation of scientific definitions and interpretations. Another source of the observed differences presumably lies in the lack of agreement on the core definition of systems biology in the scientific sphere, resulting from the different research perspectives on systems biology. Based on the premise of understanding systems biology as technoscience that we have introduced earlier, an extended discourse would be necessary to enable the different actors' participation in a fair and meaningful way in a public–scientific discourse. Hence, nonscientists need to be part of the discourse, also and especially for technosciences such as systems biology. To what extent, and whether to include them in the discussion of results, regulation, and/or science policy should be matter of further consideration. Referring to our initial point of the entangled systems of science with public, media, politics, legislation, industry, research funding, and representatives of public interest groups, a close adherence to these premises would mean that all subsystems are interdependent upon one another. It is thus of increased importance to bring the different actors, interpretations, and attitudes together and foster the exchange of perspectives and ideas (see Sect. 5.4) in order to consider the present and the future of systems biology in a concerted and grounded manner.

5.4 Scientific and Public Discourses on Science Policy: Interdependencies

Different actors contribute to the discourse on the science policy of systems biology. As we have argued before, questions regarding funding of systems biology, its value for science and society, its applications, implications, and possible necessary regulations are discussed not only by science policy and funding bodies, but also by administration, industry, nongovernmental organizations, public interest groups, and by scientists. Science policy of systems biology is reflected within in these different actors groups.

Furthermore, the discourse in the different fields of actors are not self-contained. Instead, they refer to and influence each other. The relations between the different

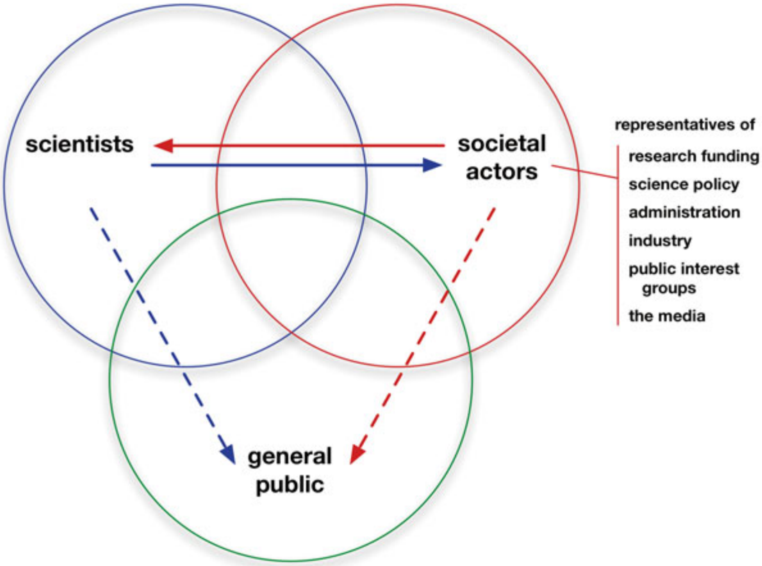

Fig. 5.2 Directions of interdepending discussion on policy of systems biology: availability of data (*solid line*: high availability of data; *dotted line*: low availability of data)

discourses can thus be described as interfaced, interconnected, and even interdependent. They not only consist of direct discussions between actors from different groups (e.g., science and politics) but also take the form of indirect interaction such as acknowledging and referring to discussions in other fields. Two types of communication on science policy exist: the direct communication between individuals and/or groups coming from different fields, and the indirect communication across different fields by referring to position papers, documents, conferences, and the like of other fields.

At this point, we analyze in more detail the mode of indirect communication. How do the different groups of actors influence each other? Where do they diverge and where do they align? We found that interactions between some actors and hence interdependencies between specific groups are much stronger than those between others. We observed, for instance, that the opinion of the general public was not discussed by the scientists in our sample, whereas public actors referred strongly to science (see Fig. 5.2).

The sociologist Peter Weingart describes this relationship between science and the public (including different actor groups) as becoming increasingly interconnected and, as a result, more tightly linked or "coupled" ("engere Kopplung"; Weingart 2001, 175). Often, and especially in resource-intensive, technical disciplines, public funding is a necessary requirement for research. Consequently, the direction of scientific research in systems biology is influenced or even determined significantly by the public and by policy makers, and not by science alone. Therefore, scientific topics develop not only a scientific, but also a social dynamic; the public's opinion influences science policy, which again influences the direction of science, which then is perceived and commentated and annotated by the public, and so on. We define these dynamic, mutual influences as interdependencies that together form an interactive system. This system is highly complex and shows no apparent dominance of a single group. Rather, it allows all individuals to work on and change the texture of the network and thus influence the interdependencies.

In this section, we analyze and discuss some of these interdependencies that emerge from our empirical analysis. By doing this, we go a step further compared to the previous section where we listened to what the different actors had to say; here we want to know how different actor groups frame and discuss the discourse of other groups.

5.4.1 Discursive Interdependencies Between Scientists and Societal Actors

The most significant interdependencies we identified exist between science and science policy (as a subgroup of the public actors; see Fig. 5.1). This is in one sense self-evident, inasmuch as the state is one of the most important sponsors of science. Science policy and funding organizations are important partners for science and research institutions because they negotiate the amount of funding that is going to be allocated to the different sectors of scientific or applied research. Not surprisingly, scientists are motivated and willing to follow the thematic agendas set by funding organizations to receive funding for their research. The role of setting agendas and trends in research is generally assigned to science policy and funding organizations, because they define themes and topics addressed in research programs and calls for proposals. These trends in funding are associated with certain funding lines or clusters of successive projects funded in the trend domain.

Such science policy decisions have far-reaching implications not only for the content of research, but also for the type of research. For instance, *project funding* privileges applied research, because application-oriented topics are usually clearly defined and can—at least in principle—be solved by a structured research agenda and within a limited time frame. Furthermore, problem-oriented systems biology research in medicine often requires, among others, the expertise of biochemists, computer scientists, and mathematicians and the cooperation of experts in interdisciplinary teams. Hence, application-oriented systems biology or medicine projects require interdisciplinary approaches, which then have a greater chance for getting monetary support. As a result, project-oriented funding also privileges problem-oriented or applied research at the expense of theoretical approaches. For example, although many epistemic problems of and in systems biology are not solved or even dealt with yet to a sufficient or even reasonable extent, science policy organizations have prioritized the establishment of mathematic modeling as a methodological approach, because it is expected to be helpful inter alia in elucidating disease mechanisms and defining new targets for the development of new drugs.

Science policy also influences the amount of money that is allocated to a new scientific development. This is closely related to the question of its *establishment* and whether it is progressing into a new phase. Interestingly, for systems biology there are strong differences regarding the state of establishment between different societal actors. They also disagree about the best direction for a science policy for systems biology. Still, most of the public actors agree in assessing systems biology as not established; it is marked as a scientific approach that is still underway and has not yet fulfilled its promises and met its announced aims. Instead, systems biology is described as a science that is still maturing and increasingly growing in importance. Consequently, more funding is needed for the future.

The influence on funding does not only run one way from the societal actors to science; there are also plenty of examples for influences on science policy from the side of science. Even if scientists are basically willing to follow the trendsetting of funding organizations, eminent scientists or science managers may have the power to *influence the initiation, the subject and the direction of research funding*. Systems biology, for example, was first put on the funding agenda because individual scientists proactively approached science policy organizations to set up pertinent funding programs. Ongoing interactions between these politically savvy scientists and science policy agents established social networks in which upcoming trends in funding and research were announced, and where the distribution of funding is negotiated.

Apart from prominent examples of proactively influencing the science policy's agenda, scientists generally care a lot about the distribution of funding as their *careers* crucially depend on the success of raising as much external funding as possible. This is needed to either support one's own position, to promote younger scientists, or to increase one's own reputation. To succeed in the competition of funding, scientists have developed different strategies. First, they refer to the program-related subjects and requirements defined by the funding organizations, which are usually defined in the topics of calls for proposals. Second, scientists communicate with colleagues in their field in order to identify innovative trends in research that may match with the trends in funding. Such networks of scientists develop and submit common proposals, in particular after having had positive experiences in collaborative work. Third, by applying for funding, these collaborative networks adapt to specific and general funding mechanisms of the funding system. Grants are, for example, primarily not given to support institutions or individuals, but to finance research projects that run within a limited budget and time frame. Once a research consortium was successful in a grant application, it may have a good chance for receiving further or even continuous funding. However, when a research project ends, the project partners usually do not know if they will be able to continue their collaboration. They have to invest a lot of effort into networking to maintain the established working relations or to adapt to the altering priorities of funding organizations, either by detecting future trends within their research area or by looking for alternative funding options.

This *impact of science on science policy* and vice versa is also discussed by public actors. They address changes in the research landscape and the establishment of new scientific approaches, as well as dependency of science on funding programs.

According to our findings, for public actors systems biology has become a routine element of biomolecular science. Hence, systems biology appears not in need of special funding, because it becomes part of the life sciences in general. In consequence, the shared perception of public actors is that systems biology will most likely become a basic element of future research programs. Here, emphasis is often put on the interconnection between scientific research and industrial application. For example, the results of fundamental research are seen as basic for the development of new analytical tools that will later be brought into application by industry. The direction of science policy supporting industrial applications thus seems to take up visions and goals of science.

Although the mutual interdependencies between science and science policy are obvious in the interviews, little can be said about the relation between science and *the public*: strikingly, in the scientific discourse, the public plays no role at all. From the scientists' view, there seems to be very little public interest in systems biology. The public too does not seem to be very interested in systems biology. Both observations are in strong contrast to the policymakers' explicit aim to increase public involvement in science and science policy. One factor identified in our interviews that limits potential public involvement is that systems biology in the social actors' discourse is perceived as highly complex, and thus as difficult to understand. Still, it is commonly stressed that the (layperson) public has to be involved in the discussion on science policy and implications of systems biology in the near future. The basic acknowledgment of systems biology seems to be sufficient until today, but it is emphasized by the interviewees that further and ongoing discussion with laypersons is needed. From our perspective, it is here necessary to reflect on when an involvement of the public is necessary, and to what ends and in what context it is induced: does it help to assess the impact of scientific research, or is the public only included to create support for future funding? Also, not all questions can be fed into the public discourse at a given time without risking an erosion of attention. As a consequence, a careful selection of the most relevant questions where public involvement is needed can help to increase the quality and outcome of it.

5.4.2 Conclusions

Science policy of systems biology must be understood as an interface—and result—of three converging discourses of science, of science policy/experts, and of the general public. Interdependencies resulting from this interface influence and change the research landscape as well as science policy and public perception of systems biology.

Our first point concerns the impact of research funding on the practice of research. Science policy *can increase dynamics in the research landscape*: project funding establishes only a temporal sustenance, and we have found evidence that some scientific and societal actors perceive that funding initiatives do not persist until the discipline is universally acknowledged as being fully established. As a consequence, this creates a momentum in the scientific community suggestion that science has to respond to this situation and to seek new research topics, modify existing ones, or adapt them to new scientific trends in order to gain access to further funding. In following this pattern, science has to change constantly, but it has to be asked whether important questions that result from previous research can and will be followed through. Also, scientists are permanently forced to adapt themselves and their professional biographies to these changing research agendas, leading to a stronger and more active competition and intensified selection. However, such an increasingly differentiated science could be counterproductive, not only for scientific biographies and careers but also for science itself as young academics, are less and less able to overlook what is being done and to follow self-defined research agendas. A new alignment between the goals of funding, the goals of science, and the requirements of sustainable scientific careers could be necessary as science not only needs—at least partially—a long-term perspective but also actors who are able to focus on fundamental and theoretical questions and self-reflection without being continuously occupied and absorbed by grant acquisition and pre-defined projects.

The second point concerns the question whether the type of science policy we observed in our study is *sustainable for science*. From the perspective of scientists, current science policy related to systems biology is seen as being not sustainable enough. Is initial funding truly effective in promoting innovation? Will the lack of mid- and long-term funding exert a detrimental effect on systems biology in the longer term? Almost certainly, systems biology will move on from basic research funding to more applied research, such as systems medicine. Based on our evidence, we must raise some doubts about whether systems biology as a basic science will last for long: did funding enable work needed to establish basic methodologies and core concepts? Or did systems biology mainly focus on pragmatic solutions for medicine and not develop (new) concepts that are transferable to other fields?

The third point of our conclusion concerns the lack of a common definition of systems biology. Could the fact that scientists, science policy, and societal actors do have different ideas about *what systems biology is* lead to conflicts? Does a highly complex field such as systems biology provoke problems with defining its main subject area and content? Such conflicts could perhaps provoke further interest in systems biology not only by science or science policy, but also by the general public. However, if opinions on and definitions of systems biology differ too much, this could also divert interest in the field and undermine public and political support.

Fourth, participation and inclusion of the public is in general seen as an important achievement from the perspective of politics, the media, and public interest groups. From the perspective of science, however, the public plays no relevant role and does not demonstrate interest. Here, we point out that we have found no prominent example where the public has been included in the assessment of systems biology. The question remains whether the public has been assigned an adequate role in the discourse described in this chapter, and, more specifically, whether the public should be more involved in the discourse on systems biology and its science policy. In the next chapter we therefore examine how systems biology is discussed in public and which consequences could arise from this discussion.

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