Infrastructure for Systems Biology Europe

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A survey/ assessment –based document detailing a vision and strategy plan for the implementation and operation of ISBE

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Background Information on WP7

Objectives of WP7

The objective of WP7 within the ISBE Preparatory Phase is to lay down a strategy, vision and advocacy framework for the implementation of the ISBE in a subsequent phase. This WP aims to attain a community-supported view on the needs, bottlenecks and potential of the various aspects of Systems Biology for area of research and development.

Deliverable 7.1 is a survey-/assessment–based document detailing a vision and strategy for the implementation and operation of ISBE.

The WP7 assists in coordinating and implementing a series of Europe-wide surveys with assessments of systems biology issues and creating a stakeholders platform. The platform will contribute to:
• Set out a common vision and goals;
• Define the areas of application;
• Identify major bottlenecks;
• Map the current infrastructure and needs;
• Identify stakeholders, as well as their visions, needs and achievements
• Provide strategic information for the definition and organisation of the data centres envisaged (ICs, DGCs and SCs).

Relationship of WP7 to other work packages:

WP7 aligns closely with the following WPs:

- WP1 Project Management and Co-ordination: WP1 and WP7 will work together on the cross-cutting topics and responsibilities to integrate results and information of all WPs to generate the overall concept of ISBE.
- WP2 Model and Data Management: Considerations around the model and data management are a central topic for the overall ISBE concept, e.g. standardization and SOPs have a high relevance and influence the strategy development how cooperation with other infrastructures, projects or initiatives might be implemented.
- WP3 Overall Infrastructure, Eligibility and Accessibility: This is a core activity of OSBE and is therefore vital for the vision, strategy and even advocacy of ISBE Also the definition of the ISBE user concepts mainly dependent on the WP3 results.
- WP4 Data Generation: Interaction needed to map the use cases identified.
- WP5 Community Building and Synergies: Synergy and interaction with different projects, infrastructures and communities are vital for ISBE, for the preparatory phase the interaction with the different user/provider communities is highly important to optimize the concept and strategy plan for ISBE.
- WP8 Modelling Infrastructure and Expertise: Input of WP8 is required on the definition of the modeling for the ISBE vision.
- WP10 Training and Education: Together with WP10, WP7 will provide a strategic basis for identification of educational needs across fields in Europe.

- WP11 Funding, Governance and Legal: WP7 will feed into WP11 with respect to the definition of funding needs and strategies, as well as with respect to advocacy at the level of funding agencies and governance.
- WP13 (Connections): on the vision of the essential role that the connections between centres and between centres and users play in achieving the integrative aims of ISBE
- WP15 Innovation, Impact and Exploitation: Liaison with WP15 to assist in providing information for the pipeline for technology and methodology exploitation and IP management, as well as a European expertise and technology matrix; the results of WP15 will also feed back to the WP3 centre structure discussion and the overall concept.

Introduction to an ISBE Vision

What is systems biology?

Systems Biology has a variety of roots, ranging from molecular biology developing into high-throughput functional genomics, to physics and mathematical biology demonstrating how modeling and theoretical concepts enable one to understand how complex properties observed in living systems may come about. Systems Biology is the science that aims to understand for any biological function, how it emerges in the actual interactions between the components of living systems and with their environment. Because virtually all components of living systems interact (very often, non-linearly) and because they all may matter for function, systems biology is tied to functional genomics. New properties arise from nonlinear interactions and thus systems biology requires precise experimental analysis of the biological system under study both with respect to its component properties and in terms of its physiology, as well as mathematical modeling of the precise interactions against the backdrop of the limitations imposed by chemistry, physics and the organization achieved by evolution.

Because living systems are the culmination of a wide variety of phenomena, systems biology requires the integration of a large number of scientific approaches that have historically developed more independently of one another. Examples include analytical chemistry, biochemistry, biophysics, mathematics, computer sciences, bioinformatics, organic chemistry, non-equilibrium statistical mechanics, classical and molecular genetics. Systems Biology is applied in existing areas such as cell biology, physiology, pharmacology, medicine, metabolic engineering, synthetic biology, and ecology.

Systems biology comes in various flavors. *Top-down* systems biology measures the dynamics of the concentrations of many or all molecules of a type (e.g. mRNA) in a living system such as a cell or an ecosystem, and then searches for patterns in this dynamics. The aim is to generate hypotheses on the behavior of the biological networks, on the nature of the interactions between the components, and on how the interactions are regulated. *Bottom-up* systems biology examines how functional properties arise from the nonlinear interactions of much fewer components, such as those of a pathway. *Middle-out* systems biology begins at some level in physiology and models how experimental observations can be understood on the basis of interactions. *S*ystems biology examines how processes at diverse levels of biological organization (e.g. transcription, metabolism and whole-body function) integrate to produce function. This leads, in the case of humans, to systems pharmacology, systems toxicology and systems medicine. Similar considerations apply to virtually all biological systems, from single cells, to small microbial communities, host-microbe interactions up to large-scale ecosystems. With the advance of the myriad of (quantitative) -omics technologies, and advanced ICT and modeling, systems biology now enables *precision biotechnology* and has the potential to substantially contribute to *precision medicine* and individualized medicine, and by connecting to patient experience, lifestyle and ambition to *personalized medicine*. Systems biology builds both upon the molecular biology that profited from the reductionist focus on single components such as genes and proteins, and on classical biology that found living systems to be so complex that all it thought it could do is observe the complexity and predict by analogy or homology rather than mechanism. We now know that the true complexity of living organisms is much higher than the two components typical for molecular biology, but not infinitely complex as supposed by classical biology. With the drastic advances in modeling and computing, this means that living systems may become predictable through a new science that differs drastically both from molecular biology and from classical biology, by focusing on the limited but large number of components of real living systems.

Systems biology is different: irreducible complexity

Network analyses have shown that in living systems virtually all molecules connect with virtually all other molecules, indirectly. Due to evolutionary pressures, virtually all molecules contribute to some function, and virtually all functions appear to be connected under some circumstances. This would seem to imply that one could not resolve the contribution of a few molecules or a pathway to biological function without simultaneously studying how all other molecules contribute to that function. And one would have to study all aspects of these contributions, which would involve many different disciplines, from mathematics to molecular genetics (see above): it would seem that Systems Biology is itself irreducibly complex.

Because Systems Biology is assigned to understanding function in terms of all components involved in setting that function, it cannot escape this problem in the way that some other disciplines can (e.g. by focusing only at one or two molecules at a time, as in molecular biology, or by looking a physiological function in terms of a few underlying physiological phenomena without linking the latter to all the contributing molecules). This makes systems biology different amongst most other sciences, with possible exceptions such as ecology, sociology and medicine.

Research groups active in systems biology are strongly limited by this problem that their object of study, be it a metabolic pathway, or the complete transcriptomics of a liver cell, is influenced in essential ways by other aspects of the biology of the organism. No research group, and not even a research institute, can have all the expertise and equipment on board to deal with any true systems biology topic comprehensively. Rather more implicitly than explicitly the same problem confronts any research group that aims to be relevant for biology, ecology or medicine.

The solutions provided by systems biology: model-assisted integration of component activities.

Systems Biology has developed a way out of this dilemma and this is model-assisted integration of activities. In this strategy, various research groups work on a more detailed part of the problem, such as the interaction between a receptor and its ligand, or the three-way interactions between a plant pathogen, an insect and and plant, and the results of their studies are integrated into a true-to-life model of the cell, organism or ecosystem that they study. The integration is facilitated by each group making a model of what they are studying and associating their experimental results organically with their model. The (sub)models of all the research groups are then integrated or, at least, interlinked, into an integral model. The result is that the implications of even a study on a minute detail for the living systems as a whole (cell, or organism) can be calculated, and thereby verified in targeted experiments. The word 'model' is here used in its meaning of mathematical and computable representation of the reality of an object.

This strategy requires a number of features that are not at all traditional to biology, although they are well known in physics and engineering: (i) inference of structures and dynamics underlying heterogeneous datasets (ii) the building of realistic and mechanistic models and submodels of this type, (iii) design motivated by these models, of experiments that are realistic vis-à-vis the limitations imposed by the biology, (iv) standardization of methodology and terminology so that experiments and models can indeed be integrated, (v) experimentation under the same experimental, *in-vivo* like, conditions, or under conditions that can be translated to those, (vi) ability to avail of all of the expertise and experimental facilities that are necessary for the sufficient characterization of a component systems, or validation of a system behavior predicted by integrated component models, (vii) access to all experimental data that are relevant for systems biology and have undergone quality control, (viii) access to already existing models, and (ix) willingness to collaborate to accomplish a common goal.

An infrastructure for systems biology; what and why?

Every new systems biology project has to deal with the issues described above. On the one hand, these may seem to present it with an immense problem: how could an even moderately sized research project get all the required expertise and equipment on board? On the other hand, all these projects have in common both the issues and the solutions suggested by systems biology. For instance, the issue of standardization is difficult, but, conceptually, the same or similar for most projects in systems biology. Furthermore, concepts generated and models made by one set of projects will be often useful for other projects. It will be highly useful therefore if all the expertise, equipment, standards, models, and integration methodologies (we shall call these together: facilities) can become available as a common set of facilities with real-time integration and real-time access to any research group active in or relevant for the life sciences. The facilities will be present at different 'stations' (i.e. locations differing both in terms of geography and discipline). They should be connected by 'railroads' enabling vary fast trains of information to pass between them, so that any research group active in systems biology or in a related discipline can avail quickly and even real-time of all the component facilities it may require. The infrastructure should help each systems biology project to employ the systems biology research strategy that is new to much of the sciences: a model-driven experimental design subdividing the total activity require to address a biological or medical question (such as dosage combination should we use for two drugs) into a number of tasks of different activities and different locations, that can then be driven and integrated by the research group real time; the approach deal with the true complexity and refrains from reducing to a number of components that are manageable for an individual research group but irrelevant for the biology, or by turning to non-predictive science of the systems as a whole foregoing its components.

An infrastructure for systems biology; why now?

Owing to technological and conceptual developments, the field of systems biology has been growing exponentially, whereby the empowerment provided by each finished project leading to a number of new projects. It has pervaded many of the modern Life Sciences because it enables their projects of great yet academic interest to connect to importance for biology, medicine, ecology and engineering at large. Large-scale projects such as the Virtual Liver Network (internet link here) demonstrate that the basics in technology development and data integration and modeling have matured to a point that they begin to accelerate true progress in the field. A broad range of on-going projects worldwide show that systems biology is becoming the central means to understand biological processes and the functioning of cells, tissues, organs and whole organisms. An increasing number of national and European programs rely increasingly on systems biology approaches to tackle biological problems in fields ranging from Medicine to Ecology to Industrial Biotechnology. Altogether, of the increasing number of successful national and European projects and initiatives in the various fields has made possible to develop the technological tools for standardized data generation, analysis, integration and modeling that prepare the ground for understanding the fundamental aspects of life through systems biology.

With this substantial growth systems biology also diverges and the different areas begin to develop their own modes of experimentation and modeling. In a few years the ways of doing things in the different areas will be so vested that there will be a strong resistance to reverse the local standards that will have developed. Models made for liver function in the body will not be able to assimilate models of metabolic pathways, and data for one pathway may have been collected at pH 7.5 whereas that for another pathway at pH 6.5. It is important therefore to begin as soon as possible with the standardization, in a way that the advantage of hooking on to the standard procedures of the infrastructure is of a benefit that is obvious to any individual research group. Standardization in annotation of gene sequences and protein structures, and standards enabling exchange and integration of models and experimental data have already been developed and are met with enthusiasm by the wider scientific community.

But there may four issues that are issues that are even more important: a revolution has occurred in the amounts of experimental data that are acquired to such an extent that, although they can be stored, they cannot always be analyzed to their full potential. The research groups collecting the data would much appreciate easy ways to analyze it and to then store it in the form of conclusions or relevant averages rather than raw data. The second issue is that the collection of the data has a high financial cost, which makes it crucial to ensure that data are collected under conditions that makes the it maximally relevant, enabling the reuse of the same data set in a number of subsequent analysis activities. Also this requires standardization and access that would be facilitated by a rapid infrastructure. The third issue is that the general public is becoming aware of the potential that some of the genomics methodologies seem to have. For instance, many will soon avail of their genome sequence and of concentrations of panels of biomarkers in their blood, whilst at the same time they are worried about debilitating diseases such as cancer, diabetes and Alzheimer's. They will wish to see that their data are treated in ways that lead to improved predictions on how lifestyle, diet and medicines may improve their well-being. The fourth issue relates to the societal impacts and costs. For instance, health care, energy or environmental costs are progressively increasing the economic burdens to national economies. Both politicians and society at large will soon begin to ask whether the life sciences can come up with methodologies that will reduce costs whilst improving the quality of life. Indeed, an important driver for the development of a comprehensive systems biology infrastructure for Europe is the urge to tackle a whole range of biological problems with of a wide societal impact (e.g. healthy aging, disease, food security, effects of global change, pharmaceutical and bioenergies, to name a few). This impact will come not only from academic research, but also in industrial, medical, agricultural and environmental applications.

The mission of ISBE

The mission of the Infrastructure for Systems Biology-Europe (ISBE) is to give life scientists in Europe easy access to an infrastructure that enables them to explore and understand the dynamic behaviour of complex biological systems, ranging from cells, to organisms, to ecosystems. Such understanding is the key to rational and effective health research and biotechnology. It is done through the integration of experimental data sets in predictive and quantitative computational models. Such approach is commonly used in other sciences (e.g. physics) and engineering and recently also shown to be highly successful in the life sciences. The ISBE will starkly enable progress in biology and medicine by providing of rapid, real-time access to all the experimental and modeling facilities, data, models, activities and expertise their project will require but that they do not avail of in their own laboratory. It will also offer the new research strategy of systems biology that facilitates integration of results through maximally realistic model representations of data and understanding, where the models themselves and be integrated to generate perspectives for biological and medical function. ISBE will herewith provide an infrastructure so that any research group anywhere in Europe can optimally contribute to the advance of European science, technology, integration and competitiveness, in many areas including medicine, drug development, biotechnology, and ecology.

To this end ISBE will create a solid pan-European infrastructure technological, intellectual and training basis and provide services allowing researchers in academia and industry to (i) collect, analyse and process data sets that are fit for integration in effective models, and (ii) build models that give insight into the functioning of biological systems.

How does ISBE differ from other research infrastructures?

The Infrastructure Systems Biology Europe will facilitate the use of the systems biology strategy by all interested life scientists. Its infrastructure will enable Europe to engage in this new type of science that is essential for great progress in the life sciences and for new and competitive applications that truly contribute to better and more efficient health care and biotechnology. The essence of ISBE is thereby to provide the infrastructure for the model-driven integration of a wide diversity of scientific activities. ISBE is an infrastructure where both the nodes (facilities) and connections (integrating the activities at the various centres) are equally important, just like a national railway system which cannot do without neither stations and nor tracks. The most unique characteristic of ISBE is that the infrastructure is built such that the projects using the infrastructure will always use one central computable presentation (model) of the system they address to direct the project in terms of experimental design and data and model integration. A second characteristic is that the infrastructure will enable scientists to make their research connect component (eg. molecular) properties with the functioning, malfunctioning, therapies or engineering of living systems.

Furthemore. ISBE will connect to and capitalize on many other research infrastructures. Examples are:

- ELIXIR, which focuses on the construction and operation of a sustainable infrastructure for biological information in Europe to support life science research for collection, curation, storage, archiving, integration and deployment of biomolecular data.
- Euro-BioImaging, which focuses on imaging; ISBE will connect researchers to those imaging facilities that focus on physiological states and on images that are suitable for model integration.
- ECRIN, which focuses on the support of multinational clinical trials, including projects in the frame of IMI.
- INFRAFRONTIER, which focuses on the establishment and use of a mouse model infrastructure for a comprehensive phenotypic analysis.
- BBMRI, which focuses on the establishment and use of European biobanks for the study of human diseases.
- EATRIS, which focuses on the support for translational medicine in the field of development of research tools and methods, protocols and data models.

Which structure and organization would best serve the aims of ISBE?

ISBE would be possibly configured as a network of centres, as indicated by fig. 1a. There would be three different types of centres, i.e. data generation centres, stewardship centres and modeling centres.

The data generation centres would be specialized on generating data under the conditions defined by the stewardship centres, typically conditions that best mimic the state in vivo, and conditions that lead to high quality and reproducible, hence standardizable experimental results. They would possibly engage in two major types of experiments, the one being experiments aimed at characterizing components and interactions in terms of dynamic behavior and corresponding parameter values, and the other experiments more at the physiological, (eco-)system level for validation of the model predictions.

The stewardship centres would ensure the standardization as well as the capture and storage of the data in model-compliant ways.

The modeling centres would have two main different tasks. One is the modeling or a newly made model in keeping with the recommendations from a stewardship centre. The other is the making of a provisional replica model of the biological system under investigation (or subsets thereof), and the association to that model of already existing submodels, as well as existing experimental data and knowledge available from the stewardship centres. The integration activity also comprises the identification and design of the experiments that should be most informative and best enable the model to answer the research questions of the project. The integration activity would also integrate the results of the project with other projects that have run or are running I parallel so as to build a process of ever improving models of a variety of parts of living organisms and ecosystems.

The suggestion by the figure that there would only be one of each type of centres is an oversimpification. Fig 1a indicates that there will be various types of stewardship centres, i.e. for data, modeling, tools and maps, also various types of data generation centres. Also the integration may be done in a variety of modeling centres, using a number of modeling methodologies.

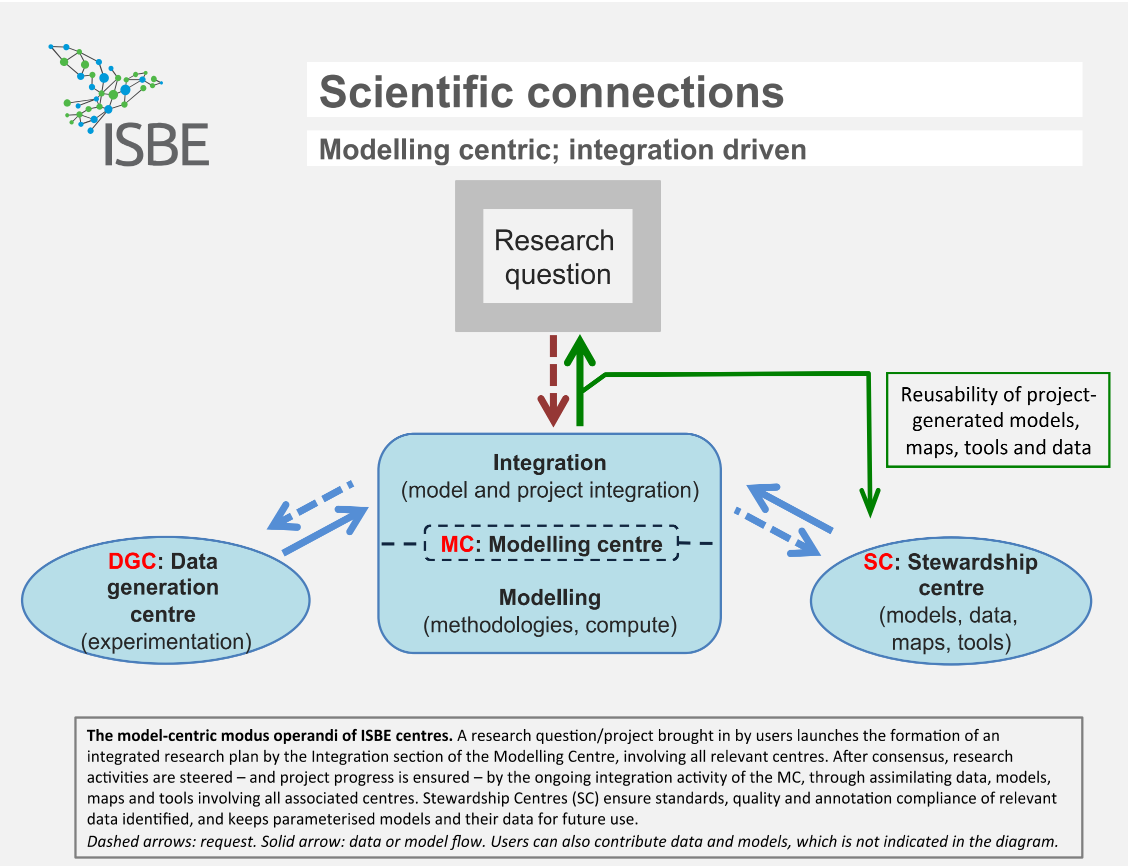

Fig. 1a: Overview about the scientific connections and interaction of needed expertise in the systems biology infrastructure for an efficient pipeline for the performance of systems biology projects.

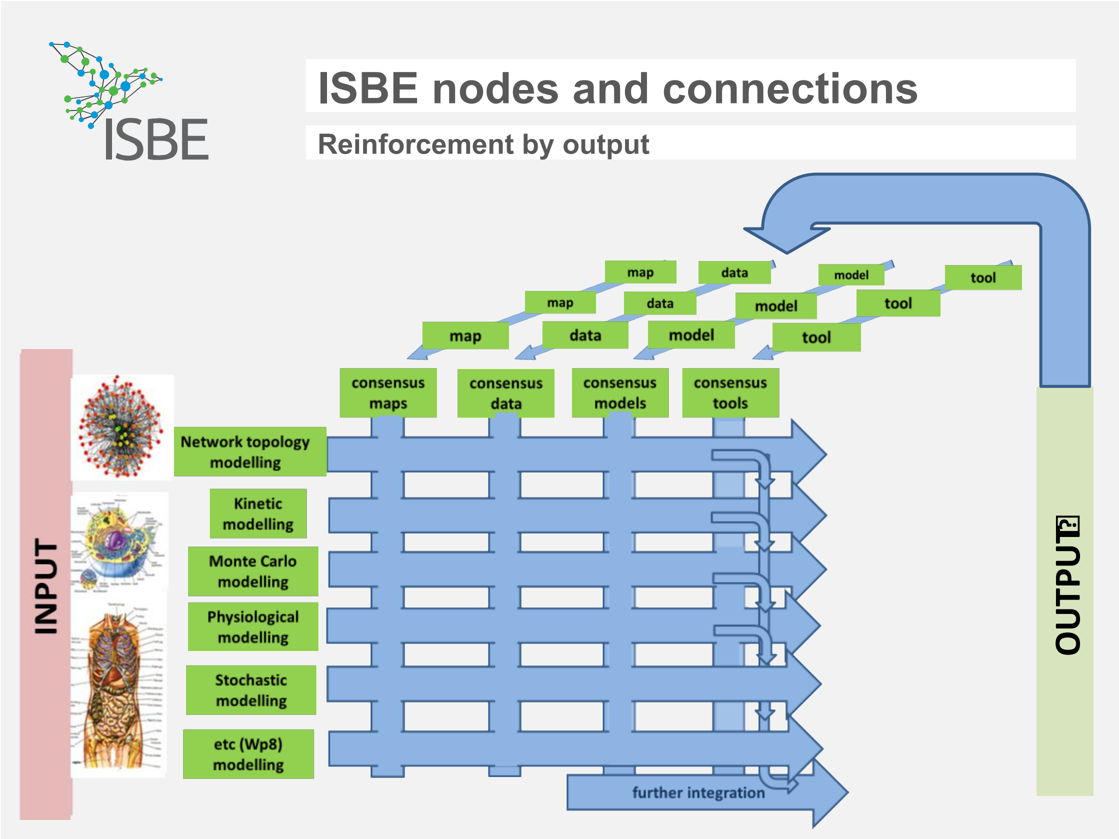

Fig. 1b: The figure visualizes the diversity and complexity of the nodes and interactions between specific approaches to perform systems biology projects. The output of the activities will also feed back to the optimization of the whole system.

The relationship between the three types of ISBE centres is depicted in figure 2:

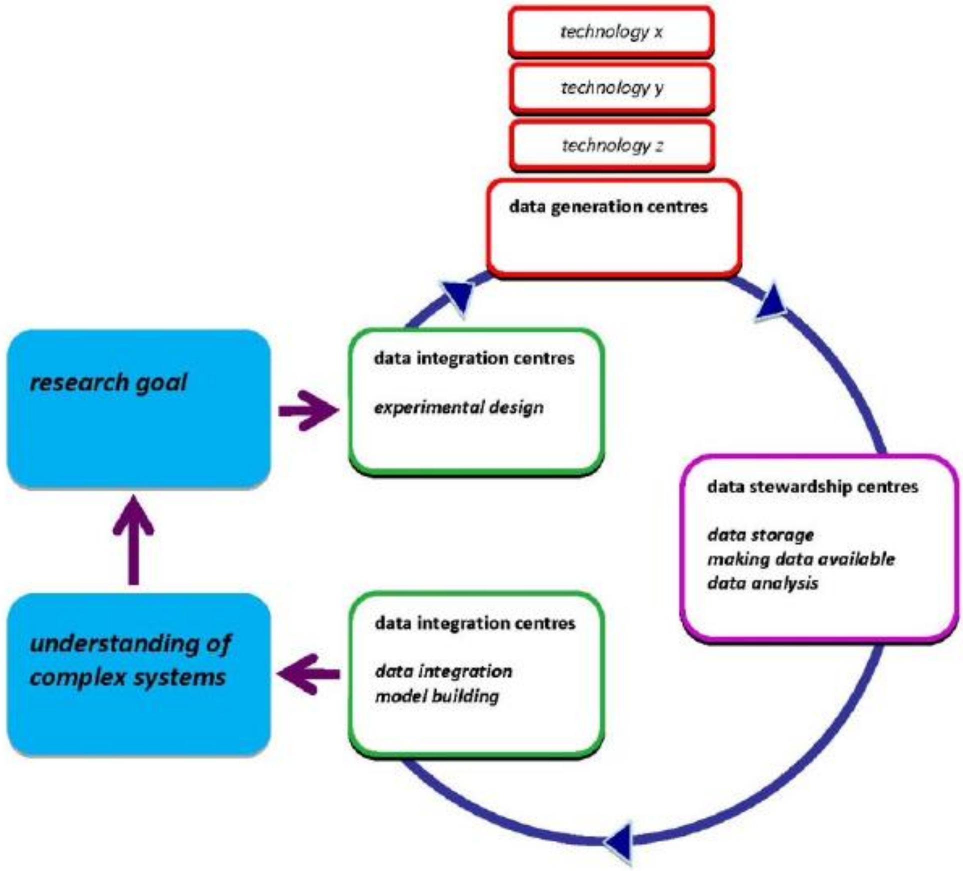

Fig.2: The systems biology cycle.

The systems biology cycle showing the elements that must be tuned to be able to perform Systems biology experience and the role the ISBE centres could play in this. Three types of centres are foreseen: *Modeling centres*, which provide expert knowledge in a wide range of modelling approaches and expertise in the combination of diverse data sets in quantitative and predictive models. *Data generation centres*, which give access to a wide range of high-end expertise and equipment essential for the generation of data sets that are fit for integration in quantitative predictive models. S*tewardship centres*, which offer expertise in data storage, curation and analysis of different types of data sets and give access to all kinds of published data sets that are useful for systems biology. ISBE centres will be tightly linked and able to work together in supporting researchers to complete multiple systems biology cycles and thus giving deep insight into the functioning of complex biological systems.

What is the main goal of the systems biology infrastructure? And what are its objectives?

The main goal of ISBE is to provide a solid infrastructure that will enable all European researchers to optimally engage in the practice of systems biology. This will produce a strong upswing of the quantity of high quality European research and of research with improved applicability in medicine, industry, agriculture and the environment.
The objectives are to:

- Put in place a research infrastructure that enables any research group that is expert on one aspect of the life sciences to have all other aspects that are important for their object of study, at their fingertips.
- Put in place a much closer and dynamic integration of tip European expertise and equipment so as to benefit all R & D in Europe
- Provide an infrastructure that will be used by the majority of future EU and large national projects.
- Provide a frame of reference for standardization, quality control and experimental and modeling methodologies
- Provide the infrastructure for the asymptotic generation through progressive integration of integral (molecules to whole) models of living organisms, tissues and ecosystems that then empower the pharmaceutical and biotechnological industries to the generation of much more effective combinations of drugs and of much more efficient production strategies for important amenables.

The pursuit of these objectives will be invaluable in contributing to transform the European Research Area into a much more productive arena thanks to the implementation throughout of systems biology

ISBE was initiated as one of the ESFRI roadmap activities. In 2012 it went into its preparatory phase with the aim of becoming fully operational in 2018. ISBE aims to be the infrastructure that empowers any member of the research and development communities with systems biology: it will provide all expertise, knowledge, technology, know-how and manpower required to understand and manage the complex systems of biology by integrating precise experimentation, mathematical modeling, data existing in literature and databases, scientific knowledge, experimental design, and technology development.

The objectives of the preparatory phase of ISBE are

- To identify the principal needs for such an infrastructure
- To identify existing bottlenecks and hurdles and to identify modes in which these can be widened
- To define the spectrum of possible applications of systems biology and its infrastructure
- To ascertain the added value of an infrastructure for Europe
- To define the elements of the infrastructure and to develop a concept for its structure and organization
- To identify its user groups and to shape the concept so as to accommodate these user groups optimally
- To develop a strategy for how connections can be established for sustainable cooperation
- To establish a business model for the implementation of the infrastructure
- To identify the added value of an infrastructure for Europe

Problem Statement

The problem is	that the complete repertoire of research expertise and infrastructura elements needed to significantly advance life science R & D is neithe affordable at any single site or organization, due to the inherent com organisms and of their interaction with the environment
The effect is	that the rate at which the life sciences develop and the effectiveness they are applied in improving the quality of life and the environment than pits full potential
The impact is	that Europe does not capitalize on its potential competitive advantag

	in this area, and may lose its edge to North America and Asia. The long term impacts are potential diminished wealth and quality of debilitating health care cost of its ageing population that it could oth an economic growth factor
A solution would be	the creation and implementation of a pan-European infrastructure fo comprehensive systems biology underpinning research in all areas of application in the life sciences, especially systems medicine.

Strategy plan

How will the ISBE consortium address the objectives?

The fundamental considerations about the structure, contents and implementation must be discussed with the different scientific communities that relate to systems biology and ISBE specifically. As the stakeholder and target groups are very much diverse, the ISBE consortium needs to involve the different communities to reflect the concepts and optimize the setup for all relevant user and provider groups.

Two of the strategies to receive this feedback from the communities:

a) Via the survey
   - The survey was developed under the leadership of WP1 and will be launched in September 2013

b) Via "Persona modeling": can be used to proof the concept by anticipating representatives of different user groups
   - The persona modeling was discussed intensively in the WP13 meeting in May 2013; please see the detailed information there.
   - An overview that is given in the report of WP13 refers to the following personas:
     > SB expert PhD student/PDRA working on systems problem (e.g. NS having worked on metabolic map)
     > Idem, but SB non-expert
     > Stakeholder from industry (define with WP15)
     > Node manager (that now also needs to provide service)
     > PI in research group that wants to use ISBE
     > Governance persona (quality control / compliance etc.)
     > Non-SB end user (e.g. clinician)
     > optionally: funding persona (if deemed relevant)

Position Statement

Target Customers and How the Infrastructure Will Meet Their Needs

For	The life science researchers, academia and industry, stakeholder groups (e.g. legal entities, public authorities)
who	need a specific expertise missing in their institution to perform systems biology projects
ISBE	
is a	comprehensive and pan-European solution connecting all relevant expertise
that	provides access to infrastructure and services for all stakeholder groups for systems biology
unlike	The fragmented knowledge and know-how in existing projects
ISBE	Will provide a "one-stop-shop" for systems biology approaches for high-quality research and large scale systems biology applications

Areas of Application for ISBE

The areas for application of systems biology and the respective infrastructure are very broad. All aspects of biology can be subject of research with the means of systems biology. These approaches include not only the fundamental aspects, but provide the basis for also a wide range of applications in the commercial field.

To provide an overview a systematic approach will help. In figure 3 the different areas of application of a systems biology infrastructure are summarised; the compilation is far from complete, but shows the huge variety of possible fields of application.

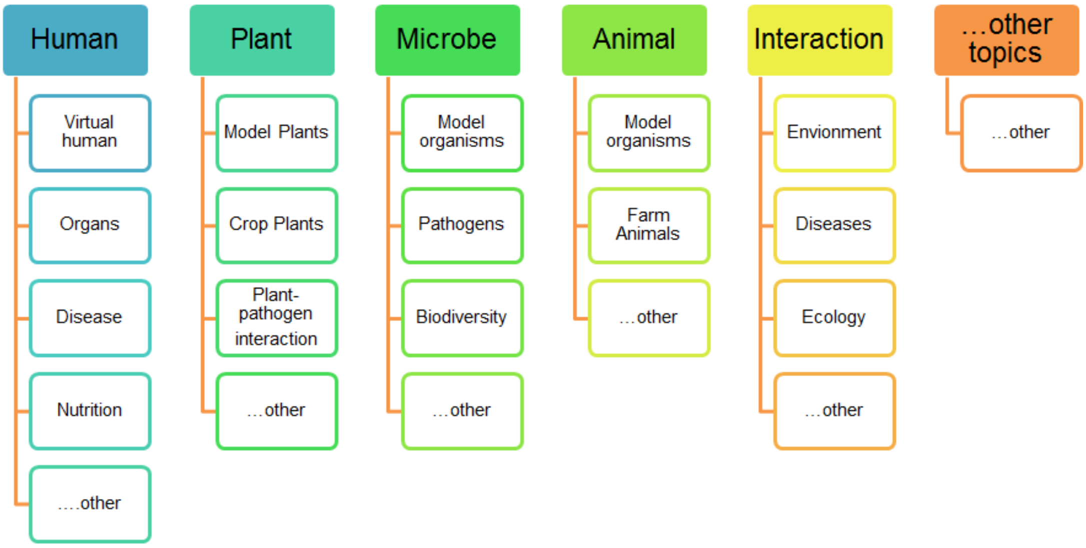

Fig. 3: Various application fields for a systems biology infrastructure.

The application fields can be summarized from the point of view of the biological system. Here we find as the principle fields human research, plants, microbes, animals. Also the various interactions between the different kingdoms can represent a whole research field. For all research fields many subtopics can be envisaged. In the area of human health research can focus on a single organ (like in the Virtual Liver Network approach), on a disease (e.g. cancer) or a method to develop new drugs.

In the plant, animal and microbe kingdoms the possibilities of research areas are multiplied because the study objects are not a single system as is the human; in these kingdoms we find a huge variety of model organisms or organisms for applications. E.g. in the plant field Arabidopsis thaliana is widely used as a model organism, but plant research include also the crop plants like rice, maize, wheat, canola, cassava, soybean and many more. The variety of organisms is multiplied by far considering the microorganism area.

The application areas may also vary with the perspective of the different user groups. In figure 4 examples from the plant and microbe field demonstrate how the focus of interest changes considering the fundamental scientists, the industry or the society as target groups.

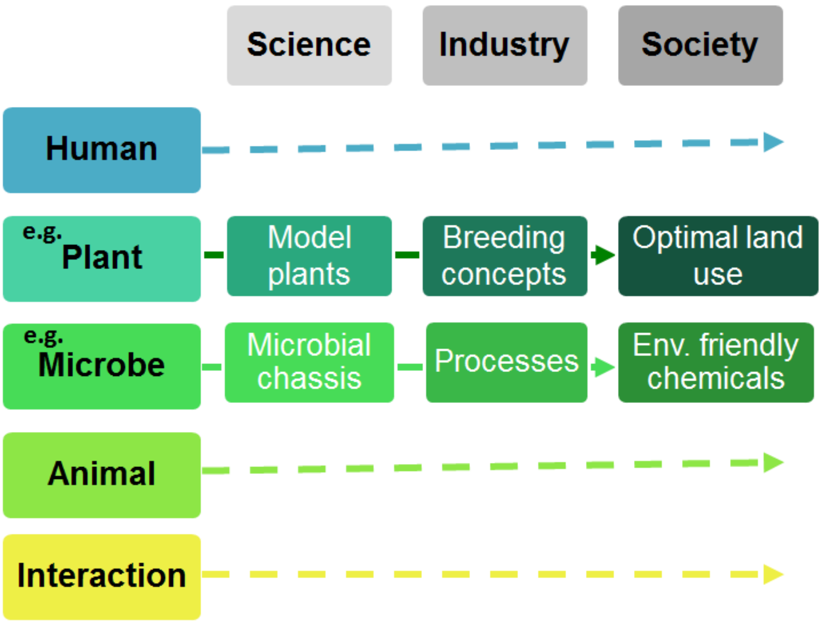

Fig. 4: Representatives from science, industry and society have a different focus of interest in using a systems biology infrastructure.

The example for the plant field mentions as major interest for the fundamental sciences the research on model plants like Arabidopsis to understand fundamental aspects of growth and development of plants, for draught stress and organ formation patterns etc. A plant breeding company might focus on seed development, male sterility and pest control. From the perspective of e.g. a ministry it could be of interest to use a systems biology infrastructure to optimise the land use or regulations on pesticide application.

Target/User Groups for ISBE

Systems biology has a high importance for the life sciences, but also for the welfare of the European Union in general because of its various application areas. Systems biology is reaching out to many areas, connecting also to non-life science research disciplines. An increasing number of larger-scale approaches addressing different biological questions or systems will be launched in the near future. These scientific questions of interest can be centered around cells (e.g. SysMO), organs (e.g. Virtual Liver Network, Virtual Gut), whole organisms (e.g. yeast and wide range of microbes) or even studying organisms in their environment. For these large-scale approaches a huge variety of expertise must collaborate to achieve the aims. In this respect, the user groups of the information derived from the model approaches might differ considerably. To achieve the paradigm shift in modern biology it is also necessary to involve the relevant stakeholder groups as advocates for systems biology.

In figure 5 the diversity of target groups linking to the ISBE activities is shown. The figure demonstrates the different user groups and communities that will connect to the infrastructure once it is implemented. A more detailed overview for the user group "industry" is given in Annex 1.

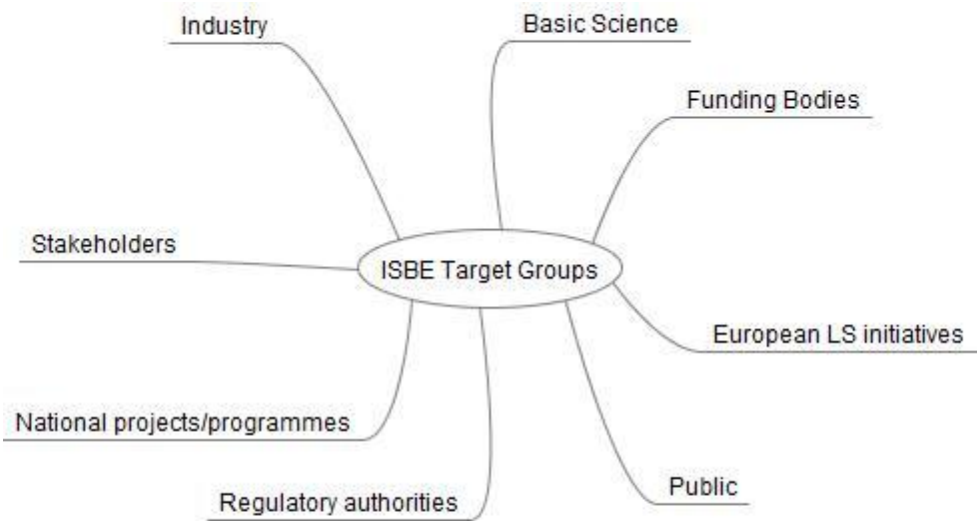

Fig. 5: Overview about the different stakeholder groups linked to ISBE activities.

The potential users of the ISBE infrastructure will be the following three major types of applicants (according to discussion status in WP3):

- small projects proposed by individual researchers or research groups
- large projects proposed by national and international research consortia
- small or large projects for commercial parties

User of the information or drivers for the launch of targeted projects (e.g. for societal or maybe also medical questions) could be stakeholder groups:

- Funding bodies
- National projects and programmes
- European life science initiatives (including ESFRI and RI infrastructures)
- Stakeholders (e.g. patient groups, regulatory bodies)
- General public (including groups like journalists etc.)

All these groups represent subdivisions, and in some cases the number of these subgroups can high with a huge diversity. These different user groups must be analysed, and the results integrated into the strategy development for ISBE according to their needs, their behavior and their activities.

The human research can serve as an example here: The groups performing fundamental science are already highly diverse; we find here representatives of the different fields in human sciences, the fundamental aspects, the diseases areas, the human nutrition, the life style etc. Also highly diverse is the group of technology developers for analytical technologies, the data processing, data management, generation of databases, generation of new tools and webservices to analyse the data, and finally the experts performing the modeling. In all these fields we also find the applications and developments for the industrial sector, including pharmaceutical companies, cosmetics, food and feed, prevention etc. Users of the infrastructure and the information and knowledge generated can

include also other stakeholder groups like patient organisations, health insurance companies, ministries, NGOs etc.
In the ideal case ISBE prepares for all the various user groups and responds to their needs and questions efficiently. In this respect the planned survey and persona modeling will support the concept development of ISBE efficiently to consider the various relevant perspectives.

Value of ISBE

Key factors for the value of ISBE

What is the added value that ISBE can contribute to the scientific community that nobody or nothing else can provide?

To meet the demands and challenges of a European infrastructure for systems biology ISBE considerations on the value of ISBE will contribute to the development of an appropriate structure and roadmap.

Added value by providing access to an infrastructure for systems biology:
Researchers from academia and industry will benefit from the systems biology infrastructure because it

- covers the whole pipeline from data acquisition to integration and modeling
- integrates all expertise needed
- provides fast access to a wide variety of specific expertise (including the biological sectors)
- allows a faster execution of research projects or programs because the pipelines are already established
- allows the efficient access and use of existing information (e.g. datasets in high quality produced by standard processes)
- allows the efficient use of the research budget based on an existing professional pipeline

Added value for the advancement in science:
The infrastructure for system biology will also contribute to advance science because it

- produces new and integrates existing knowledge and advances the building of a knowledge base for Europe
- will provide the optimal infrastructure to allow the efficient performance of large-scale approaches in biology (similar to Virtual Liver Network)
- represents a “think tank” function: ISBE will develop into a hub where information is integrated and existing needs, gaps, and challenges can be identified. Derived from the “think tank” activities recommendations can be made policy makers which are the upcoming topics that need to be addressed (function as consultant for science policies and pan-European strategies)
- Central contact points for international activities

Added value by overall training and capacity building:
As systems biology approaches will increase in the future, therefore the demand in personnel with skills data integration and modeling will increase dramatically. Europe needs training and capacity building on a broad scale to

- Generate personnel with high level expertise in the areas data integration and modeling via dedicated programs
- Generate a basic knowledge of systems biology for all life scientists via integrating training modules in university programs and by specific courses for established researchers

Added value for economy and society:
With its very broad spectrum of applications and new products Systems Biology will be a vital driver for innovations in Europe; it will make a considerable contribution to the creation of new job opportunities and increase the wealth and well-being of the European citizen. An infrastructure for systems biology will increase the chances for Europe-based companies, especially SMEs, to generate new products, processes and services deriving from on systems biology.

Added value for Innovation Union:
Research infrastructures are key for the development of innovation as they connect with all relevant actors in one field. They also support the translation and implementation of national policies in the European Research Area. Systems biology is a vital driver to overcome fragmentation of research in Europe and stimulate innovation because of its highly interdisciplinary character. The infrastructure connects to a broad spectrum of life science communities and creates added value by integrating expertise and knowledge for the benefit of all.

ANNEX 1

Detailed overview for the user group “industry” as an example for possible connections with ISBE