



The EUREKA *InSysBio* Cluster



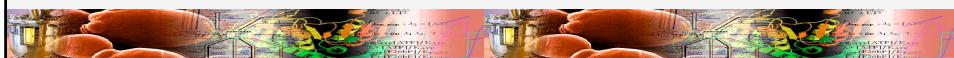
**A European Industry-driven Initiative on
*Integrative Systems Biology***




InSysBio:

**Presentation
at the
Kick-off Meeting of *NiSIS*
European Co-ordination Action
*'Nature-inspired
Smart Information Systems'*
5 March 2005, Aachen**

M Pfaff, BioControl Jena GmbH







InSysBio:


**Major Points
addressed in this Talk:**

- **Contents and Status of *InSysBio***
- **Potential Links with *NiSIS***





InSysBio: The EUREKA Framework

- **Members: 33 Countries (including the EU)**
- **National Contact Points: 3 Countries**
- **Associated Member: 1 Country**
- **Chairmanships:**
 - July 2002 – June 2003: Denmark
 - July 2003 – June 2004: France
 - July 2004 – June 2005: Netherlands
- **Clusters** are established for **strategic projects**,
such as *InSysBio*




www.eureka.be



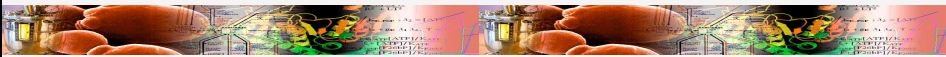
 **InSysBio: The Activities (Past & Present)**


- First Ideas for a EUREKA Cluster 'Virtual Cell' – Mid 2003
- Brussels Meeting – November 2003
- Paris Meeting – February 2004
- **White Book** finalised – June 2004
- **EUREKA Status** obtained – June 2004 (**E! 3365**)
- Brussels Kick-off Meeting – September 2004
- Heidelberg Meeting at ICSB – October 2004
- **First Call for Project Proposals** – Spring 2005
- Further Meetings, Setting up the Organisation etc – 2005



 **InSysBio: The General Description**

- Project: **E! 3365 INSYSBIO**
- Status: **Announced 18 June 2004**
- Title: **Integrative Systems Biology Cluster**
- Area: **Medical & Biotechnology**
- Duration: **5 Years**
- Start Date: **01 September 2004**
- End Date: **31 August 2009**
- Costs: **500 M€, 600 Man Years (estimated)**
- Projects: **50 with 2-7 Participants (estimated)**
- Funding: **by the National Member States (up to 50%)**




 **InSysBio: The Participants (Current)**


- ~~Sanofi-Synthelabo (FR)~~
- [GlaxoSmithKline (UK)]
- [Bayer (DE)]
- DSM (NL)
- Novo Nordisk (DE)
- Unilever (UK)

Large Companies

- Aureus Pharma (FR)
- BioControl (DE)
- Biomax (DE)
- ChipManTech (FI)
- Molecular Networks (DE)
- Nonlinear Dynamics (UK)
- Physiomics (UK)

SMEs

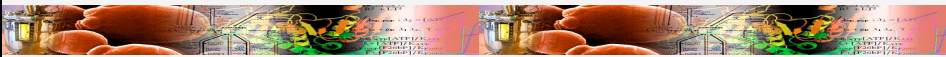



 **InSysBio: The Participants (Current)**

- Vrije Universiteit Amsterdam (NL)
- CNRS (FR)
- Centre for Bioinformatics Hamburg (DE)
- Biosystems Informatics Institute Newcastle (UK)
- Matimop – Israeli Industry Centre for R&D (IL)

University/Research/Administration


It is the explicit aim of the Cluster to continue to engage more partners, particularly among SME's and large industrial companies to achieve the ambitious goals defined by the programme.



 **InSysBio: The Contributions**

Country	Contribution [%]
France	29
United Kingdom	29
The Netherlands	14
Denmark	11
Germany	10
Finland	7

Initially Estimated Contributions to the Projects by Country
(subject to change)



 **InSysBio: The General Aim**

InSysBio


aims to promote

Industry-driven R&D Projects in Systems Biology

to reinforce the competitiveness

of the European Pharma and Food Industries







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InSysBio: The Core of the Matter

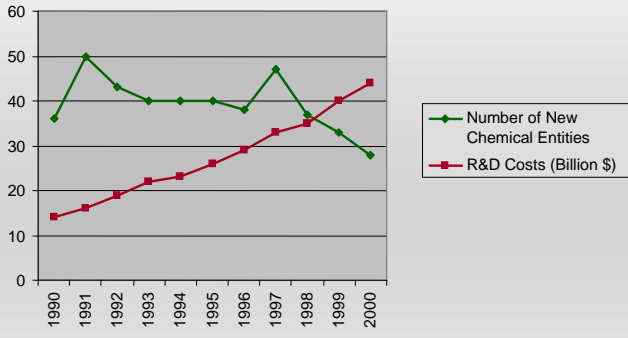
In the core of the *InSysBio* Initiative are **applications that use Systems Biology** approaches, methods and tools **in an integrative way** to solve **real-world problems** in **pharma and food** research, development and production





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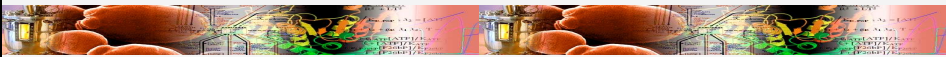
InSysBio: The Motivation




Year	Number of New Chemical Entities	R&D Costs (Billion \$)
1990	36	14
1991	50	16
1992	43	18
1993	40	21
1994	40	23
1995	40	26
1996	38	29
1997	47	33
1998	36	36
1999	33	40
2000	28	44

R&D Costs and Drug Discovery

Source: Decision Resources Inc., Pharmaceutical Research and Manufacturers of America (PhRMA)







InSysBio: The Motivation

Drug discovery and development is an interdisciplinary, **expensive and time-consuming** process.

From target identification to regulatory approval, **companies invest** an average of **\$900 million** and **~15 years** in research for a single new drug.

The estimation of cost, due to **failure** (9 out of 10 drug candidates fail) is approximately **75% of the total cost**.

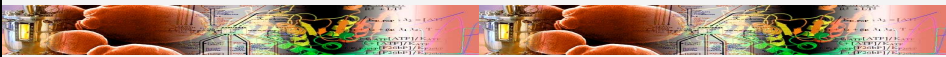



InSysBio: The Motivation

How to make this process **less failure-prone** and how to **speed it up** to save money and time?

Keys:

- **Information/Data** abundantly available today
- Approaches, such as **Systems Biology**




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InSysBio: The Notion of SB


Systems Biology is the study of living organisms in terms of their underlying network structure rather than simply their individual molecular components.


*A '**system**' can be anything from a **gene regulatory network** to a **cell**, a **tissue**, or an **entire organism**.*

*Because Systems Biology requires investigation of all interacting components simultaneously, **high-throughput, quantitative technologies** are essential.*

***Computational approaches** are also required to handle and interpret the volumes of data necessary to understand complex biological systems.*

www.sysbio.org/index.stm




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InSysBio: The Vision of SB

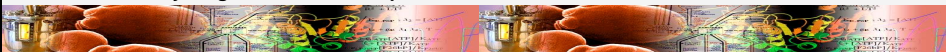
The challenge for Systems Biology is to transform the pharmaceutical industry by providing a means for identifying pathways that are critical to disease, and discovering both on- and off-target effects of compounds.

The concept of a linear drug discovery and development spectrum is being replaced by an iterative process, where knowledge gained on a systems level is applied at various points in a continuum.

The dynamic nature of biology is not easily modelled. However, by combining disparate types of data that interpret changes in genes, proteins, metabolites on a cellular level, it will comprise a set of parameters that when used together can provide a definitive means of diagnosis and evaluating drugs that alter disease outcome.

Using a computational approach, a pathway can be connected with a clinical endpoint and a small molecule drug. This will eventually create predictive medicine that will improve the process of drug development and increase the number of efficacious compounds.

www.beyondgenome.com/isb.asp



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InSysBio: The Target

Genomic Target sequence → Proteomics → Functional determination → Target validation → Assay development → HTS → Efficacy models → Drug leads

Targeting the entire Value Chain for Drug Discovery


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InSysBio: The Integration

Interactome

- DNA → Genomics
- mRNA → Transcriptomics
- proteins → Proteomics
- reactions → Fluxomics
- metabolite → Metabolomics



Integrating all Levels of Information available



***InSysBio:* The Specific Aims**

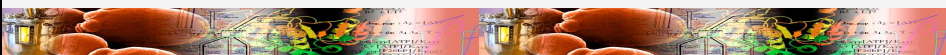
***InSysBio* Activities will promote**


- The **integration and analysis of existing data** in a homogeneous and accessible way
- The **development of integrative modelling tools** to better model biological systems
- The **creation of integrative models for applications** in pharma and food R&D



***InSysBio:* The 3 Work Areas**


- **Integrative Data Management Tools**
- **Integrative Modelling Tools**
- **Integrative Applications**




 **InSysBio: The Work Area A)**

Integrative Data Management Tools

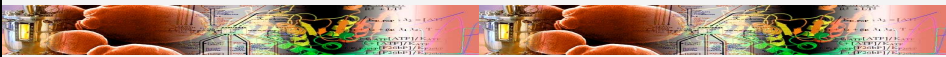
- **Data Integration Tools**
 Technical tools required to achieve integration and analysis of the data available at the Cluster partners in the various European countries
 'Middleware' solution to centralise in a common and accessible way the different data sources (databases, flat-files, publications, websites ...)
- **Semantic Integration Solution**
 Semantic Integration above the technical 'middleware' integration layer will provide understanding of the information objects gathered from the heterogeneous databases
- **Global Semantic Level Framework**
 Global meta-model will be developed above to integrate data and tools, will create coherence between the Work Areas, will be implemented with a variety of standards




 **InSysBio: The Work Area B)**

Integrative Modelling Tools

- **Mathematical Modelling Tools**
 that involve generic aspects and such that concentrate on each of the relevant levels of biological organisation
 also tools to integrate the level-specific tools into a whole-cell/organism modelling tool
 1. Nanoscopeic tools for small molecules, macromolecules and their interactions
 2. Mesoscopeic tools for supra-macromolecular and sub-cellular structures and for cellular pathways and networks
 3. Microscopeic tools for the cell and for cell populations
 4. Macroscopic tools for above and beyond the cell, i.e. for the tissue, organ and organism
 5. Generic tools that span all levels of Computational Systems Biology







InSysBio: The Work Area C)

Integrative Applications

- **Meta Integration of Systems Biology Applications**
of relevance to the drug and nutraceutical development pipeline
and to improved food speciality ingredients
- **Generic Models and 'omics' Data Integration
including Computer Replica**
of individual cells and micro-organisms and also cell populations and tissues
for studying physiology and behaviour under varying environmental and
process conditions
- **Improved Visualisation and User Interaction
with High-dimensional Complex Models**



InSysBio: The General Rules

EUREKA provides a simple set of criteria for projects:


- Involve at least 2 partners from different EUREKA member states
- Focus on the application and/or development of advanced technologies with a relevant level of innovation
- Aim at a marketable product, process or service

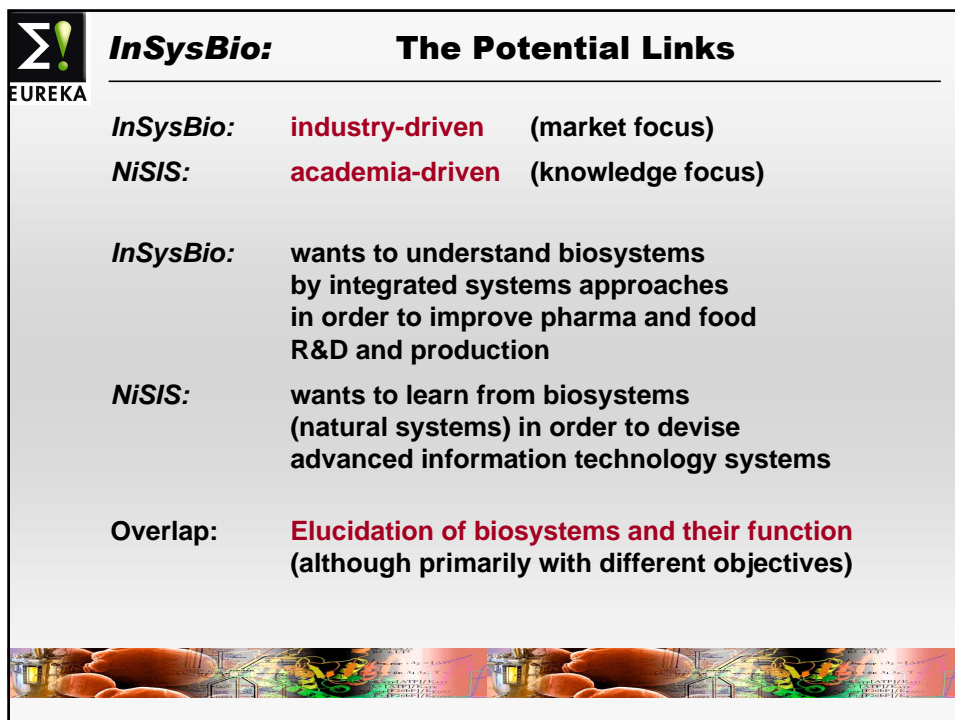
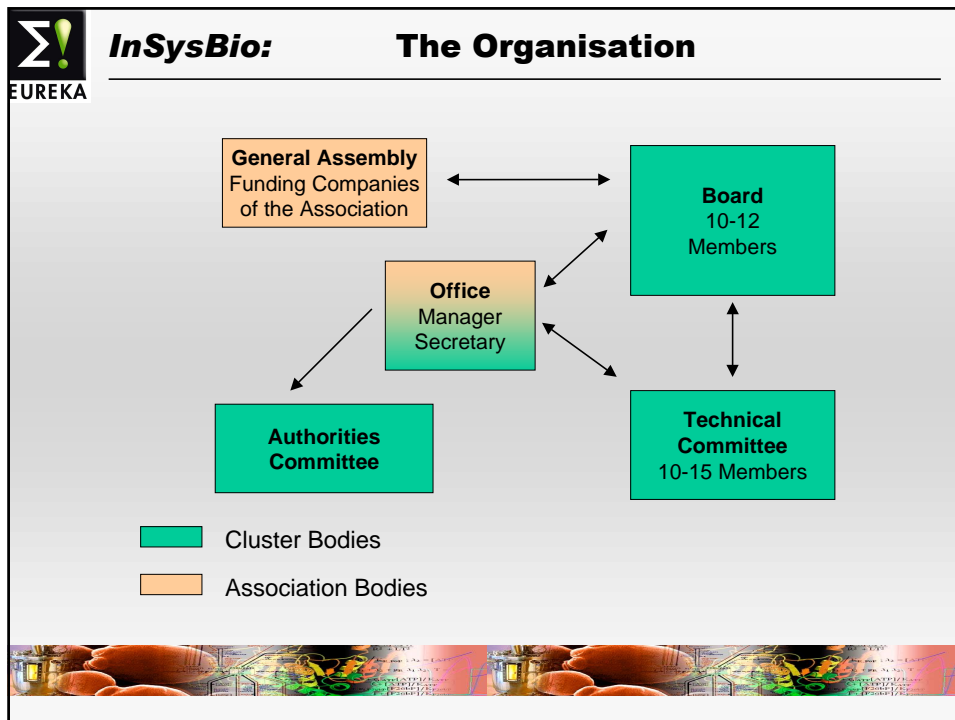
IPR Issues:


- Case-by-case partnership agreements in projects

Obligations:

- After the individual project's approval
contribution by the project partners
to the running costs of the organisational structure of the Cluster,
probably as percentage of this project's budget
(still to be finalised in detail)





**InSysBio: The Potential Links**

Way forward?

In general, '**Cross-Fertilisation**' appears to be **possible**.

Please **attract potential partners, in particular from industry,**
for the two initiatives.

Then, on a **case-by-case** basis the **collaboration potential**
should be checked.

In general, **links between the two initiatives should be kept**.

... Further Ideas?
... Open for Discussion!

Thank you!

