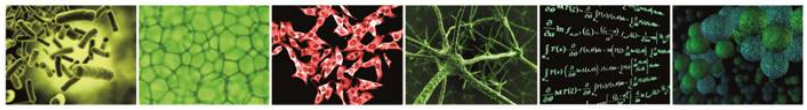


2-nd workshop

"Networking Systems Biology: academia-industry"

Luxembourg, 8.-9. October 2015

REPORT

Organizers: ERASysAPP – ERA-Net for Systems Biology Applications (http://www.erasysapp.eu/).

Location: Maison du Savoir, 2, avenue de l'Université, L-4365 Esch-sur-Alzette, Luxembourg

Organizing Committee

- Egils Stalidzans (Latvian Academy of Sciences, Latvia)
- Frank Glod (National Research Fund, Luxembourg)
- Karine Briand (National Research Fund, Luxembourg)
- Petra Schulte (Projektträger Jülich, Germany)

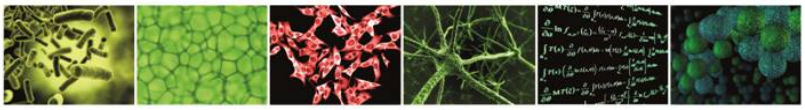
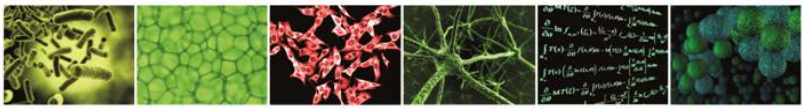


Table of contents



Introduction

The full title of ERASysAPP (www.erasysapp.eu) project is "Systems Biology Applications – ERASysAPP" (app = application = translational systems biology). The project aims to promote multidimensional and complementary European systems biology (SB) projects, programs, and research initiatives on a number of selected research topics with a particular focus on applications – or in other words so called "translational systems biology" research approaches (application-oriented and/or industry-relevant).

In order to reach our ambitious goals, ERASysAPP has been outlined to initiate novel activities and impulses for SB in the ERA. Taking past successful developments and achievements into account, ERASysAPP continues and builds on work, which has been performed by the previously funded successful ERA-Net on SB, ERASysBio and its spin-offs ERASysBio+, SysMo and SysMO2 (www.erasysbio.net). This is advantageous, since it allows for the efficient use of past experiences and tangible results of ERASysBio and will guarantee for maximum synergistic effects. Apart from setting up joint transnational calls and giving impulses for industry to apply more SB approaches, ERASysAPP will focus on horizontal topics such as improved data management and sharing, training and networking with national, transnational, and EU SB initiatives as well as programs outside the ERA.

In addition to other activities, two workshops focusing on networking between academia and industry have been organized. The first one took place 14-15. May 2014 in Berlin. The workshop described in this report is the second and last one within ERASysAPP project. The workshop was devoted to two topics: 1) data exchange and standards and 2) intellectual property rights (IPR). A detailed program of he workshop is presented in the Annex 1.

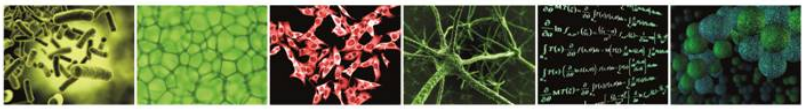
1. Standards and data exchange in systems biology

1.1. Introduction

Common language is important in any collaboration, especially in industry-academia collaboration. Besides differences in goal setting, time scale of operation and criteria of success also common language in data exchange and standards are necessary. Improvements in the field of data exchange and standards have to be made continuously in growing scientific fields including SB.

Ideally, scientists should have a long-term focus taking into consideration the impact of standards and data exchange on the longer term – thinking beyond the project, beyond their own career. The current state and future was discussed in different aspects.

The workshop section on standards and data exchange was started by introductory lectures by experts of the field: Susanne Hollmann (project NORMSYS), Martin Golebiewski (HITS gGmbH and ISO/TC 276, Biotechnology) and Wolfgang Mueller (HITS gGmbH) and continued in group discussions led by the lecturers.



1.2. Discussion results

1.2.1. Data exchange

Centralised infrastructure for data exchange is needed. Existing organizations already engaged in similar activities should be involved because of developed appropriate governance mechanism. The central platform could be operated by consortium (e.g. Infrastructure for Systems Biology Europe (ISBE)) naturally implementing both data standardization and data exchange.

How could a centralized and standardised infrastructure for SB support data integration?

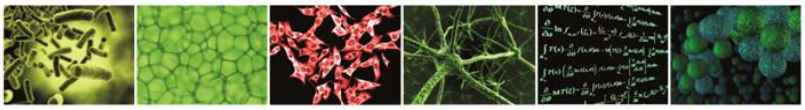
- It has to define clearly: what is a standard, when and how it has to be used.
- It has to organize the management of information on the data (interlinkage, comparability) because just availability does not help: application has to be made easy to be widely accepted. Intuitive and self-explanatory system should be created for that.
- Infrastructure should focus both on data gathering and data quality setting at least minimal data quality to be satisfied.
- Centralised explicit help desk for modelling and data processing would facilitate data exchange quantity and quality.
- Infrastructure could develop checkable criteria for good-enough data sharing.
- Centralised infrastructure could facilitate and mediate inclusion of modelers into experimental design assuring generation of data applicable for modeling targeted when possible.
- Data citation as positive incentive should be stimulated in the community.

What are the risks or drawbacks of a more centralized and standardised infrastructure?

- Duplication of standards/organizations involved in standardization may occur causing "competition" and fragmentation.
- Different infrastructures may become too much niche focused.
- Lack of link with community may develop – community agreement on standard is required to become popular and widely used.
- Cultural differences and traditions regarding data sharing (sharing is good/bad) may block some cases of exchange.
- Most developed countries may be losing competitive advantage sharing their advances.
- Undue or excessive influence of institutions and countries hosting the infrastructure.

Data/model/result exchange motivators

- Linkage to funding – scientists need to be forced to use it by funders. Data exchange requirement (requirement to use a certain system) should be implemented in calls as precondition.
- Training and education regarding standards and exchange tools will facilitate the exchange.
- Mutual interest of academia and industry representatives is an important natural driving force for data exchange and data quality.
- Availability of user-friendly data exchange system.



- Data should be public because academic research is paid mostly by public (tax payers) money.
- Acknowledgement for data publishing could be similar as in case of publications, could be included in performance indicators for scientists
- Application of data exchange friendly standards may be requested by publishers.
- Data integration discussion as sanity check may detect problems that will cost more at a later stage.
- Community acceptance is sometimes more motivating than a system with theoretically best fit for purpose.

Motivation of industry to exchange data

- Direct benefit to get access to he data or to get the data analysed.
- Positive publicity may be valuable for industry.
- Motivation may be limited only to pre-competitive stage.
- Hope for advantage together with public partner (e.g. IMI, most of the time sharing with the team, sharing across EFPIA).
- Well developed secrecy regulation may encourage industry towards data exchange.

What are the risks and hurdles in data exchange within/between academia and industry?

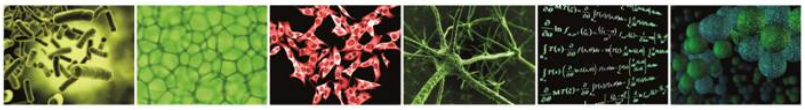
- Low acceptance of standards by scientists – even though required for bringing the product to the market.
- Use of different incompatible standards may complicate communication and cause misunderstandings.
- Different attitude in intellectual property issues may inhibit data exchange.
- Different ideas about the scope of data to be shared may lead to disagreements even when the data exchange idea generally is accepted by both sides.

Dreaming about ideal solution of standards and data exchange

- Central curation.
- Standards and data exchange helpdesk.
- Easy metadata.
- No „overpublication fear" (fear to publish more data than minimally necessary).
- One data type = one general standard, open and free to use.
- Automatic generation of scientific papers from data.

1.2.2. Standards

Looking at the scope of standards applicable for SB it was found that there is no big need for new standards (only standard for data quality metrics was mentioned as missing) and the existing standards are not impediment. It may change in time depending on the number of competing standards in particular areas. The main issue is not the number of standards but their acceptance.



In contrast to community standards, official standard, for instance ISO, certified organisations can work only with other certified ones. That may limit the wide implementation of some official standards. Proprietary standards may hinder exchange, but some of them (e.g. for microscopy data) can be transferred into more generic standards (e.g. OME).

Industry usually does not like to have legally binding standards (unless it gives you an advantage on the market, when you implement the standard, but your competitors do not). It depends on business models, but often community or ISO, CEN and other standards might support access to the market.

Standards can improve the transfer of research results into industrial applications because integration of research results is easier. CDISC (http://www.cdisc.org/) for clinical data is a good example. Different licensing mechanisms might be needed for academia and industry (e.g. standards can be freely accessed by academia, but industry has to pay). CDISC refers to ISO standards.

How to improve acceptance of standards in the community?

- Funders and publishers can implement precondition of implementation of particular standards.
- Critical mass of people needs to start applying the standards and others will follow.
- Business partners can request application of standards (e.g. for certification).
- Principal investigators (PIs) should facilitate use standards in their groups.
- Practical training facilitates implementation of standards on site.

1.2.3. Recommendations on data exchange and standards

- Centralised organisation dealing with data exchange and standards would be needed to facilitate efficiency improvement of research and academia/industry collaboration.
- Acceptance of standards by community is critical for their implementation. Funders and publishers can force and/or facilitate standard implementation by strict qualification rules.
- Easy applicable data exchange systems supported by training can facilitate data exchange process.

2. Intellectual Property Rights in Systems Biology: industry and academia collaboration

2.1. Introduction

The implications of Intellectual Property Rights (IPR) on synthetic biology are intensively discussed in the synthetic biology community. The main goal of synthetic biology is the design and creation of organisms with new biological features, which has especially raised a lot of concerns regarding the impact of patenting practices on research and access. The

community of systems biology (SB) has so far not widely implemented or discussed IPR-related issues. However, they are one of the important elements in collaboration between industry and academia and it is, therefore, important to consider to what extent IPRs may act as an incentive or barrier to research in the area of systems biology (SB) and in collaborations between industry and academia.

Three Intellectual Property (IP) experts were invited to start the discussion at the workshop on a professional level. Notably, these three experts have also been involved at a similar workshop within the context of EraSynBio and have studied IP issues in biology, including synthetic biology. All speakers are authors of very interesting publications devoted to IPRs in synthetic biology, including the co-authored paper: Minssen T., Rutz B., van Zimmeren E., (2015) *Synthetic biology and intellectual property rights: Six recommendations*. Biotechnology Journal, 10, pp. 236-241, DOI 10.1002/biot.201400604.

Berthold Rutz (Germany) from the European Patent Office is a senior patent examiner in the field of biotechnology. He has a special interest in synthetic and systems biology and the use of open and collaborative innovation models in these fields as well as technology transfer.

Timo Minssen (Denmark) from the University of Copenhagen is Associate Professor of IP- & Innovation Law. As scientific advisory board member of the Copenhagen Centre for Regulatory Sciences (CORS) and co-head of the Copenhagen Biotech & Pharma Forum (CBPF), he is a frequent lecturer on various biotech & pharma related topics with many publications in leading international journals. He is also a regular contributor on Harvard Law School's "Bill of Health" blog. At present he is working on a book in pharma & life science competition law with Oxford University Press.

Esther van Zimmeren (Belgium) from the University of Antwerp is a Research Professor in the area of IP law and Governance. She is specialised in IP law and the public and private governance of IP related issues at the European and international level. She has collaborated with scientists and practitioners from various disciplines on the implications of IPRs in different sectors and has written several peer-reviewed articles on the potential role of collaborative innovation and licensing models for dealing with IPRs.

Taking into account the wishes of participants the discussion was not split into different groups as it was planned initially, but all participants were involved in one major workshop on this complex theme. The three above-mentioned experts were available for questions and were actively involved in the discussion.

Experts during panel discussion (from left to right): Berthold Rutz, Esther van Zimmeren and Timo Minssen.

2.2. Outcomes of discussion

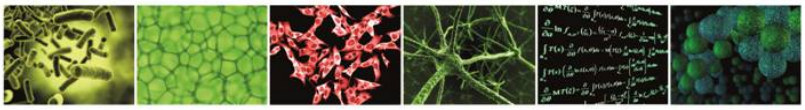
2.2.1. General questions raised to stimulate discussion

- How to align the needs of academia and industry in SB?
- What should be protected by IPRs, by which IPRs, how and when in SB?
- What are the most appropriate IPR strategies for different business models in SB?
- How will the current and future role of standards develop in SB and how does it interrelate with IPRs?
- Need for changes in IP policy at the EU level?

2.2.2. General IPR issues in systems biology

IPR issues cannot be avoided and should be addressed pro-actively

Early in the discussion it was found that IPR issues cannot be avoided: any creation, also in research, belongs to the "creator" by default if nothing else is agreed. Even a declaration that a certain technology or work is freely available is in fact based on the existence of IPRs and implies a particular type of licensing with specific rights and obligations for the creator and for the users.



A short survey among participants revealed that typically researchers in SB try to avoid IP issues in two different ways:

- By using freely available resources without any specific limitations,
- By not dealing with IP related issues concerning their own work and by declaring it freely usable, which in fact implies a certain type of free licensing.

As a result, interesting research findings are out in the public domain and the potential return on investment of public money via IP is lost!

Another phenomenon is that interesting compounds, diagnostics or other inventions are discarded because of lack of IP. Companies claim that it is too risky to invest in further developing research results that could be used by anybody (by their competitors notably!).

The tendency to avoid IP issues may be a consequence of the fact that researchers lack appropriate knowledge on IP issues resulting in an underestimation of the importance of IP in research in general and in collaboration with industry in particular. But different IP rights follow different rules, have different price and different potential uses.

IP peculiarities in SB

Some of SB aspects regarding IPR are:

- usually research is highly collaborative, and hence, ownership to IPRs and access rights will generally need to be shared among many parties (unless agreed otherwise) with different objectives and interests;
- the origin of each contribution is not always traceable, which creates challenges in terms of discussions regarding ownership of IPRs;
- the exact impact of each contribution is not always measurable and assessable, which also creates challenges in terms of discussions regarding ownership of IPRs;
- increasing importance of standardization and thus potentially the issue of standard-essential patents (cf. in 2.2.3.).

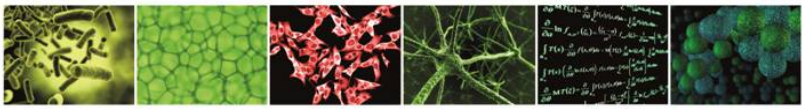
IP peculiarities in industry and academia

Typical industry and academy approach to IP is different.
Typical industry perspective:

1) focus on problem,
2) develop solution,
3) value proposition,
4) selling in a market,
5) protect technology as derivative of business concept.

Typical academia perspective:

1) focus on research,
2) develop solution,
3) look where it can be applied.



The above-mentioned differences are the reason why most IP resulting from academic research will not be valuable to industry. See also "Rembrandts in the attic: Unlocking the Hidden Value of Patents" (a famous economics book in the late 90s) observing that most IP is not used and the importance of finding potential buyers, licensees.

Therefore, the role of Technology Transfer Offices (TTOs) with respect to IP-related issues as mediator between academia and industry is essential, in view of:

- focus on business development,
- patent expertise,
- scientific expertise,
- critical mass,
- experience.

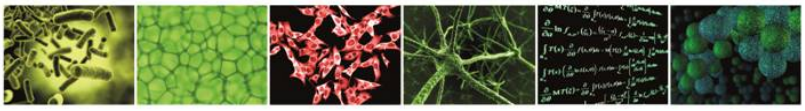
Difficulties dealing with IPR

- Funders impose a requirement that the results of publicly-funded research is widely disseminated but the actual responsibility of how this should happen rests with the researchers.
- In many countries the employee/employer relationship is relatively complex and there are significant differences between countries (e.g. "Arbeitnehmererfindergesetz", professor privilege).
- IP negotiations with potential investors (companies, pharma, biotech etc.) are complicated.
- Possibility to patent should be taken into consideration in decisions about when to publish. This is especially relevant as no real grace period exists in Europe, whereas it does exist in a several other important jurisdictions.
- Public organisations are perhaps not best placed to hold patents and to manage and exploit them in a responsible, commercially relevant manner.
- Technology Transfer Offices (TTOs) are often not considered as partners by the researchers and collaboration does not function as well as it should.

IP strategies can be developed in accordance with the needs of a particular sector, technology, partners, etc.

- Different IP strategies can be employed, for example invention may not just be licenced to a single partner, in some cases it may be wiser to block its use by others, in order to have a competitive advantage, whereas in other cases it might be more interesting to license very broadly.
- Different licensing types can be applied: exclusive / non-exclusive.
- One should be aware of the potential consequences of disclosing research results when trying to find partners, but raise interest in the patent filling.

Approaches to support and facilitate IP protection, when considered desirable



Funders should set money aside for IP counselling in project calls, so that IP does not get compressed or lost at implementation stage.

IP is increasingly used as one of the performance indicators to identify the success of a research project, but in practice this requires a complex analysis because the actual (commercial) value of patents is often uncertain:

- focus on numbers of patents results in the application and maintenance of many useless patents;
- careers of researchers/scientists should not be dependent on the number of patent filings;
- patent filings say nothing about the value of the patents once granted (no quality control at that stage);
- successful licensing/market entry seems to be a better criterion.

IPRs are not enough discussed in the SB community

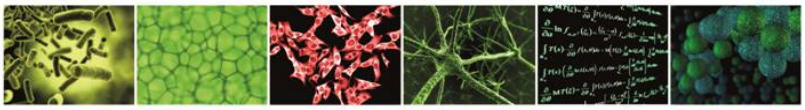
Participants believe that IPR issues are not sufficiently discussed in the SB community. The three introductory lectures that were part of this workshop have named many aspects that most workshop participants were not aware off. That led to a suggestion to have IPR issues on the agenda of different coordination undertakings like ERA-Nets (ERASysAPP, ERA IB) or ISBE as a project with a longer perspective.

That could be done by:

- dedicating a special Work Package to IP,
- organizing training on IP,
- arranging contact persons to consult about IP,
- central legal/IP counsellor.

IP related proposals

- SB institutions, initiatives or projects (for instance, ISBE, ERA-Nets) should include IP issues as one of the items in their programs to assure development of ”best practices”.
- IP management can take place in many different ways, but should at all times be tailored to the needs of a certain sector, technology, community, etc. Alternative strategies for managing IP resulting from collaborative SB projects could be explored in more detail, e.g. examining possibilities for consortia/community to set up a responsible IP strategy, maintaining incentives for investment while keeping openness, “AB tests” for/against IP (like Amazon website marketing tests), sharing the revenues in a fair way, licensing freely within the community.
- IP spin-outs (for instance, EMBLEM (http://www.embl-em.de/), ISIS (http://isis-innovation.com/) etc.) may be an appropriate and responsible way for certain institutions for dealing with IPRs and therefore it is important to learn more about such



models. More transparency and better search engines to conduct more efficient freedom to operate analysis.

2.2.3. Standards related IP issues

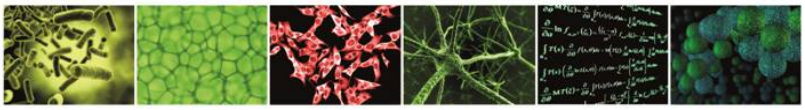
Standards are needed to ensure quality of data, interoperability of systems, exchange of data and models. Interaction of open (community) standards and proprietary formats (e.g. microscopes, Open Microscopy Environment (OME)) has to be taken into account.

Different (types of) SB related standards are available, such as:

- pharma standards for biomarkers;
- PharmML (pharmacokinetics/pharmacodynamics modelling): under development, freely available:
    - initiated by researchers, joined by big pharma,
    - enabling collaboration between pharma and academia,
    - education can be standardised,
    - streamlines application;
- Predictive Safety Testing Consortium (in collaboration with Food and Drug Administration (FDA));
- Snomed-CT: example for de-facto standard:
    - disease ontology in medicine,
    - has to be licensed,
    - non-profit standards organisation,
    - generated knowledge cannot be distributed further.

IP issues in collaborative SB standards

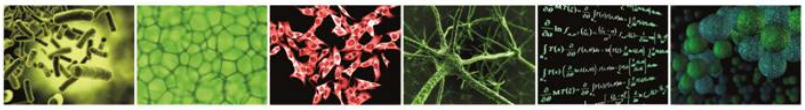
- There is a need to clarify copyrights and database protection rights of data- standards documents.
- Can official “authors” be selected by community?
- GPL: let sign every author of more than 7 lines?
- Should IPR be assigned to organisation?
- Increasing importance of standardization and thus potentially the issue of standard-essential patents.
- Risk for standard essential patent hold-ups and patent trolling scenarios based on the increasing standardization efforts in SB.



- Possibility to get inspiration from FRAND (Fair, Reasonable, and Non-Discriminatory) licensing policies in the information and communications technology (ICT) standard sector. But careful study of pitfalls and peculiarities of SB necessary.
- Consider very controversial recent Court of Justice of the European Union (CJEU) case law regarding interim injunctions enforced by standard-essential patent (SEP) holders in standardization situations. C- 170/13, Huawei v ZTE (2015) and its actual or potential impact on SB.
- Proposal: "FAIR" (Findable, Accessible, Interoperable and Reusable) instead of "FRAND" terms for licensing standard essential patents in SB.
- Not inly IP issues important for exchange of data, standards and open innovation. Also how to tread personal data transfer to other countries, such as the US, has to be considered very carefully in light of CJEU in Case C-362/14 Maximillian Schrems v Data Protection Commissioner (October 2015).

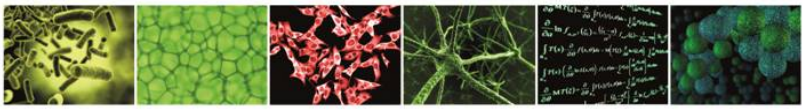
3. Conclusions and recommendations

- Centralised organisation dealing with data exchange and standards would be needed to facilitate efficiency improvement of research and academia/industry collaboration. FAIRDOM in collaboration with ISBE could be good candidates.
- Acceptance of standards by community is critical for their implementation. Funders and publishers can force and/or facilitate standard implementation by strict qualification rules.
- Easy applicable data exchange systems supported by training can facilitate data exchange process. FAIRDOM and COMBINE are good examples.
- SB institutions, initiatives or projects (for instance, ISBE, ERA-Nets) should include IP issues as one of the items in their programs to assure development of "best practices".
- IP management can take place in many different ways, but should at all times be tailored to the needs of a certain sector, technology, community, etc. Alternative strategies for managing IP resulting from collaborative SB projects could be explored in more detail, e.g. examining possibilities for consortia/community to set up a and implement responsible IP strategy, maintaining incentives for investment while keeping openness, "AB tests" for/against IP (like Amazon website marketing tests), sharing the revenues in a fair way, licensing freely within the community.
- IP spin-outs (for instance, EMBLEM, ISIS etc.) may be an appropriate and responsible way for certain institutions for dealing with IPRs and therefore it is important to learn more about such models. More transparency and better search engines to conduct more efficient freedom to operate analysis.

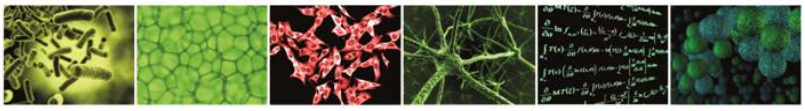


Annex 1. The program of the workshop

Day 2: 08.10.2015. (Thursday)		
TIME	**ACTIVITY**	**REMARKS**
12:00 - 12.30	**REGISTRATION AND SNACKS**	Egils Stalidzans, Frank Glod
12:30 - 14:00	**Lunch, start of workshop "Networking industry-academia"**	
14.00 - 14:10	**WELCOME** • Welcome and introduction to ERASysAPP	Petra Schulte, Project ERASysAPP
14.10 - 14:45	**Participants introduction round**	
14.45 - 15:00	**Why do we need standards? prerequisites, needs and recommendations to improve data exchange and technology transfer with and within industry**	Susanne Hollmann Project NORMSYS
15.00 - 15:15	**Standardising activities in systems biology and beyond: COMBINE and ISO**	Martin Golebiewski HITS gGmbH, Germany and ISO/TC 276 ,Biotechnology
15.15 - 15:30	**FAIRDOM: Standards-compliant data management**	Wolfgang Müller HITS gGmbH
15.30 - 16:00	**Coffee break in POSTER HALL**	
16.00 - 16:05	**Instructions for work in groups on Standards and data exchange**	
16.05 - 17:00	**Work in groups on Standards and data exchange**	Participants are split in 3-4 groups
17:00 - 17:30	**Group reports on Standards and data exchange**	
18:00 - 19:30	**Guided tour combining** Luxembourg Centre of Systems Biomedicine (LCSB) **and a special visit of the Belval High Furnace**	
19:30 - 21:00	**Dinner in the Belval area**	
Day 3: 09.10.2015. (Friday)		
8.30 - 9:00	**Coffee Break**	
9.00 - 9:30	**When Technicality Meets Morality: Patenting of Systems Biology Inventions**	Berthold Rutz European Patent Office,

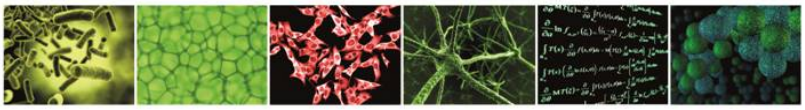


	under the EPC	Germany
9.30 - 10:00	**Open Innovation, Standardization and IPRs in Systems Biology**	Timo Minssen, University of Copenhagen, Denmark
10.00 - 10:30	**Alternative Tools for Dealing with Intellectual Property Rights in Systems Biology: Patent Pools and Clearinghouses**	Esther van Zimmeren University of Antwerp, Belgium
10:30 - 10:45	**Instructions for group work**	
10.45 - 11:15	**Coffee break**	
11.15 - 12:30	**Work in groups on IP issues**	Participants are split in 3-4 groups
12:30 - 13:00	**Group reports on IP issues**	
13:00 - 14:00	**Lunch, end of workshop "Networking industry-academia"**	



Annex 2. List of participants

Title:	First Name	Last Name:	Institution:	Country:
1	Rolf	Apweiler	EMBL-EBI	United Kingdom
2	Uldis	Kalnenieks	University of Latvia	Latvia
3	Francisco	Azuaje	Luxembourg Institute of Health (LIH)	Luxembourg
4	Susanne	Hollmann	University of Potsdam	Germany
5	Margarida	Gama-Carvalho	BioISI - Institute for Biosystems and Integrative Sciences	Portugal
6	Yuri	Kogan	Optimata	Israel
7	Martin	Golebiewski	HITS gGmbH	Germany
8	Raivo	Vilu	Tallinn University of Technology	Estonia
9	Esther	van Zimmeren	University of Antwerp	Belgium
10	Artemis	Hatzigeorgiou	Hellenic Pasteur Intsitute	
11	Babette	Regierer	LifeGlimmer GmbH	Germany
12	Clemens	Ostrowicz	University of Luxembourg - LCSB	Luxembourg
13	Maria Manuela	Nogueira	European Institute for Systems Biology and Medicine	France
14	Eldad	Taub	Optimata	Israel
15	Thomas	Sauter	University of Luxembourg	Luxembourg
16	Timo	Minssen	University of Copenhaguen	Danemark
17	Ronan	Fleming	University of	Luxembourg



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18	Simona	Stoian	UEFISCDI	Roumania
19	Müller	Wolfgang	HITS	Germany
20	Olga	Krebs	HITS	Germany
21	Venkata	Satagopam	LCSB, University of Luxembourg	Luxembourg
22	Egils	Stalidzans	Latvian Academy of Sciences	Latvia
23	Paul	Wilmes	University of Luxembourg	Luxembourg
24	Simona	Stoian	UEFISCDI- Romania	Romania
25	Rob	Diemel	ZonMw	Netherlands
26	Viorel	Vulturescu	UEFISCDI	Romania
27	Anne	Boeter	ZonMw	Netherlands
28	Reinhard	Schneider	LCSB Luxembourg	Luxembourg
29	Jorge	Goncalves	LCSB, University of Luxembourg	Luxembourg
30	Berthold	Rutz	European Patent Office	Germany
31	Frank	GLOD	National Research Fund Luxembourg	Luxembourg
32	Thomas	Dentzer	Luxinnovation	Luxembourg