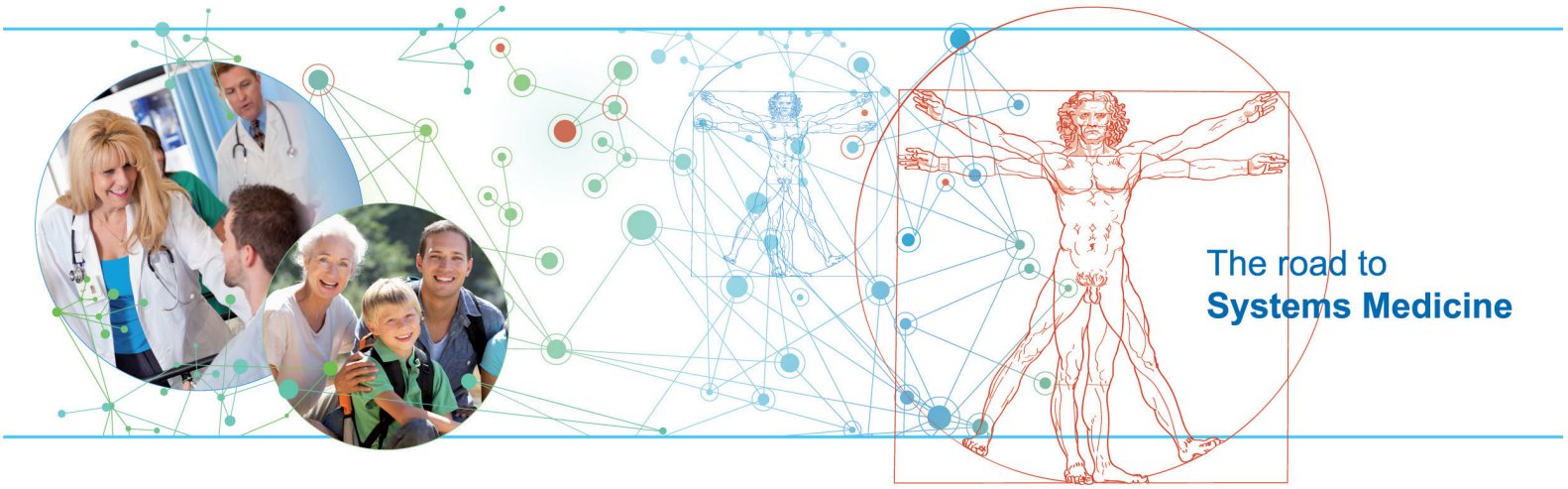
CASYM EUROPE

Coordinating Action Systems Medicine
Implementation of Systems Medicine across Europe

SEVENTH FRAMEWORK PROGRAMME



Europe-wide inventory of industry involved in Systems Medicine

REPORT

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INTRODUCTION AND AIM

Why an industry inventory for Systems Medicine?

Many consider modern medicine to bring huge potential to the healthcare market. The integration of clinical and omics data in computer models will lead to rationally based cost-effective drug and technology development. CASyM aims to speed up innovation in translational activities. As part of its objective to create an implementation strategy for *Systems Medicine* across Europe, CASyM inventoried the potentials and barriers of *industry* towards the medical and healthcare application of Systems Medicine (Systems Medicine). This inventory is part of CASyM Work Package 4 – Strengthening innovation activities, technology transfer and exploitation. In this report, CASyM outlines best practices with the aim of inspiring scientists, company management and investors to create new business based on a Systems Medicine approach.

METHODOLOGY

A three step methodology

This report is based on questionnaires and interviews with representatives from industry working in small and medium enterprises (SMEs) and large companies. As a general rule, a three-step methodology was used:

1) Online questionnaire
2) Telephone interview
3) Combined summary of questionnaire and interview

Interview candidates were initially contacted by e-mail. Candidates included full and associated CASyM partners, personal contacts of CASyM members and attendees at stakeholder events. There were no criteria for candidate selection and anyone interested in the subject could take part in an interview. Many of the interviewees were (co)founder of their company or CEO. Most of them came from European companies.
Several weeks before an interview, the candidate was sent an online questionnaire (see default questionnaire, section 7.1). Questionnaires were completed before interviews took place. During the interviews, the questions and answers from the questionnaire were discussed. When answers were unclear to the interviewer, additional questions were asked to clarify their meaning. The duration of each telephone interview was typically 45-60 minutes. All interviews began with the interviewer stating the *CASyM definition of Systems Medicine*: 'The implementation of systems biology approaches in medical concepts, research and practice, through iterative and reciprocal feedback between data-driven computational and mathematical models as well as *model-driven* translational and *clinical investigations and practice*'. In short, Systems Medicine is the *application of systems biology methods in medical practice*. Usually, within two weeks after the interview, the interviewer prepared a summary of the information provided in the questionnaire and the interview. This summary was sent to the interviewee for correction and approval. All approved summaries are included in the appendix (section 6). For privacy reasons, the answers to question 9 in the default questionnaire ('person or organization recommended for further contact') has been omitted from the interview summaries.

RESULTS

Numbers

This report is based on 16 interviews with representatives from industry (27 companies were contacted; response rate: 60%). In this report, the participating organizations are classified as large pharma (7), large technology (1), SME pharma (3), SME *in silico* (3) and other (2).

Systems Medicine – known and appreciated

Systems Medicine is highly appreciated by the companies interviewed. It is considered one of the key technological and scientific developments and challenges in the coming10-20 years. Industry considers the search for blockbuster medicine no longer sustainable because it involves huge costs and the outcomes of clinical trials are hard to predict and often disappointing. In the past, blockbuster drugs worked mostly for single-cause diseases and for 'the average person'. However, it is now clear that many diseases are multifactorial and cannot be treated with a single medicine. Moreover, recent technologies have shown us that the human being is complex and that humans can differ a lot from each other. Therefore, the companies interviewed identified alternative approaches and have started to implement them in their core business. Systems Medicine is one such approach. Industry uses Systems Medicine to model and simulate patients groups (generic, child, gender, genotype), drug action and drug distribution. This is followed by laboratory experiments and comparison with real patient data. In relation to the companies interviewed, Systems Medicine can be applied well in oncology, cardiovascular diseases, neurodegenerative diseases, ageing, immunology, inflammation and chronic disorders.

There are slight differences in the way that SMEs and large companies use Systems Medicine:

- Large pharma companies use Systems Medicine approaches in a translational way to get the best results out of their clinical trials, to understand diseases at a mechanistic and molecular level and to understand the action of drugs in human physiology using modelling and simulation. The pharmaceutical industry recognizes that it is generating more and more data, but that it often falls short in fully leveraging data for decision making. Applying Systems Medicine will improve the interpretation of available data. It should result in a holistic, integrated view of disease and treatment options. In this way, better and quantitative decisions are expected to be made for patients and the economy.
- Technology-driven industry aims to use Systems Medicine to predict the causes of disease and treatment results for use in medical imaging, personal diagnostics and personal therapy (*non-drug*, e.g. ultrasound, chemo, radio). It uses **ICT-based tools to model and simulate human physiology and apply computer models for personalized and predictive healthcare.**
- *SMEs* vary a lot in the way they use Systems Medicine approaches. Most SMEs are positioned on niche markets. Some companies specialize in silico approaches and make *models* in order to understand diseases. The models are based on the literature and are fed with patient data, either virtual data or data from real samples and biopsies, and are further developed for subsets of patients. Other SMEs are positioned in diagnostics and use Systems Medicine approaches to stratify patients in order to select those who will best respond to a treatment. Finally, some SMEs test approved drugs combination in order to find new treatments.

Successful application of Systems Medicine

Industry believes that Systems Medicine approaches will lead to better drugs or technology, further geared towards personalized treatments. There are various demonstrator and close-to-market projects that underpin the success of the approach, both in an industrial and academic setting, and show that in certain disease areas, Systems Medicine results in more accurate disease knowledge and treatment options than classical approaches. This has convinced some companies to proceed and expand the Systems Medicine approach in their area of business. Many others argue that a much larger portfolio of proof of concept studies is needed to convince the entire field of clinicians, academic and industrial collaborators and investors.

In pharmaceutical companies, many of the drug compounds tested using Systems Medicine are in the pre-clinical or clinical trial phase. As a defined concept, Systems Medicine has not been around long enough to have led to drugs that are already on the market. Companies need some ten years to translate new concepts into products. As a consequence, it is too early to prove that the application of Systems Medicine reduces a product's time to market.

A promising application of Systems Medicine that is already being used by several SMEs to develop new treatments involves *in silico* models of human disease pathways. They are based on literature research and non-confidential information on *existing* drugs and experimental results and are used to predict drug effects that may not be known and are not claimed by the manufacturer of the registered drug. Often a combination of two such registered drugs leads to the development of an innovative and more accurate therapy with fewer side effects.

Many companies consider *public-private partnership (PPP)* [1] a successful concept for an evolving field like Systems Medicine. In a PPP, industry (both large companies and SMEs) joins forces with academic groups of scientific excellence. Usually, a PPP is established in a field where fundamental knowledge is lacking and further exploration is needed. As such, a PPP is interesting for both types of partners. Industry rarely invests in a PPP in an area that it considers to be its own core business (e.g. development, clinical trials and marketing of specific drugs).

Gaps and needs in the application of Systems Medicine

Before Systems Medicine can become part of the daily routine in industry, several hurdles must be overcome:

- There is a need for a wide range of demonstrator and proof of concept (POC) studies, especially for *in silico* modelling:
  - In some *companies*, higher management wants additional proof to fully convince themselves of the suitability of *in silico* modelling approaches compared to traditional drug discovery methods (from lead to phase III trials).
  - In a *clinical* setting, systems and modelling approaches are considered too abstract. Its value is therefore not appreciated. Thus, confidence in this approach would benefit routine clinical practice.
  - *Regulators* must be convinced of the validity of *in silico* modelling approaches.
- There is a need for training and human resources. There are only a few trained systems biologists that understand clinical needs, and vice versa there are only a few medical doctors who are trained in data-driven and quantitative approaches. As a consequence, there are too few ambassadors for Systems Medicine in their respective daily practices.

[1] A public-private partnership is defined as collaboration between research institutions and industry, defined as a long-term arrangement whereby one or more research institutions collaborate(s) on a project with one or more private partners, each party retaining its own identity and responsibility, and working on the basis of a clear and appropriate allocation of tasks and risks.

- Sustainable funding is required to develop strong new business in this discipline. Such funding should come from industry as well as governments. SMEs are dependent on collaboration with academic and clinical partners, especially in the start-up phase, and they often find it difficult to obtain funding for projects that must lead to POCs.
- Many human diseases prove to be much more complex than anticipated. Understanding disease mechanisms costs a lot of time and effort.
- The quality and availability of clinical phenotypic data is presently insufficient. Patient samples need to be standardized. Access to data needs to be facilitated. Biobanks should have sufficient sample material to enable re-analysis of samples. These are prerequisites for the integration and interpretation of data.
- There are many European initiatives in systems approaches. These initiatives should work together and become a single voice for the community.
- Governmental rules and guidelines should be unified. There are too many country-specific laws and reimbursement mechanisms.
- Public-private partnerships in national or European consortia require early integration into emerging projects, easy-to-follow processes for project partnership and access to contact points and partnership forums.
- Potential buyers at large pharmaceutical companies have not yet developed the expertise to discriminate between providers of in silico approaches.

SMEs using in silico approaches mentioned gaps specific to their business:

- In the field of medical technology and informatics, SMEs face strong competition from academia and large companies
- IT know-how is difficult to protect
- SMEs have limited internal resources for joining projects outside the core business of the company
- There is a strong need for proof of concept to convince potential clients
- There is a need to communicate the different technologies developed, their complementarities and how they should be used

Business models for the application of Systems Medicine

Business models for Systems Medicine depend largely on the area of the research and type of industry.

For large pharma, the current business model for developing blockbuster drugs is no longer sustainable. Companies are therefore searching for different models in order to:

- Develop more patient-specific products in a shorter period of time. A holistic, integrated view of disease and treatment options is needed first. Once such fundamental knowledge has been obtained, drugs for specific subpopulations can be developed. Applying Systems Medicine will facilitate better and quantitative decisions for both patients and the economy.
- Gain access to knowledge through cooperation. A PPP with academia and SMEs is considered effective for rapidly obtaining scientific knowledge. The required scale of investment is so large that it will not be provided outside of a partnership model. In general, academic partners are best in up-front science. Moreover, university clinics have access to patients. On the other hand, industry is usually best in understanding diseases and turning a discovery into a marketable

product. In a PPP, research can be considered a “phase 0” trial (prospective, monitor efficacy, no treatment) using small patient groups. Risks and rewards should be shared between academia and industry.

For SMEs, several models are considered advantageous:

- Knowledge generation by modelling, where the intellectual property (the model) is kept within the company and the output of the model is sold.
- Discovery and development of drug candidates and generation of pieces of intellectual property (IP), until an inflection point is reached to trigger interest from large pharma. Then, either a licensing deal is agreed or a portfolio of IP is sold to a virtual standalone company (single asset company) financed by a venture capitalist and/or pharma company.
- Business services and intellectual property on new lead and drug targets facilitating industry collaborations.
- Combination of existing drugs (or drugs close to the market) and the beneficial effect of that combination predicted in silico. Regulative demands are expected to be easier met when existing drugs are used.
- Fee-for-service is valued by some, but is rendered unprofitable by others.
- Use of pension funds to attract a more stable and long-lasting investment. This approach consists of applying the financial engineering technique of securitization to drug candidate assets.
- Cooperation with healthcare insurance providers and healthcare providers. As an example, in the USA, health care providers cooperate with physicians in the clinic in order to minimize costs and optimize therapy.
- Awareness of the perspective and procedures of regulatory authorities and making that an integrated component throughout all steps of research and drug development.

Industrial needs from policy makers

Industry representatives mentioned several needs that must be met by national governments, funding agencies and the EU:

Proof of concept portfolio: industry would appreciate CASyM compiling and hosting a POC portfolio on its website. The interviewed persons believe that company management would be more open towards Systems Medicine if its success stories were validated and readily available. Moreover, POC may facilitate access to the market for the procedures of regulatory authorities.

Open access to data: the information and data generated in publicly funded research projects should be openly available for everyone. Open access to data, knowledge and expertise is crucial to ensure that not only funded projects but the field as a whole benefit from the massive amount of funding invested in this area.

Funding programmes specifically for disruptive industrial innovation: national governments and the EU should facilitate disruptive innovation by means of specific funding schemes allowing for cooperation between scientists from academia, industry and clinics.

International trade federation of SMEs: one SME explicitly recommends the creation of a trade federation of SMEs in order to help non-experts discriminate between the various approaches (bioinformatics, mathematical modelling, heuristic modelling, etc.). The main objective is to reduce the market's opacity and thus facilitate adoption.

CONCLUSIONS

Improve the interpretation of disease data

Industry is very interested in Systems Medicine, and many companies in the field of modelling, technology development and drug development are already applying it. Systems Medicine is considered a requirement for a better understanding of disease mechanisms, portfolio optimization and for identifying new technology, drug targets and patient subsets. Systems Medicine will accelerate the development of personalized medicine.

Collaborate

Public-private partnerships are highly appreciated and considered crucial because they combine different areas and traditions in science and healthcare. PPPs should always start and end with the needs of the patient. Open discussion should facilitate a clear focus on the gaps and technological challenges of the future (not of those of today).

Proof of concept

Presently, there are only a few cases showing proof of concept and this collection needs to be enlarged. However, there is a lack of robust and widespread proof of concept that restrains industry in making large-scale investments in the Systems Medicine approach. Industry would benefit from an online POC portfolio and a 'global standard' of quality guidelines for in silico approaches.

Provide access to data

Improved mechanisms for accessing and using patient data are required for research purposes while the privacy of the patient is ensured. Computational models can only be created and used accurately when a sufficient amount of high-quality data is available and a data management infrastructure has been implemented. The focus should be on specific disease subsets represented by homogenous and well-characterized patient subpopulations.

OUTLOOK

Future CASyM work and events aimed at industry

CASyM will keep up to date with the developments and needs of industry. CASyM WP4 will continue to interview representatives from industry and promote the Systems Medicine approach. In addition, during various stakeholder meetings, industry will be specifically targeted. All results will be disseminated via the CASyM website.

- The feasibility of a CASyM proof of concept webpage by industry will be tested in early 2014. On this page, industry will showcase POCs and may thereby attract collaborators.
- Innovative projects and initiatives will continue to be pursued and industrial representatives will be interviewed and made aware of Systems Medicine until the end of the CASyM initiative. The results will be discussed in the WP4 industry/academia group and disseminated online.
- Annually, in spring 2014, 2015 and 2016, a one-day workshop will be organized for SMEs and university research groups looking for international partners, funding or visibility. The goal is for both parties to present their ideas and proof of concepts for collaboration in Systems Medicine. Each workshop will include a roundtable discussion and presentations of innovative projects on a defined subject. Around 50 people will participate in each workshop. These workshops will be organized collaboratively by WPs 4 and 6. The first workshop is planned for 10 April 2014 in Lyon, France.
- Near the end of CASyM (2016) a wrap-up meeting will be organized for industry and other interested stakeholders. Industry will have the opportunity to interact with academia, hospitals, patient organizations, regulators and governmental organizations. Participants may contribute to a continuation of CASyM. The meeting will also serve to address the next steps after CASyM, such as discussing a concept for a European Association of Systems Medicine.

ANNEXES

Interview summaries

Default questionnaire

Coordinating Action Systems Medicine
Implementation of Systems Medicine across Europe

WP4 - Strengthening innovation activities, technology transfer and exploitation

Systems Medicine is the **application of systems biology methods to medicine**, in CASyM defined as "The implementation of Systems Biology approaches into medical concepts, research and practice, through iterative and reciprocal feedbacks between data-driven computational and mathematical models as well as **model-driven** translational and clinical investigations and practice´´

Public-Private Partnership (PPP) is a collaboration between research institutions and industry, defined as a long-term arrangement whereby one or more research institutions collaborate(s) on a project with one or more private partners, each party retaining its own identity and responsibility, and working on the basis of a clear and appropriate allocation of tasks and risks.

Your organisation:

Name person:

Function person:

Address:

E-mail:

Website:

Organisation type:

Involved in CASyM:

Date interview

1.	**Are you familiar with the term Systems Medicine as defined above?**	*No / Yes, since…*	
2.	**Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?**		
3.	**Does your organisation apply Systems Medicine according to the definition above?**	*Yes / No* *If yes, please elaborate here and below:*	
		Number of projects:	
		General topic of projects:	
		Type of projects: (e.g. PPP, purely industrial)	
		Approximate total budget of Systems Medicine projects:	
4.	**What are best practices you are aware of in Systems Medicine projects in terms of innovation and exploitation?**	*Please provide examples (innovations, case studies, proofs of principle and success stories):* - *Which one?* - *Who was involved? Contact names / details?*	
5.	**What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?**	*Please, provide examples*	
6.	**In which way can Systems Medicine be important for industry in the future?**	*Please, elaborate*	
7.	**What would be a good business model to apply for Systems Medicine?**	*Please, elaborate*	
8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	*If yes, please elaborate. E.g. type of projects, number of projects, which department, collaboration with other organisations*	
		Number of projects:	
		General topic of projects:	
		Type of projects: (e.g. PPP, purely industrial)	
		Approximate total budget of projects:	
9.	**Which person / organisation do you recommend we should contact as well?**	*Please provide us with the contact information (name, organisation, department, function , email and phone number.)*	
10.	**Any recommendation or comment on the subject of Systems Medicine ?**		

Interview Adriano Henney

Your organisation:	**Obsidian Biomedical Consulting (OBC) & Virtual Liver Network (VLN)**
Name person:	Adriano Henney
Function person:	Owner (OBC) Programme Director (VLN)
Address:	University of Heidelberg, Im Neuenheimer Feld 267, 69120, Heidelberg, Germany
E-mail:	adriano.henney@obsidian-biomed.com adriano.henney@virtual-liver.de
Website:	www.virtual-liver.de
Organisation type:	1-man consulting company (OBC) National flagship research programme (VLN): 250 participants, 69 Principal Investigators, 44 Projects and 40 Institutions in Germany, including SMEs and Pharma
Involved in CASyM:	Associated partner
Date interview	25 March 2013

1.	**Are you familiar with the term Systems Medicine as defined above?**	Yes, since it was first proposed	
2.	**Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?**	Yes, the Virtual Liver programme is focused on delivering to the clinic in a way that reflects the Systems Medicine agenda	
3.	**Does your organisation apply Systems Medicine according to the definition above?**	Yes, in my opinion Systems Biology represents a toolbox that can be used in various disciplines, like in medicine. In the VLN, liver physiology in health and disease is studied, e.g. fatty liver, inflammation, regeneration following injury. In the VLN board, several clinicians are present.	
		Number of projects:	44
		General topic of projects:	Multiscale modelling of liver function and physiology
		Type of projects: (e.g. PPP, purely industrial, collaboration with others)	Academic and industrial, working as an integrated network. It's largely academic. The industrial partners are Bayer and one *in silico* SME. The companies have a more applied / translational view and projects are at the interface of clinical pharmacology. Two clinics (Stuttgart and Kiel) have patient studies. As a flagship programme, VLN does not have deliverables, but aims for scientific blueprints.
		Approximate total budget of Systems Medicine projects:	The VLN budget is 44 M€ over 5 years

4.	**What are best practices in Systems Medicine projects in terms of innovation and exploitation?**	'Systems Medicine' hasn't been going long enough as a defined concept to have success stories in my view, but SysBio applied to medicine as a forerunner has had some success stories: the use of the ion channel heart model to support registration by the FDA of Ranolazine is an example. Some other examples of utility were shown in cancer studies to understand mode of action also (e.g. Iressa- Hendricks et al)	
5.	**What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?**	- Many cultural aspects related to reluctance to accept the approaches; - Failure to understand what Systems Medicine and SysBio are; - Lack of clarity what precisely are the clinical imperatives to address and how best to deliver what a patient and clinician need to implement approaches; - Building confidence in the clinic that Systems Medicine is of added value - Time constraints of practicing clinicians - Fragmentation in EU, thereby lacking a single voice of the systems approach. CASyM should aim for leadership, with one person as the "ambassador". - Too few interactions with regulatory authorities We have to deliver: - Example models across scales - Evidence that Systems Medicine is of utility in the clinic	
6.	**What would be a good business model to apply for Systems Medicine?**	Difficult to pinpoint to one business model, since Systems Medicine by definition represents a variable toolbox. Joint ventures seem to be the most promising, presently. In general, business could profit from: -Improved understanding of the dynamics of disease, leading to more efficacious, tailored therapies. -Impacts on the patient, the discovery and development of new medicines and the design of more efficient clinical trials	
7.	**In which way can Systems Medicine be important for industry in the future?**	I would suggest that the model devised by the BMBF to fund the Virtual Liver Network could be a useful blueprint/ starting point to consider	
8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	Yes, see all the answers above	
		Number of projects:	
		General topic of projects:	
		Type of projects: (e.g. PPP, purely industrial, collaboration with others)	
		Approximate total budget of projects:	
9.	**Any recommendation**	CASyM should make a proposal for Horizon2020, in which physiology, medicine and patients are addressed.	

Interview Alain Huriez

Your organisation:	**EPEMED**
Name person:	Huriez
Function person:	Chairman
Address:	Luxembourg
E-mail:	ahuriez@epemed.org
Website:	www.epemed.org
Organisation type:	non for profit
Involved in CASyM:	No, but present at the second CASyM stakeholder meeting, round table 'What business models for industries involved in Systems Medicine?', Lyon, 25 March 2013.
Date interview	17 May 2013

1.	**Are you familiar with the term Systems Medicine as defined above?**	Yes, since 2011. EPEMED is not involved in CASyM, but is in general aware of Systems Medicine, biomedicine and integration of data. On an international level, we are in contact with industry in France and with the Luxembourg Centre of Systems Biomedicine.	
2.	**Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?**	Yes, as a method for discovery of new targets, portfolio and research optimization, data integration and validation of current marketed drugs. Systems Medicine may fundamentally alter biotechnology into generation of more precise drug targets. Analysis and knowledge about interaction and integration of genes and proteins will lead to optimized use of the data and will show the relevance of the data. Systems medicine or systems biology will bring another approach in optimization of current drug targets and the generation of new, better targets. EPEMED can be considered a think tank or lobby among stakeholders, developing a concept for realizing personalized medicine in Europe. Through the production of knowledge like by webinars, white papers, position papers and conferences and market assess studies we try to create awareness and guiding decision makers to stimulate research in personalized medicine. The goals of EPEMED are broader than just Systems Medicine. Partners in EPEMED include large and small pharma companies, IT and diagnostic companies, clinicians, etc. EPEMED members pay a member fee. In our view the difference between Systems Medicine and Personalized medicine is small, since both concepts focus on market access. In the future, our studies other project and might be systems medicine.	
3.	**Does your organisation apply Systems Medicine according to the definition above?**	No, EPEMED is a non for profit association dealing with Personalised medicine.	
		Number of projects:	N/A
		General topic of projects:	

		Type of projects: (e.g. PPP, purely industrial)	
		Approximate total budget of Systems Medicine projects:	
4.	**What are best practices you are aware of in Systems Medicine projects in terms of innovation and exploitation?**	Not fully aware	
5.	**What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?**	My guess is that examples should be provided and sustainable funding would be required to develop strong new business in such discipline. Commercial proof of concept of new drug targets is needed. The discipline is fully recognized to qualify for funding. A full translational research towards business is needed. Investors should pay for it.	
6.	**In which way can Systems Medicine be important for industry in the future?**	For portfolio optimization and finding new drug targets. Areas include neurodegenerative disease like Parkinson, ageing, immunology, inflammation, chronic disorders and more. Systems biomedicine would very well apply in these areas.	
7.	**What would be a good business model to apply for Systems Medicine?**	Services business and intellectual property on new lead and drug targets, allowing industry collaborations. Service companies would be good, when the Intellectual Property is kept within the company. Fee-for-service companies will not be viable in this area.	
8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	Yes, personalized medicine	
		Number of projects:	We finance one project, funded by our members.
		General topic of projects:	We organize a conference
		Type of projects: (e.g. PPP, purely industrial)	Market access hurdles and challenges in Europe for drug diagnostics, The focus is on molecules that are already approved together with a biomarker that is approved by the EMA. In the future we will fund more projects, always with a maximum duration of one year.
		Approximate total budget of projects:	150 k€

Interview Andreas Schuppert

Your organisation:	**Bayer Technology Services**
Name person:	Andreas Schuppert
Function person:	Key Expert
Address:	Germany
E-mail:	andreas.schuppert@bayer.com
Website:	*www.bayertechnology.com*
Organisation type:	Large pharmaceutical company
Involved in CASyM:	Full partner
Date interview	13 March 2013

1.	**Are you familiar with the term Systems Medicine as defined above?**	Yes	
2.	**Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?**	Yes, we expect significant contributions to improved efficiency of the pharma R&D workflows. By using systems approaches, Bayer aims to obtain *information*. Bayer claims state of the art in Systems Medicine worldwide.	
3.	**Does your organisation apply Systems Medicine according to the definition above?**	Yes, since we do Systems Pharmacology since more than 10 years for customers in Pharmaceutical and Biotech Industry worldwide. Moreover, we invest significantly in own research and academic collaborations. We simulate patients by modelling the patient (generic, child, gender, genotype) and model drug action and distribution. Bayer employs well trained modellers and systems biologist, decreasing wet lab research in favour of in silico research.	
		Number of projects:	Appr. 10 running at present. In all, 50 projects have been initiated.
		General topic of projects:	Systems Pharmacology, modeling of drug action in man, optimization of clinical trials. Focus on cardiology, hematology, oncology, diabetes.
		Type of projects: (e.g. PPP, purely industrial, collaboration with others)	All kinds. Mostly industrial projects (clinical trials). PPP with academia through the Virtual Liver Network and in BMBF funded grants. The strategy for PPP is to extend existing, fundamental knowledge.
		Approximate total budget of Systems Medicine projects:	Appr. 3 million euro's annually
4.	**What are best practices in Systems Medicine projects in terms of innovation and exploitation?**	Real success stories are limited, due to the lack of PoC. It will take 10 years to get a drug, developed by using systems medicine approaches, into the clinic.	

5.	**What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?**	-Data driven approaches are sufficiently available, but mechanistic modelling is limited yet. -Human resources (trained systems biologists) are limited at the moment -Budget in clinic and health care sector is scarce -Medical doctors are not trained in data driven and quantitative approaches, thus need to get convinced that Systems Medicine is of help in their daily practice	
6.	**What would be a good business model to apply for Systems Medicine?**	- Cooperation with health care insurances and health care providers. In the USA health care providers cooperate with physicians in the clinic in order to minimize costs and optimize therapy - By providing Systems Medicine services to other companies. Overall, the business model depends on the scientific progress in a certain area	
7.	**In which way can Systems Medicine be important for industry in the future?**	Improvement of the drug R&D efficiency	
8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	Yes. Systems Biology, however, has not proven to aid in curing disease or prediction in the clinic	
		Number of projects:	Appr. 10
		General topic of projects:	Biomarkers, Biological Networks, Multi-omics approaches, molecular approaches.
		Type of projects: (e.g. PPP, purely industrial, collaboration with others)	
		Approximate total budget of projects:	Appr. 3 million euro's annually
9.	**Any recommendation**	Through open discussion, get a clear focus on the gaps and technological challenges of the future, not of those of today. Focus on the need of the patient. International collaboration (including PPP) is crucial, since it combines different areas and traditions in science and health care.	

Interview Claus Bendtsen

Your organisation:	**AstraZeneca**
Name person:	Claus Bendtsen
Function person:	Head Computational Biology
Address:	UK
E-mail:	claus.bendtsen@astrazeneca.com
Website:	*www.astrazeneca.com*
Organisation type:	Large pharmaceutical company
Involved in CASyM:	Full partner
Date interview	12 March 2013

1.	**Are you familiar with the term Systems Medicine as defined above?**	Yes	
2.	**Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?**	In part. We recognize that we are increasingly generating data, but often fall short in our abilities to fully leverage data in our decision making.	
3.	**Does your organisation apply Systems Medicine according to the definition above?**	Yes, in order to form an integrated understanding of our data in support of investment decisions. AstraZeneca started 3 years ago in Systems Medicine.	
		Number of projects:	Over 10
		General topic of projects:	Many disease areas except for neuroscience. The aim of the projects is to increase quantitative understanding as well as hypothesis generation. In this way a more informed decision making in clinic and better understanding of disease will be generated. Models should be more than just descriptive and must show efficacy and safety. The models should be more than statistical and should help in design of pre-clinical assays, identify (plasma) biomarkers and aid in understanding the design and the results of clinical trials.
		Type of projects: (e.g. PPP, purely industrial, collaboration with others)	Mostly purely industrial but examples of PPP, CROs and consultancies.
		Approximate total budget of Systems Medicine projects:	(not disclosed)

4.	**What are best practices in Systems Medicine projects in terms of innovation and exploitation?**	NIH white paper on Systems Pharmacology There are some proofs of concept in cardiovascular area and oncology. In oncology, experimental data are generated, cells screens performed, xenografts and animal models used and clinical trials performed. In cardiovascular area, ion channels are modelled, electrophysiology performed, data are available and clinical trials performed.	
5.	**What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?**	The limiting factor is not so much the limited number of successful models, but the complexity of human disease and the data availability Areas that are not yet well understood: - Inflammation (respiratory), infection (therapy resistance mechanisms) and immunology, since models are complex and difficult to make - Neuroscience, since in clinical trials brain measurements cannot be performed and good brain models are not available	
6.	**What would be a good business model to apply for Systems Medicine?**	The current business model in pharmaceutical industry is not sustainable. Therefore, AstraZeneca is searching for different models. One of them is Systems Medicine, in order to get a holistic, integrated view of disease and treatment options and make more sense out of available data. In this way, better and quantitative decisions are expected to be made for patient and economy.	
7.	**In which way can Systems Medicine be important for industry in the future?**	More informed decisions for drug development and better outcomes for patients.	
8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	Yes, increasingly during the last 10 years	
		Number of projects:	Hundreds
		General topic of projects:	There are a few systems biology projects, in order to get a basic understanding of cell function. These projects are different from the abovementioned Systems Medicine projects
		Type of projects: (e.g. PPP, purely industrial, collaboration with others)	An increasing number of PPP are performed. These projects are beneficial for basic understanding of health and science.
		Approximate total budget of projects:	(not disclosed)

Interview François-Henri Boissel

Your organisation:	**Novadiscovery**
Name person:	François-Henri Boissel
Function person:	Chief Executive Officer
Address:	60 avenue Rockefeller 69008 Lyon, France
E-mail:	francois.boissel@novadiscovery.com
Website:	www.novadiscovery.com
Organisation type:	SME
Involved in CASyM:	Associated Partner
Date interview	13 and 27 March 2013

1.	**Are you familiar with the term Systems Medicine as defined above?**	Yes, since 2000. The company Novadiscovery started in 2010, basing its science on this emerging field.
2.	**Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?**	Undoubtedly yes. The seamless integration of biomedical knowledge and real-world patient data will dramatically improve our understanding of disease processes, open up avenues for new treatments, rationalize R&D spending by reducing in-vivo/in-vitro trial-and-error, enable personalized treatment decision-making and optimize healthcare delivery.
3.	**Does your organisation apply Systems Medicine according to the definition above?**	Systems medicine is at the core of Novadiscovery's expertise. We develop mathematical models of diseases in a variety of areas (cancer, cardiovascular, infectious diseases, etc.) in order to identify and develop innovative treatments as well as deliver personalized medicine capabilities. Novadiscovery applies Systems Medicine by working with a team of “biomodelers”, typically trained as engineers and/or mathematicians (MSc) supplemented by a strong background in biology/biomedical sciences (PhD). The biomodelers read scientific literature on specific diseases, extract information on all mechanisms involved in a particular disease (from genes to populations) and assign a strength of quality of the information extracted (or “quality score”) to the way the studies are set up. In most cases, studies and knowledge extracted are discussed with scientific experts (typically clinicians expert in the disease). The biomodelers then build a multi-scale (dynamic) mechanistic graphical model, using biological, clinical and real world patient data as well as data from drug candidates. This first deliverable is called the “Knowledge Model”. It is a multi-layered map of all the mechanisms involved in the disease of interest (see Appendix 1). This Knowledge Model is then converted into mathematical equations and ultimately computer code. It becomes a “Formal Model”. In parallel, a “Virtual Population” of patients is developed, taking into account real-world patient data drawn from epidemiological studies or biological datasets. By combining the Formal Model and the Virtual Population, a large number of assumptions can be tested in a predictive framework (see Appendix 2), thanks to the discovery of the Effect Model Law (see Appendix 3). In this framework, the

<table>
<tr><td></td><td></td><td colspan="2">benefit of a potential drug is reflected by the difference between the incidence of an event caused by illness in treated patients in relation to untreated patients, using the same virtual target population. By varying the characteristics of the target population, effects of drug candidates can be tested on specific patient populations, thereby leading towards personalized medicine.</td></tr>
<tr><td></td><td></td><td>Number of projects:</td><td>Currently 4 R&D programs, 1 fundamental research and 1 technology development project.</td></tr>
<tr><td></td><td></td><td>General topic of projects:</td><td>R&D: lung transplantation, acute stroke, sepsis, lung cancer.

Fundamental research: biomedical knowledge and uncertainty management.

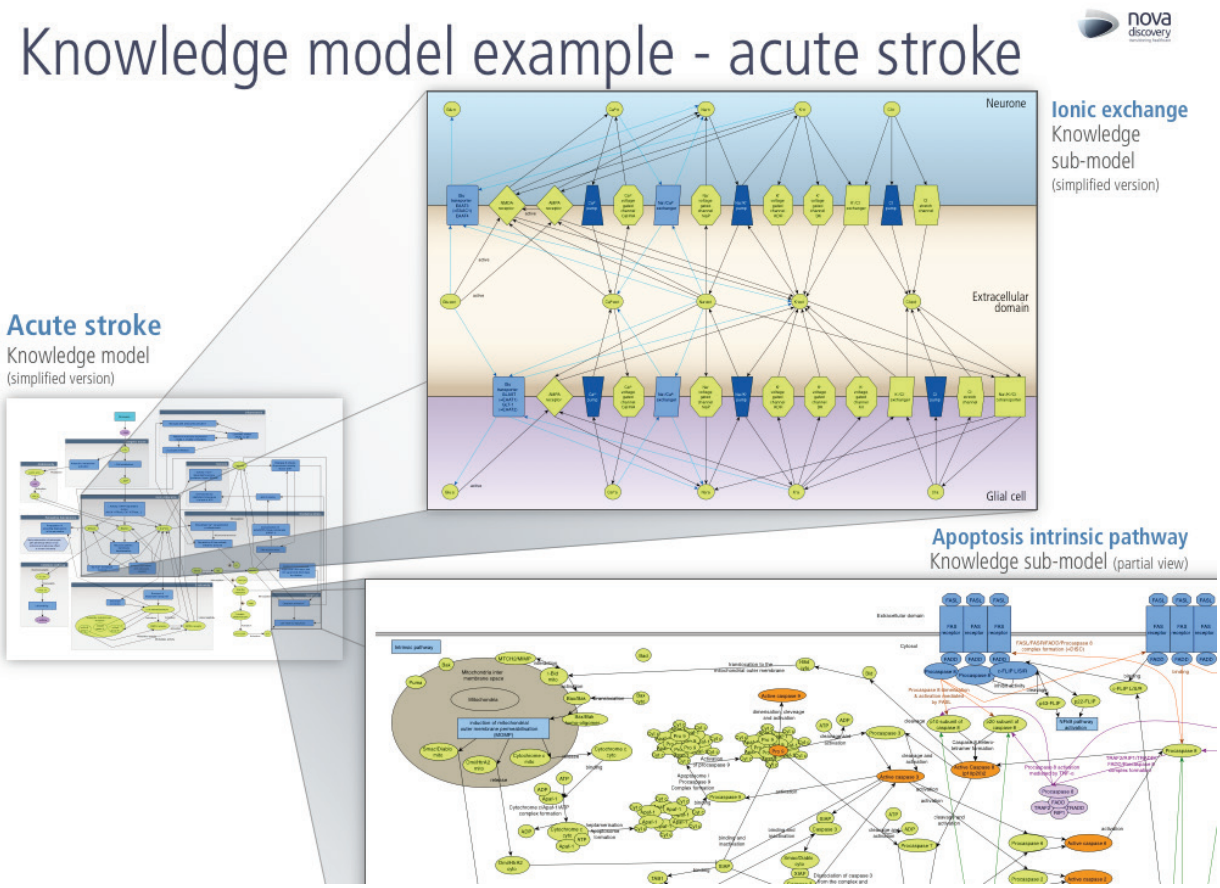
Technology development: knowledge and data management, modeling and simulation platform (see Appendix 4).</td></tr>
<tr><td></td><td></td><td>Type of projects:(e.g. PPP, purely industrial, collaboration with others)</td><td>A mix of (i) internal, (ii) collaborations partially funded through research grants and (iii) industrial partnerships.</td></tr>
<tr><td></td><td></td><td>Approximate total budget ofSystems Medicine projects:</td><td>Currently circa1 million euro’s, expected to grow 10x within the next 24 months.</td></tr>
<tr><td>4.</td><td>What are best practices in Systems Medicine projects in terms ofinnovation and exploitation?</td><td colspan="2">In terms of best practices, we are developing internally our own SOPs with regards to knowledge and uncertainty management, quality control, therapy responder profiling, etc. Another fundamental element Novadiscovery is engaged in is the development of a formal evaluation framework to help regulators and pharma companies understand how to assess Systems Medicine simulation results.
Novadiscovery has produced or assembled (based on previous work from Nova’s researchers before the company’s incorporation) a number of PoCs ranging from dose-effect prediction to new indication identification. Please refer to the PoC posters attached in a separate document.</td></tr>
<tr><td>5.</td><td>What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?</td><td colspan="2">Widespread adoption of Systems Medicine is currently hindered by a lack of convincing success stories and PoC. What is needed is a large-scale proof of concept applied to a drug R&D program where the value of in silico technology can be established.

Gaps towards widespread in silico modelling approaches and Systems Medicine:
- Regulators need to get convinced of its validity
- Higher management of large pharma companies need to be convinced of its suitability, compared to traditional drug discovery methods (from lead to phase III trials)
- Modelling is not yet understood by many people and is therefore not appreciated
The Systems Medicine field would benefit from a ‘global</td></tr>
</table>

		standard' of quality guidelines for in silico approaches. This standard should be made by scientific and clinical experts. Agencies (regulators & payers) should be involved in the process as they will be instrumental in the widespread adoption of systems-based approaches throughout the industry.	
6.	**What would be a good business model to apply for Systems Medicine?**	There are broadly speaking two segments where Systems Medicine can be applied: new drug R&D and medical practice. With regards to the former, given the technology's lack of maturity and poor traction with large pharma, both modelling software licensing and fee-for-service models are currently thought not to be viable. Another approach would be to focus on a proprietary R&D model. This is highly capital intensive and should preferably not be executed along a traditional biotech model. The recommended approach is to structure a virtual pharma ecosystem where the original IP is generated using Systems Medicine (new target(s), repurposing, combinations) before it is transferred to a standalone single or portfolio Asset Company which in turns receives funding from venture capitalist firms. The assets are then licensed out to a large pharma once a first inflection point is reached. This approach consists in applying the financial engineering technique of securitization to drug candidate assets. The product/market fit for personalized medicine applications in daily medical practice is certainly easier to establish. However, start-ups will face issues with regards to distribution channels, direct involvement in regulatory matters (possibly so far as to conduct trials) and limited exit opportunities. More generally, Novadiscovery expects providers of Systems Medicine solutions to gradually evolve from a cost-plus pricing tactic to a value-based one once the ecosystem accumulates sufficient evidence.	
7.	**In which way can Systems Medicine be important for industry in the future?**	Systems Medicine is the only way forward to put breakthrough innovation back at the heart of the drug discovery process. There is a significant amount of knowledge available about disease mechanisms that can only be structured and made actionable through Systems Medicine approaches.	
8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	The core is Systems Medicine. All of our aforementioned R&D projects draw on the full scope of systems-based methodologies, from cellular level up to population level.	
		Number of projects:	
		General topic of projects:	
		Type of projects:(e.g. PPP, purely industrial, collaboration with others)	
		Approximate total budget of projects:	
9.	**Any recommendation**	We fully support the CASyM and similar initiatives as we are convinced that "coopetition" among the players is the most suitable strategy at this stage of the market's development. Unfortunately, a number of SMEs are stuck in a "competition" mode which effectively curtails the widespread adoption of these game-changing approaches. We strongly recommend the creation of an international trade	

		federation of SME providers in order to help non-experts discriminate between the various approaches (bioinformatics, mathematical modelling, heuristic modelling, etc.). The main objective is to reduce the market's opacity and thus facilitate adoption. Novadiscovery has indicated it would gladly take the lead in setting up this federation. One of the single most important levers to accelerate adoption is, in our mind, the agencies (regulators & payers). Significant emphasis should be laid on helping these stakeholders understand the benefits of Systems Medicine. Once this primary objective is achieved, we can assume large pharma will naturally invest in it.

The knowledge model



The Knowledge Model consists in a series of entities involved in the disease mechanisms. These entities are grouped into submodels to facilitate exploration and documentation. In the particular case of sepsis, those submodels are:

- The inflammatory response;
- The molecular model of both the coagulation and the fibrinolytic pathways;
- The molecular model of cell energy metabolism cascade;
- A phenomenological model linking the fall in ATP production to the failure of a representative organ;
- The model of immune system response.

The modelling process

The modelling process at Novadiscovery consists in a series of sequential steps before the delivery of a validated disease model.

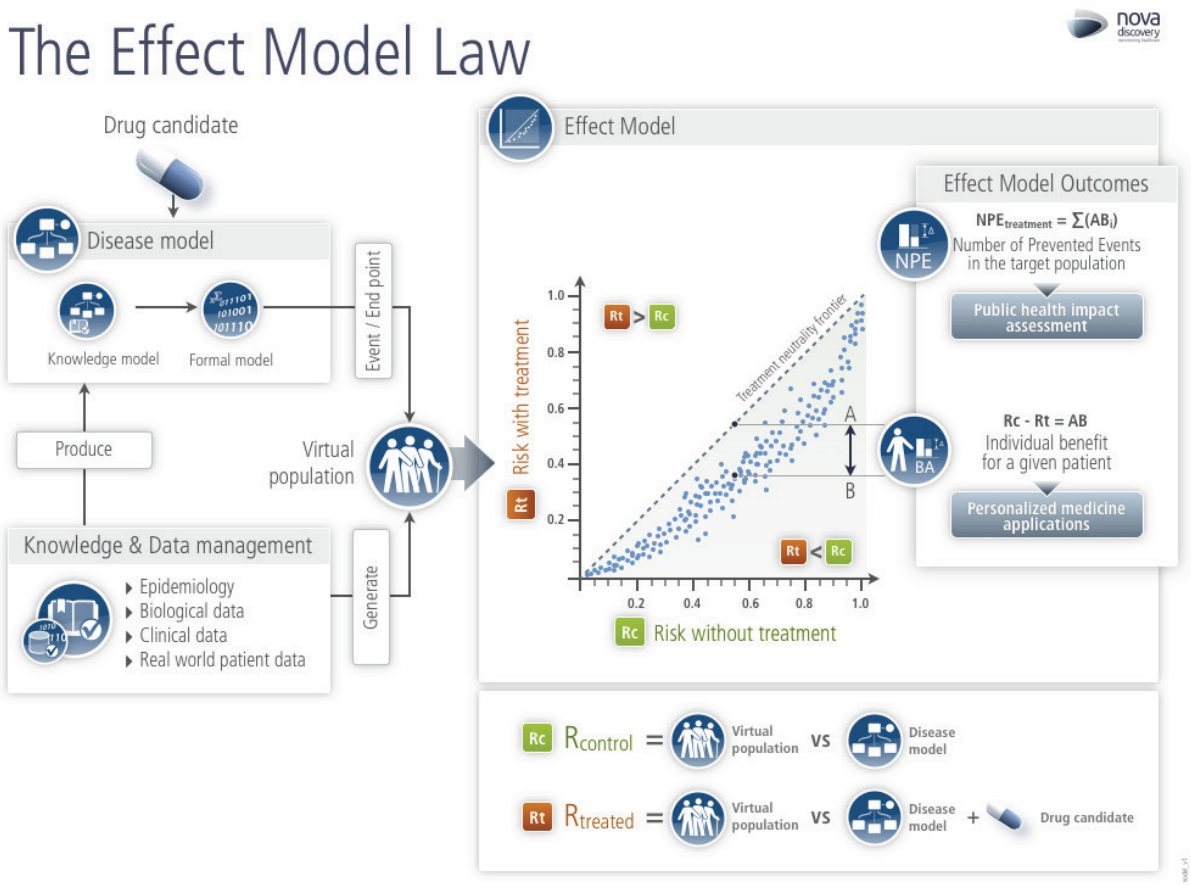
First, a Knowledge Model is developed in partnership with disease experts. It consists in a graphical representation of all the entities that have been identified as playing a role in the disease mechanism.

Once validated, the Knowledge Model is converted into a Formal Model, i.e. a series of mathematical equations. These are in turn converted into computer code to enable simulations.

The Virtual Population is developed in parallel to the disease model.

The calibration is performed with available data. Model validation consists in a two-step process: first, the model is operated to reproduce experimental data that was not used during the calibration process. Then, the model is operated to tryand reproduce knowledge that was not formerly incorporated into the Knowledge Model design phase.

The effect model law



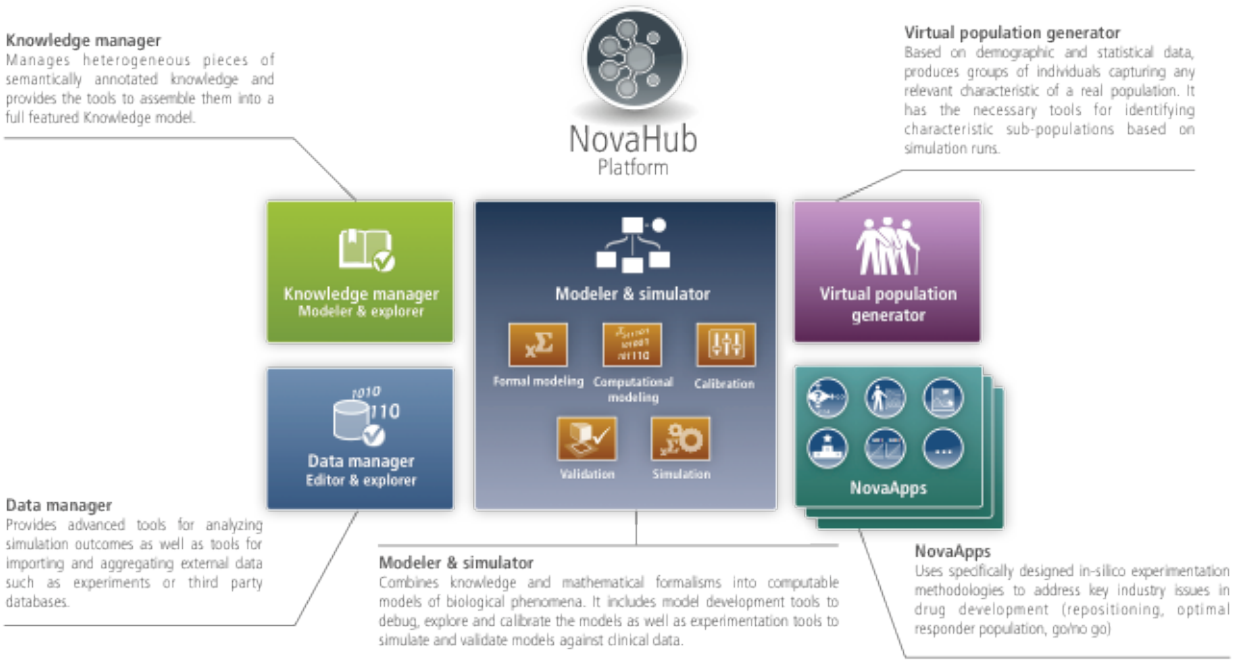
The Effect Model Law states that a natural relationship exists for each individual between the frequency (observation) or the probability (prediction) of a morbid event without any treatment and the frequency or probability of the same event with a treatment. This relationship is called the Effect Model. It applies to a single individual, individuals within a population, or groups. The relationship is specific to a therapy, a disease or an event, and a period of observation.

In a personalized medicine context, the effect model enables the prediction of the (absolute) benefit of a treatment for a given patient.

By summing up absolute benefits over the entire population of patients, it enables the early prediction of the treatment's public health impact with the estimation of the Number of Prevented Events.

Evidence of the existence of the Effect Model Law is supported by empirical observations, simulations as well as a theoretical demonstration.

Modelling simulation platforms



Novadiscovery is developing a modelling and simulation platform to support its research efforts. It is a collaborative environment which enables the seamless integration of partners to a given project.

Interview Manuel Gea

Your organisation:	**BIO-MODELING SYSTEMS**
Name person:	Manuel Gea
Function person:	Co-founder; CEO
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E-mail:	manuel.gea@bmsystems.net
Website:	www.bmsystems.net
Organisation type:	SME
Involved in CASyM:	No, but present at the second CASyM stakeholder meeting, round table 'What business models for industries involved in Systems Medicine?', Lyon, 25 March 2013.
Date interview	18 July 2013

1.	**Are you familiar with the term Systems Medicine as defined above?**	Yes, since 2010. We pioneered this area and were invited by the EC for the workshop 'from systems biology to systems medicine' in 2010 where we presented best practices in late phase Creutzfeldt-Jakob disease.
2.	**Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?**	Yes, BMSystems applies the systems medicine approach since 2004.
3.	**Does your organisation apply Systems Medicine according to the definition above?**	Yes, except we only develop non-mathematical models for discovery. In our view, life mechanisms cannot be described by Cartesian tools. Instead, we use heuristic models (problem solving approach evaluating each step in a process, from different points of view, using all available qualitative data, searching for satisfactory rather than optimal solutions). BMSystems develops *in silico* models of human disease pathways, based upon literature research, and non-confidential information of existing drugs and experimental results. By combining two of such registered drugs, we develop innovative therapy without side effects, since our models predict drug effects not known and claimed by the producer. Subsequently, collaborating companies validate our models in the lab and in small patient cohorts for their proof of concept. This approach is quite successful and since 2006 we make profit. We are already delivering results that led to patents and spin-off companies (Pherecydes Pharma) and out licenses (New Co). A new model for a novel therapy for Parkinson disease was developed and the validation phase will soon start. In the future, the spin-off companies may discover new drugs or perform clinical trials. BMSystems employs both biologists and informaticians. We developed Computer-Assisted Deductive Integration (CADI™) proprietary methodologies and tools for Disease understanding / (re)definition, Target discovery / validation, New therapeutic strategies, and New association / combination of existing drugs. CADI combines organic non-linear integration (brain intelligence) and *in silico* data processing power (collecting,

		structuring and manipulating data) to build validated biological interaction maps that describe biological reality. It can describe the dynamics of a pathological process and/or a pathological status vs. control and allows to switch from "symptomatic" to "causal" medicine, predicting and identifying pertinent biomarkers and proposing new therapeutic strategies. The CADI models belong to the non-mathematical holistic and heuristic class of models. It does not make exact maps of the complex reality, but makes pertinent representations that gather the minimum knowledge and intelligence necessary to describe a living process in a defined context and allows researchers to take the best possible decisions for the best possible results.	
		Number of projects:	5 programs under development: Decius(chronic anxiety) Idunn (neurodegenerative diseases therapy)Psy Lico (schizophrenia and bipolar diseases), New Co (done, spin-off company of CEA life Sciences one of our key our research partner launched; psychotropic medication) Pherecydes Pharma (done, spin-off company launched; developing bacteriophages (phages) to rapidly detect and/or kill a large range of bio threats). Synthons (industrial biotech) is now finished as a program.
		General topic of projects:	Discovery of new mechanisms and proposition of new therapies. Go / no go decisions for next phase programs.
		Type of projects: (e.g. PPP, purely industrial)	These programs are collaborative programs with partners that have experimental capabilities and clinical expertise. These programs are self funded; because we do not want to disclose our methodology / models since that they are the basis of our company.
		Approximate total budget of Systems Medicine projects:	Self funded confidential programs of approximately 1M€ each.
4.	**What are best practices you are aware of in Systems Medicine projects in terms of innovation and exploitation?**	Not aware of real success except our own programs, because of the complexity of systems medicine that requires multi-scale inter systems cross talks modelling.	
5.	**What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?**	Scientists and experts should stop searching under the street light. We need disruptive thinkers that aim for things we can do instead of what we should do. We need to learn about human physiology, talk to patients and get a holistic view. We need generalists instead of specialists. Medical doctors need to understand modelling, and vice versa. Our company is looking for veterinarians, paediatricians or coroners with a strong broad biology physiology and genetic	

		background, because they are used to treat patients that cannot speak, so they are trained to use heuristic problem solving approach . And we search for informaticians/biologists from the former Eastern Europe, since due lack of availability of computers they are used to use their brain and imagination.	
6.	**In which way can Systems Medicine be important for industry in the future?**	The systems medicine could be of some help for diseases where animal models do not simulate the disease (CNS).	
7.	**What would be a good business model to apply for Systems Medicine?**	PPP with industrial partner, clinicians and SME. The business model of BMSystems is to develop heuristic models/platforms that are kept as own property of the company and are not sold. Costumers pay fee for service: pathways, results and visual representation for their specific aim and area. We prefer long-term relationships. Customers include major pharmaceutical and, cosmetics companies and for industrial biotech chemical, environment and energy companies. In an area that BMSystems has no experience in, we prefer to co-develop with a partner (academia or industry). In an area in which we are experienced, we are more in the lead and choose established partners to collaborate with. BMSystems as a company stays with its core business of heuristic modelling. When IP is generated, the patents are placed in spin-off companies, aimed at developing therapies.	
8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	Yes, for areas where human tissue samples cannot be used (e.g. brain), we use animal models	
		Number of projects:	6
		General topic of projects:	Systems biology and Translational medicine
		Type of projects: (e.g. PPP, purely industrial)	
		Approximate total budget of projects:	
9.	**Any recommendation**	How to support real disruptive innovations? The European Commission should better support and give real chances to people and companies that think differently. The European Commission should not structure its selection process on the consensus of experts only, since that eliminates disruptive innovation. The non-consensus of experts about a program should be a good starting point to orientate the program to a specific evaluation process BMSystems is working on.	

Interview Phillipe Sanseau

Your organisation:	**GlaxoSmithKline**
Name person:	Philippe Sanseau
Function person:	Global head Computational Biology
Address:	Gunnels Wood Road, Stevenage, SG1 2NY, United Kingdom
E-mail:	philippe.x.sanseau@gsk.com
Website:	www.gsk.com
Organisation type:	Large pharmaceutical company
Involved in CASyM:	Associated partner; GSK was involved in preparative initiatives leading to CASyM
Date interview	14 March 2013

1.	**Are you familiar with the term Systems Medicine as defined above?**	Yes, since 2011	
2.	**Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?**	Yes, Systems Medicine is an important scientific component within the next 10-20 years. This is driven by the nature of the data available and the computational tools being developed. For example, it is likely to impact our mechanistic understanding of drugs, their targets and the diseases context (potential impact is on all major phases of the drug development pipeline). It could reduce attrition and costs in drug development. Some of challenges are around, demonstrating clearly value in a medicine development context. We should not underestimate the cultural challenge, either since it is likely to lead to a different way of working with data, different interactions etc.	
3.	**Does your organisation apply Systems Medicine according to the definition above?**	Yes, mainly categorized as Systems Pharmacology. Biological modelling at GSK is relatively small and has limited resources, but would like to invest in this area. There is some mechanistic modelling going on, but at present it is mainly qualitative data analysis.	
		Number of projects:	Appr. 7
		General topic of projects:	Systems pharmacology Biological networks (e.g. genes, diseases, etc), Synthetic biology, Pathways analysis. Respiratory and immuno-inflammation. Near future: microbiome.
		Type of projects: (e.g. PPP, purely industrial, collaboration with others)	Industrial and in collaboration with academic researchers in a PPP. GSK chooses to work with academia as much as possible and has opened data from clinical trials to society. By sharing data GSK aims to attract new collaborators.
		Approximate total budget of Systems Medicine projects:	(not disclosed)

4.	**What are best practices in Systems Medicine projects in terms of innovation and exploitation?**	- Application to specific scientific questions where systems medicine approaches are the best way (scientifically and financially) to solve the problems. - In our case we work on specific case studies rather than large projects. We do it early in drug development, and integrate Systems Medicine with classical PK/PD modelling from phase I to phase II.	
5.	**What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?**	Truth vs. buzz. We need realism in what can be delivered by Systems Medicine. Presently, biological in silico modelling is not yet really trusted as being beneficial in drug development outside PK/PD modelling	
6.	**What would be a good business model to apply for Systems Medicine?**	-Pre-competitive activities in common biological pathways, disease models, tools (especially if no compounds are included) -Shared risks and rewards between academia and industry (can include projects with compounds) -Work with external experts	
7.	**In which way can Systems Medicine be important for industry in the future?**	- Reducing attrition and costs (e.g. faster development, less patients, no animal studies, better biomarkers) - Improved mechanistic understanding of target/drug relationships - Greater understanding of diseases underlying physiology, pathways -Feasibility studies, providing value and competitive advantage -Potential to cure diseases / more personalised approaches -Making decision making faster: go on with drug candidate or stop the project	
8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	Yes	
		Number of projects:	Appr. 20-25
		General topic of projects:	Examples: Translational biomarkers, Rapid translation into experimental studies, Pathways analyses, Diseases networks, Cell function
		Type of projects: (e.g. PPP, purely industrial, collaboration with others)	PPP, purely industrial and in collaboration
		Approximate total budget of projects:	

Interview Johannes Schuchhardt

Your organisation:	**MicroDiscovery**
Name person:	Johannes Schuchhardt
Function person:	Chief Scientific Officer
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Website:	www.microdiscovery.de
Organisation type:	Industry - SME
Involved in CASyM:	Full partner
Date interview	7 February and 5 April 2013

1.	**Are you familiar with the term Systems Medicine as defined above?**	Yes. MicroDiscovery is a full partner in CASyM. The reason to join is a fundamental scientific interest in systems medicine as well as the chance that systems medicine gets commercially important.	
2.	**Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?**	Yes. MicroDiscovery is a bioinformatics company providing software solutions and data analysis in the areas of innovative diagnostics, personalized medicine and biomolecular research. MicroDiscovery focuses on the areas of custom software development for biomedical applications, analysis of next generation sequencing data, statistical data analysis by targeted algorithms and houses a profile database containing various –omics data generated in cross-omics high throughput studies. It is an SME of approximately 20 people. MicroDiscovery's clients include biotechnology and pharmacy companies and academic institutions.	
3.	**Does your organisation apply Systems Medicine according to the definition above?**	Partially according to the definition. MicroDiscovery is involved in data analysis and data management projects, including data-driven computational and mathematical (mainly statistical) models, developing concepts. The work does not yet include model-driven translational and clinical investigations and practice. In two projects (see below) data management is performed in the context of medical questions. Through a profile database high throughput data are made accessible for biologists and clinicians in terms of visualization, statistical analysis, correlation (e.g. gene-protein level) and integration. Beyond data analysis, previous research projects include the construction and simulation of mathematical models for metabolic diseases with a focus on type II diabetes. In addition projects in systems biology have been performed in cooperation with the Max Planck Institute for Infection Biology addressing dynamics of NFkappaB signalling. The project is model-driven, not aiming to understand a disease. So MicroDiscovery does have experience with mathematical modelling (models where formulated in terms of stochastic and non-stochastic differential equations) but sees its expertise and role primarily on the data driven side of systems medicine.	
		Number of projects:	A supportive role in several projects.

		General topic of projects:	Two projects are funded by the EU and by the Ministry of Education and Research (BMBF). - Colon cancer project, in cooperation with Charité University Berlin - Glioma / brain tumor project, in cooperation with the National Institute of Biology and the Blood bank of Slovenia
		Type of projects: (e.g. PPP, purely industrial)	PPP
		Approximate total budget of Systems Medicine projects:	
4.	**What are best practices you are aware of in Systems Medicine projects in terms of innovation and exploitation?**	The opportunity to cooperate in PPP with outstanding academic groups is highly valued. The reason to work on governmental funded projects is that they give MicroDiscovery the opportunity to keep up with the scientific developments, come into contact with organizations, and gives the general option to develop novel methods.	
5.	**What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?**	The impression is there is still a conceptual gap between the data driven approaches relying on simplified (usually linear) statistical models and the model driven approach usually coming along with the formulation of very specific questions. In any case, achieving full validation of a (molecular) model is usually very cost intensive, because many parameters need to be tuned or checked. Costumers usually have little interest in software improvements or new software from other companies. Next to this, excellent academic groups often produce open source products instead of trying to commercialize it in cooperation with a company. Finally, there is a fierce competition in getting a software product to the market.	
6.	**In which way can Systems Medicine be important for industry in the future?**	Commercially, Systems Medicine data management can be important for industry. The fields of image analysis in particular brain imaging may bring a number of interesting applications. For a bioinformatics oriented company commercialisation can be challenging, because the market is still very much guided by a hardware oriented paradigm, this is observed at least in biotechnology. Scientifically, it is difficult to judge if and which Systems Medicine tools and models can be important for industry.	
7.	**What would be a good business model to apply for Systems Medicine?**	- Model based consulting - Decision support processes, using mathematical models. These may be difficult to sell or to attract potential clients, though - Correlating imaging data (e.g. MRI) with statistical or mathematical models or data interpretation tools. In terms of systems medicine this should extend towards disease prognosis and diagnosis - Extending software products for data management towards clinical analysis - Supporting mobile access to patient information for the clinician - Supporting mobile testing of diseases	

8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	Three projects are on the topic of translational research.	
		Number of projects:	3
		General topic of projects:	One of the projects is in cooperation with the Leiden University Medical Centre and focuses on Cancer biomarkers and the development of tools for decision support for clinicians. Other projects are addressing evaluation of clinical data in the context of neuro-degenerative diseases and typically employ classification systems (machine learning),and multiple markers for diagnostic or prognostic tasks.
		Type of projects: (e.g. PPP, purely industrial)	PPP
		Approximate total budget of projects:	

Interview Manfred Hendlich & Thomas Klabunde

Your organisation:	**Sanofi-Aventis**
Name person:	Manfred Hendlich Thomas Klabunde
Function person:	Translational Bioinformatics Coordinator (MF) R&D Head Computational Biology & Bioinformatics (TK)
Address:	Industriepark Höchst, Building H831, 65926 Frankfurt, Germany (MH)
E-mail:	Manfred.Hendlich@sanofi.com Thomas.Klabunde@sanofi.com
Website:	
Organisation type:	Large pharmaceutical company
Involved in CASyM:	Full partner
Date interview	19 March 2013

1.	**Are you familiar with the term Systems Medicine as defined above?**	Yes, since approximately 2010	
2.	**Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?**	Yes, - Improved translation of preclinical findings - Improved understanding of complex diseases - Patient stratification Furthermore, Systems Medicine can be used to find the correct dosing in the clinical situation and be used in telemetric medicine	
3.	**Does your organisation apply Systems Medicine according to the definition above?**	Yes, in a systems pharmacology way in e.g. diabetes research, but not applied to the patient yet	
		Number of projects:	Appr. 10 (Sanofi employs 25 experts in this field)
		General topic of projects:	Different aspects of Systems Medicine are applied in a variety of projects, e.g. target credentialing, biomarker discovery, PK/PD modelling Oncology and diabetes Drivers of disease and drug candidates, including mechanistic modelling and data analysis
		Type of projects: (e.g. PPP, purely industrial, collaboration with others)	PPP and purely industrial In the IMI initiative (PPP) disease progression is researched and results flow toward clinical environment
		Approximate total budget of Systems Medicine projects:	
4.	**What are best practices in Systems Medicine projects in terms of innovation and**	Not aware of any	

	exploitation?		
5.	**What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?**	Missing knowledge of context specific biological networks topology and dynamics. Access to patient data / not enough longitudinal epidemiologic studies. Improved mechanisms for using patient data for research purposes are required while ensuring data privacy aspects. Data management infrastructure is not optimal. In USA data from trials and patients are more easily shared than in Europe. The EU needs to focus more on data sharing and be less strict in data privacy. Otherwise, medical breakthroughs will not occur in EU.	
6.	**What would be a good business model to apply for Systems Medicine?**	- Cooperation of large pharma with SME and academia, in order to rapidly obtain scientific excellent knowledge. This can be considered as a "phase 0" trial (prospective, monitor efficacy, no treatment) using small patient groups (Charite university Berlin and Heidelberg university) -Systematic mapping of diseases -Model based drug discovery	
7.	**In which way can Systems Medicine be important for industry in the future?**	Improved translation of preclinical findings, Target credentialing, drug combinations, patient stratification	
8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	Yes, systems biology, translational medicine and model-based drug discovery	
		Number of projects:	Appr. 10
		General topic of projects:	-Improve translation of preclinical findings. IMIDIA to understand the role of the pancreatic beta cell in the generation of diabetes; modelling of glucose-insulin homeostasis and drug action to translate animal in vivo and human in vitro data into computational prediction of drug effect in humans -Pathway and network understanding -Omics
		Type of projects: (e.g. PPP, purely industrial, collaboration with others)	PPP and purely industrial
		Approximate total budget of projects:	

Interview Anthony Rowe

Your organisation:	**Janssen R&D (Johnson&Johnson)**
Name person:	Antony Rowe
Function person:	Informatics
Address:	High Wycombe, Buckinghamshire, UK
E-mail:	arowe4@its.jnj.com
Website:	www.jnj.com
Organisation type:	Healthcare/Pharmaceutical
Involved in CASyM:	No, but present at the CASyM stakeholder meetings in Lyon, 25 March 2013, and St.Andrews, 13 May 2013.
Date interview	19 July 2013

1.	**Are you familiar with the term Systems Medicine as defined above?**	Yes, since I got involved in IMI projects in 2010. The Innovative Medicines Initiative (IMI) is an public-private partnership between the European Union and the European Federation of Pharmaceutical Industies and Associates (EFPIA) aiming to speed up the development of better and safer medicines for patients.	
2.	**Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?**	Systems Medicine is seen as a key areas of strategic importance to the informatics teams. To design better therapies, systems approaches are crucial in obtaining an overall, integrated view. Persons with a background in systems approaches, machine learning and simulation of disease pathways are working in each of the five therapeutic areas that J&J covers: Neuroscience, Immunology, Cardiovascular, Infectious Disease and Oncology.	
3.	**Does your organisation apply Systems Medicine according to the definition above?**	Yes, I am involved in eight IMI projects that have Systems Medicine approaches for collecting patient samples, do biological profiling, using systems biology in areas like severe asthma and colon cancer.	
		Number of projects:	Personally 5-10 J&J wide appr. 20-50
		General topic of projects:	In each of our five therapeutic areas there are elements of Systems Medicine research
		Type of projects: (e.g. PPP, purely industrial)	PPP like IMI, internal, collaborations with university and sometimes collaboration with SME when they have specific expertise like IT
		Approximate total budget of Systems Medicine projects:	Not known, but might amount up to 80 M€
4.	**What are best practices you are aware of in Systems Medicine projects in terms of innovation and exploitation?**	Some IMI projects that started 3 years ago are now starting to provide case studies, but they have not yet delivered a best practice. As an academic case study, the chronobiology project presented by Francis Levi in the CASyM stakeholder meeting in Lyon was a good example. It included patient	

		recruitment, sample and data analysis, modelling and SOPs. Public-private partnerships are important in areas where there is little knowledge, or when it gives access to additional patients for inclusion in trials. PPP provides a mechanism to share costs to enable studies at a scale that is cost prohibitive for any single organisation. Our best experience with PPP is when a new and specified area is investigated and a new dataset is built, since this often leads to a real shared vision and goal of the team. Especially the younger generation is very open to cooperate in such a team.	
5.	**What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?**	Over-promising and under-delivering. At present, routine discovery and validation of biomarkers using a Systems Medicine approach still seems unrealistic. It needs more time and effort to become a routine. There are no short cuts. In this respect, the reductionist approach is of additional value, since it gives information on details and specified areas. Systems Medicine has to demonstrate its own effectiveness before it will be widely accepted as a methodology by our traditional drug discover teams.	
6.	**In which way can Systems Medicine be important for industry in the future?**	By developing reusable platforms for research that industry can contract/collaborate with to explore research into specific patient populations	
7.	**What would be a good business model to apply for Systems Medicine?**	Currently, it is only the PPP model that works for system medicine, since the technology is unproven and the costs are high. The required scale of investment is so large (20-40 M€ for a single study) that it will not be provided outside of a partnership model.	
8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	Yes, systems biology approaches are becoming more common to help disease understanding and in the area of poly pharmacology. Informatics tools that help to translate between human and pre-clinical data are being evaluated and will see more use in the upcoming years.	
		Number of projects:	20
		General topic of projects:	Biomarker discovery and validation
		Type of projects: (e.g. PPP, purely industrial)	PPP, internal, collaborations
		Approximate total budget of projects:	

Interview Birgit Schoeberl

Your organisation:	**Merrimack Pharmaceuticals**

Name person:	Birgit Schoeberl
Function person:	VP of Research
Address:	One Kendall Square, Suite B7201, Cambridge, MA 02139, USA
E-mail:	bschoeberl@merrimackpharma.com
Website:	www.merrimackpharma.com
Organisation type:	Biotech
Involved in CASyM:	Associate partner
Date interview	18 August 2013

1.	**Are you familiar with the term Systems Medicine as defined above?**	Yes. I obtained my PhD in Systems Biology 13 years ago. The natural extension of Systems Biology is Systems Medicine i.e. implementation of Systems Biology approaches in medical concepts, research and practice. Personally, I expanded my work to Systems Medicine by joining Merrimack Pharmaceuticals about 10 years ago. Merrimack was founded on Systems Biology. We are using Systems Biology to understand the mechanisms underlying disease and use this understanding to design novel oncology drugs.	
2.	**Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?**	Yes, Systems Medicine is part of our 'DNA' and we use it throughout the drug development process. Merrimack as a company emerged from Systems Biology efforts at MIT and Harvard. We plan to use our continuous learning to advance the field of Systems Biology and Medicine. The implementation of Systems Biology is a major challenge. At Merrimack, we believe that interdisciplinary teams are key to success. Currently, Merrimack has 260 employees; 90 percent of our researchers are experimentalists and 10 percent are modellers.	
3.	**Does your organisation apply Systems Medicine according to the definition above?**	Yes. We aim to mechanistically understand the driving forces of tumor growth and to use those insights to develop novel medicines. Based upon literature, proprietary experimental preclinical and clinical data, we develop computational models with the goal to identify patients most likely to respond to our therapies and to define the clinical development strategy. Presently, we have six oncology therapeutics in clinical development.	
		Number of projects:	Six clinical, two pre-clinical and a number in discovery phase
		General topic of projects:	Oncology
		Type of projects: (e.g. PPP, purely industrial)	Mostly private-academic partnerships. In PPP, we

			collaborate with scientific groups of academic excellence with common interests.
		Approximate total budget of Systems Medicine projects:	N/D
4.	**What are best practices you are aware of in Systems Medicine projects in terms of innovation and exploitation?**	Merrimack internal projects: MM-121: signal inhibitor for multiple cancers (breast, ovarian, lung), currently being tested in a broad clinical development program in collaboration with Sanofi Oncology. MM-111: bispecific signalling inhibitor currently in Phase2 clinical testing for gastric cancer Academic work by Peter Sorger, Doug Lauffenburger and Mike Yaffe (Koch center at MIT) or LungSys project of the DKFZ in Germany.	
5.	**What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?**	- Insufficient quantitative data of high quality available to allow the building and use of computational models - Broad, interdisciplinary education is needed - Pitfalls: inability to collaborate and communicate	
6.	**In which way can Systems Medicine be important for industry in the future?**	Systems Medicine helps Merrimack, and the industry as a whole, to understand complex biological systems, identify new targets, and to design better drugs. Systems Medicine ultimately helps scientists, doctors and researchers put personalized medicine to practice. A Systems Medicine approach can shorten development times and costs.	
7.	**What would be a good business model to apply for Systems Medicine?**	From a business perspective, Systems Medicine can best be implemented in an integrated pharmaceutical company or used by healthcare providers (hospitals, insurances) to help optimize care.	
8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	Systems Medicine, also known as Systems Biology at Merrimack, is part of our DNA. We also strive to do outreach as a platform for our research, as we have partnerships with patient advocacy organizations, like the Pancreatic Cancer Action Network (www.pancan.org) to educate patients and physicians about Systems Medicine.	
		Number of projects:	>6
		General topic of projects:	oncology
		Type of projects: (e.g. PPP, purely industrial)	PPP
		Approximate total budget of projects:	N/D

Interview Bernd Eisele

Your organisation:	**VPM – Vakzine Projekt Management**
Name person:	Bernd Eisele
Function person:	CEO and Chief Medical Officer
Address:	Mellendorfer Str. 9, Hannover, Germany
E-mail:	eisele@vakzine-manager.de
Website:	www.vakzine-manager.de
Organisation type:	Service provider
Involved in CASyM:	No
Date interview	27 August 2013

<table>
<tr><td>1.</td><td>Are you familiar with the term Systems Medicine as defined above?</td><td colspan="2">Yes, since 2011 when I visited LCSB in Luxemburg. They are performing Systems Medicine on Parkinson’s disease.</td></tr>
<tr><td>2.</td><td>Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?</td><td colspan="2">Yes. Also, for VPM Systems Medicine will become of importance.</td></tr>
<tr><td rowspan="5">3.</td><td rowspan="5">Does your organisation apply Systems Medicine according to the definition above?</td><td colspan="2">No, not yet, but we plan to apply it in the future.
VPM started 10 years ago. At that time a better vaccine for lung tuberculosis was needed, both in terms of immune efficacy as safety. The ministry funded the project; our collaborators were in the Paul-Ehrlich-Institute, involved in medicinal product legislation. We started with our philosophy of backward planning, from clinical testing backwards toward the lab. In that way, no important steps in a drug registration document will be missed. Now we are doing a similar approach on the subject of bladder cancer, driven by a clinical need.</td></tr>
<tr><td>Number of projects:</td><td>Currently we have 5 drug targets, of which 1 is in clinical phase and 3 are in pre-clinical phase. We would like to license in or license out and do the co-development.</td></tr>
<tr><td>General topic of projects:</td><td>Vaccine candidates, e.g. for the prevention of human cytomegalovirus, (HCMV) infections, or interferon for treating multiple sclerosis and hepatitis C.</td></tr>
<tr><td>Type of projects: (e.g. PPP, purely industrial)</td><td>Our research is a collaboration of researchers, clinicians and regulatory bodies.</td></tr>
<tr><td>Approximate total budget of Systems Medicine projects:</td><td></td></tr>
</table>

4.	**What are best practices you are aware of in Systems Medicine projects in terms of innovation and exploitation?**	Not aware.	
5.	**What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?**	There are a lot of strict rules getting a drug candidate from the lab to phase III trials and ultimately the patient in a clinic. Not only rules on safety, but also on distribution and marketing and the starting material has to be clearly defined. We have to follow these, to get a product in a registration document. When there is only one red flag in all of the steps, nobody will licence it.	
6.	**In which way can Systems Medicine be important for industry in the future?**	- Identifying potential new products - Insight in the mechanistic level of disease - Address clinical needs	
7.	**What would be a good business model to apply for Systems Medicine?**	VPM would not change much in its current business model of 1) backward planning and 2) in collaboration with regulators. VPM uses a Project Management group, working in a structured way, keeping the regulators independent since VPM is in charge ofr preparing the advice. Systems Medicine might add to this business model.	
8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	Translational medicine and product development	
		Number of projects:	15
		General topic of projects:	Lung disease, cancer, vaccines, ALS. There are many common pathways in diseases.
		Type of projects: (e.g. PPP, purely industrial)	collaboration with Academia, VC, biotech and big pharma
		Approximate total budget of projects:	
9.	**Any recommendation?**	Do not neglect challenges in the regulatory path, even when the idea is brilliant!	

Interview Hans Hofstraat

Your organisation:	**Philips Research**
Name person:	Hans Hofstraat
Function person:	Vice President
Address:	High Tech Campus 34, 5656 AE Eindhoven, the Netherlands
E-mail:	Hans.hofstraat@philips.com
Website:	www.research.philips.com
Organisation type:	Industrial Research Organization
Involved in CASyM:	To be determined
Date interview:	28 August 2013

1.	**Are you familiar with the term Systems Medicine as defined above?**	Yes, since we are working on many concepts derived from a systems medicine way of thinking in our healthcare research program. Philips is an active participant in the FP7 program Virtual Physiological Human that aims for **i) patient-specific computer models for personalised and predictive healthcare and ii) ICT-based tools for modelling and simulation of human physiology and disease-related processes**
2.	**Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?**	Yes, since in the future healthcare will become quantitative, measurable, tailored to the person and to some extent pre-emptive, and hence cost effective. Systems Medicine is one of the approaches that supports reaching this objective. Philips is working at the interface of medical technology and biology. Our research often involves a solution based on a combination of Measurement (imaging, physiology, in vitro diagnostics) and Modelling (statistical and algorithmic). The model is a combination of biology and technology. Our research is data driven. It involves data generation and processing, and data-based modelling and prognosis. We aim to identify the cause of disease and predict the treatment result.
3.	**Does your organisation apply Systems Medicine according to the definition above?**	Yes, with noting that we do not develop medicines, but are involved in healthcare solutions based on medical technologies, such as medical imaging, personal diagnostics and therapy (e.g. digital pathology, image-guided interventions, electrophysiology, vital signs monitoring). Some areas and examples from Philips Research: - Radiation therapy and radiation oncology treatment planning: location of tumor and metastases, of vulnerable organs, tumor modelling, dosed radiation, modelling of damage to surrounding tissue. - Biological pathways underlying tumor growth: pathway diagnosis, study of tissue pathology and design of an optimal treatment plan.. - Cardiovascular modelling and interventions: minimally invasive image-guided treatment of atherosclerosis, ultrasound-aided local treatment of arrhythmia. - Neurology/neurodegenerative diseases: get a better, objective view on Alzheimer's disease.

<table>
<tr><td></td><td></td><td colspan="2">- Respiratory models of the lung, e.g. COPD: image and measure the respiratory performance of patients
- Support in Intensive Care Units: patient monitoring (pO2, ECG, heart rate). Monitoring vital signs of patients at a distance in ICU's. Reduce false alarms and identify earlier life-threatening situations through intelligent interpretation of the data.</td></tr>
<tr><td></td><td></td><td>Number of projects:</td><td>Dozens</td></tr>
<tr><td></td><td></td><td>General topic of projects:</td><td>Solutions based on medical technologies and data intelligence.</td></tr>
<tr><td></td><td></td><td>Type of projects: (e.g. PPP, purely industrial)</td><td>PPP and industrial. In our research always multidisciplinary teams are involved consisting of bioinformaticians, physicists, clinicians, biologists and engineers, most often involving clinical partners and users, including patients. We adopt a 'co-creation' approach to the research projects we are involved in.</td></tr>
<tr><td></td><td></td><td>Approximate total budget of Systems Medicine projects:</td><td></td></tr>
<tr><td>4.</td><td>What are best practices you are aware of in Systems Medicine projects in terms of innovation and exploitation?</td><td colspan="2">Many of the VPH projects. A good example is the euHeart project (www.euheart.eu), which was a European research initiative targeting the personalized diagnosis and treatment of cardiovascular disease. It was a close collaboration between clinicians, researchers, SME and academia.</td></tr>
<tr><td>5.</td><td>What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?</td><td colspan="2">- Systems biologists often work far from daily clinical practice.
- Animal models and in vitro models are difficult to translate into the clinic</td></tr>
<tr><td>6.</td><td>In which way can Systems Medicine be important for industry in the future?</td><td colspan="2">By delivering healthcare solutions that improve people's lives: the patient and the healthcare system have to benefit from it. Some examples:
- Prevent that people must seek complex treatment through the provision of earlier diagnosis or pre-emptive action.
- Provide the most effective treatment, tailored to the person.
- Provide more efficacious and higher quality solutions.
- Provide effective treatment outside the hospital, e.g. manage patients at home.</td></tr>
<tr><td>7.</td><td>What would be a good business model to apply for Systems Medicine?</td><td colspan="2">Provision of meaningful solutions with proven outcomes by
- Addressing a clinical unmet need.
- Applying cost-effective care
- Applying high-quality, 'first-time-right' care
Systems medicine can provide the means to provide healthcare to patients in an objective (instead of subjective) manner, providing proven outcomes.</td></tr>
</table>

8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	User need inspired research and development. Every solution we develop is geared towards the patient in a translational approach.	
		Number of projects:	Dozens
		General topic of projects:	Solutions based on medical technologies and data intelligence.
		Type of projects: (e.g. PPP, purely industrial)	PPP's, industrial (with partners), multidisciplinary research ('co-creation').
		Approximate total budget of projects:	

Interview Dimiter Dimitrov

Your organisation:	**Diavita Ltd**

Name person:	Dr Dimiter Dimitrov
Function person:	CEO
Address:	
E-mail:	dimiter.v.dimitrov@gmail.com
Website:	www.diavita.org
Organisation type:	SME
Involved in CASyM:	Associate partner
Date interview	25 September 2013

1.	**Are you familiar with the term Systems Medicine as defined above?**	Yes, since 2011	
2.	**Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?**	Yes, it is the most promising challenge in medicine, concerning strategic aspects, role on portfolio and research plans. Systems Medicine should be focussed to improve health care, to address the needs of the patient. The term Systems Medicine should be popularized so that many stakeholders and the general public get familiar with it and get to appreciate it.	
3.	**Does your organisation apply Systems Medicine according to the definition above?**	Yes, Diavita is an SME investigating the nutritional systems biology of the gut microbiome and analyzes and implements large amount of data from the “gutome” funnel. The focus is on computational / medical bioinformatics. Disease areas include diabetes and obesity. The company started in 2011 and consist of a physician (Dimitrov) and two IT specialists. Currently, Diavita is interested in collaboration through FP7 and Horizon2020.	
		Number of projects:	2
		General topic of projects:	Modelling gut host-microbiome interactions. In the projects clinical samples are collected and hardware and software are installed.
		Type of projects: (e.g. PPP, purely industrial, collaboration with others)	Collaboration with local university and clinic
		Approximate total budget of Systems Medicine projects:	To be determined. The projects are temporarily on hold awaiting funding from local or European sources
4.	**What are best practices you are aware of in Systems Medicine projects in terms of innovation and exploitation?**	eTricks and Transmart Initiatives. These projects are in their starting period, are based upon good ideas and contain PPP.	

5.	**What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?**	- For an SME, it is very hard to start up in an emerging field like Systems Medicine. We depend on local and European funding in order to establish collaboration and obtain proofs of concept. - Currently, the main challenge is to teach physicians and medical researchers in systems approaches. - Similarly, it takes time to train IT specialist in biological and mathematical modelling. - Statistics and integration of data is a challenge	
6.	**In which way can Systems Medicine be important for industry in the future?**	Translatability. Systems Medicine seems very relevant for pharmaceutical companies when their projects are in late stage of clinical trials.	
7.	**What would be a good business model to apply for Systems Medicine?**	- Interaction between different parties (academic and industry) - Communicate and connect basic and clinical scientists, since they speak different languages	
8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	Yes, we try to, but their practical implementation depends on obtaining funding resources.	
		Number of projects:	
		General topic of projects:	
		Type of projects: (e.g. PPP, purely industrial)	
		Approximate total budget of projects:	
9.	**Any recommendation?**	It is highly appreciated that there is a platform like CASyM that harbours a community for Systems Medicine stakeholders. In order to strengthen the community, I would suggest to increase the frequency of distribution of a CASyM newsletter.	

Interview Ad van Gorp

Your organisation:	**Lead Pharma**
Name person:	Ad van Gorp
Function person:	CEO
Address:	Kapittelweg 29, Nijmegen, the Netherlands
E-mail:	Ad.vanGorp@leadpharma.com
Website:	www.leadpharma.com
Organisation type:	SME
Involved in CASyM:	Associate partner
Date interview:	4 October 2013

1.	**Are you familiar with the term Systems Medicine as defined above?**	Not aware of this term, but we are very much involved in systems biology and drug development.	
2.	**Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?**	Yes and we are already applying it. Lead Pharma is an SME with 30 persons. We have a large bioinformatics group. The focus of our research is on small molecules using structure based drug design (crystallography and organic chemistry). By a systems biology approach we model proteins and pathways, validate targets and test substances in cell and animal systems.	
3.	**Does your organisation apply Systems Medicine according to the definition above?**	We work on a common mechanism in age related diseases in the areas of chronic heart failure, origin of tumor, auto immune diseases and nuclear receptors.	
		Number of projects:	3
		General topic of projects:	See above
		Type of projects: (e.g. PPP, purely industrial)	Drug development is purely industrial. In other areas we cooperate a lot with universities.
		Approximate total budget of Systems Medicine projects:	
4.	**What are best practices you are aware of in Systems Medicine projects in terms of innovation and exploitation?**	We know that former company Organon used systems medicine in all their research, including data mining, RNA research and translational research.	
5.	**What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?**	- Difficulties in re-producing data from literature / academic studies - Lack of means (budget and equipment) - Governmental funding of innovative and high risk research is mainly aimed at academia and not enough on industry - In a PPP, the academic and industrial partners can have different objectives, e.g. publication vs. product development	

6.	**In which way can Systems Medicine be important for industry in the future?**	Systems Medicine represents a mind shift in thinking about drug development. It should be used in a very focussed way in your company processes, otherwise you'll lose yourself in data and details.	
7.	**What would be a good business model to apply for Systems Medicine?**	Presently, we form partnerships with large pharmaceutical companies. This allows us to invest in our research. Ultimately, we aim to fully develop and produce a drug by ourselves.	
8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	All of our projects are based upon data mining, -omics and profiling on protein and pathway level	
		Number of projects:	
		General topic of projects:	
		Type of projects: (e.g. PPP, purely industrial)	
		Approximate total budget of projects:	
9.	**Any recommendation?**	Aim to get industry enthusiastic about and involved in CASyM.	

Interview Elena Sebokova

Your organisation:	**Elena Sebokova is reflecting her personal opinion, based upon experiences working at Hoffmannn La Roche**
Name person:	Elena Sebokova
Function person:	Vice Director Cardiovascular metabolism
Address:	Bachlettenstrasse 29, Basel, Switzerland
E-mail:	elena.sebokova@gmail.com
Website:	www.roche.com
Organisation type:	Large pharmaceutical company
Involved in CASyM:	No, but present at stakeholder meetings
Date interview	4 October 2013

1.	**Are you familiar with the term Systems Medicine as defined above?**	Yes, since 2006. In my department we are working on combining –omics data with clinical phenotypes, cohorts of healthy and diseased persons, and bioinformatics, statistics, modelling and prediction. The areas include diabetes, metabolism and cardiovascular diseases.	
2.	**Does your organization render Systems Medicine as one of the key technological and scientific developments / challenges within the next 10-20 years?**	Yes, I consider it very important, since blockbuster drugs are not likely anymore. Instead, we need more efficacious medicines, select subgroups of patients and treat them. In fact, many pharmaceutical companies are already applying systems medicine as research strategy.	
3.	**Does your organisation apply Systems Medicine according to the definition above?**	Hoffmann La Roche is working in the areas of oncology, infectious diseases, cardiovascular and metabolism, and neuroscience. There is no department of systems medicine, but we have project task forces that use Systems Medicine approaches.	
		Number of projects:	>10
		General topic of projects:	Many in oncology and CNS, due to availability of biomarkers and imaging data. Somewhat less in polygenic disease like e.g. cardiovascular.
		Type of projects: (e.g. PPP, purely industrial)	Depending on the questions and the knowledge we have and the availability of clinical samples, we may do the projects ourselves or join with academic partners in a PPP.
		Approximate total budget of Systems Medicine projects:	

4.	**What are best practices you are aware of in Systems Medicine projects in terms of innovation and exploitation?**	The best practices are in the area of single gene cancers, e.g. FDA approved medicines for breast cancer (her2 positive), lung cancer and skin cancer. In the area of osteoporosis we have developed tests, based upon proteomics data and biomarkers. The efficiency in treatment is now under investigation.	
5.	**What are gaps and pitfalls towards the medical and healthcare application of Systems Medicine?**	This depends on the way Systems Medicine research is done. - Quality and availability of clinical phenotypic data. Samples need to be standardized. Biobanks are needed, having sufficient sample material that makes re-analysis of samples possible. - Standardization of methodology, preferably worldwide. - Within the EU there are differences in governmental support in Systems Medicine.	
6.	**In which way can Systems Medicine be important for industry in the future?**	Coming from a pharmaceutical background, I'm certain that industry in personalized healthcare and pharma can gain from Systems Medicine application	
7.	**What would be a good business model to apply for Systems Medicine?**	The R&D combination of pharma and diagnostic industry can lead to development of better prototypes.	
8.	**Does your organisation apply related methodologies (e.g. systems biology, translational medicine) ?**	Yes, both pre-clinical and clinical research is necessary. It is basic research using imaging, in vitro and in vivo techniques, with a focus on application in a disease area.	
		Number of projects:	
		General topic of projects:	
		Type of projects: (e.g. PPP, purely industrial)	
		Approximate total budget of projects:	
9.	**Any recommendation or comment on the subject of Systems Medicine ?**	- Existing funding programmes need consolidation - The EC needs to be and stay involved - The information and data that are gathered in publicly funded research projects should be openly available for everyone. Open access to data, knowledge and expertise is crucial, otherwise the field as a whole will not benefit from the massive amount of funding put into this area.	

Acknowledgements

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Steering Committee - The following officials, as part of the Scientific Steering Committee, are involved in the scientific coordination of CASyM:

Charles Auffray - European Institute for Systems Biology & Medicine - EISBM, France
Mikael Benson (Deputy Speaker) - Linköping University Hospital, Sweden
Rob Diemel - The Netherlands Organisation for Health Research and Development, The Netherlands
David Harrison (Speaker) - University of St. Andrews, United Kingdom
Walter Kolch - University College Dublin, Ireland
Frank Laplace - Federal Ministry of Education and Research, Germany
Francis Lévi - Institut National de la Sante et de la Recherche Medicale, France
Damjana Rozman (Deputy Speaker) - University of Ljubljana, Faculty of Medicine, Slovenia
Johannes Schuchhardt - MicroDiscovery GmbH, Germany
Olaf Wolkenhauer - Dept. of Systems Biology & Bioinformatics University of Rostock, Germany

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