



BMBF-Funding Initiative `Systems of Life – Systems Biology`

Platform
Modeling / Bioinformatics

Coordinator: Prof. E. D. Gilles

Kick-Off-Meeting, Heidelberg, April 19, 2004

Platform partners



Humboldt University, Berlin:

Prof. H.-G. Holzhütter, Charité, Mathematical Modeling

Prof. R. Heinrich, Biology, Theoretical Biophysics

Prof. T. Höfer, Institute for Theoretical Biophysics

Prof. A. Herrmann, Biology, Molecular Biophysics

Prof. H. Herzel, Institute for Theoretical Biology

Prof. J. Reich, MDC for Molecular Medicine, Bioinformatics



EML Research, Heidelberg:

Dr. U. Kummer, Bioinformatics and Computational Biochemistry

Dr. R. Wade, Molecular and Cellular Modeling



MPI DCTS, Magdeburg:

Prof. E.D. Gilles, Systems Biology

Prof. S. Schuster, Univ. Jena, Bioinformatics

Mission

- ❑ The platform `modeling / bioinformatics` is devoted to the foresighted development of methods and tools for the efficient construction, analysis, integration and exchange of complex mathematical models in systems biology.

- ❑ The platform interacts with all partners of the initiative by:
 - Providing novel methods and tools for the systems-level analysis of the hepatocyte.

 - Conducting specific research projects in cooperation with the partners to develop methods, tools and standards.

Key objectives of research and development

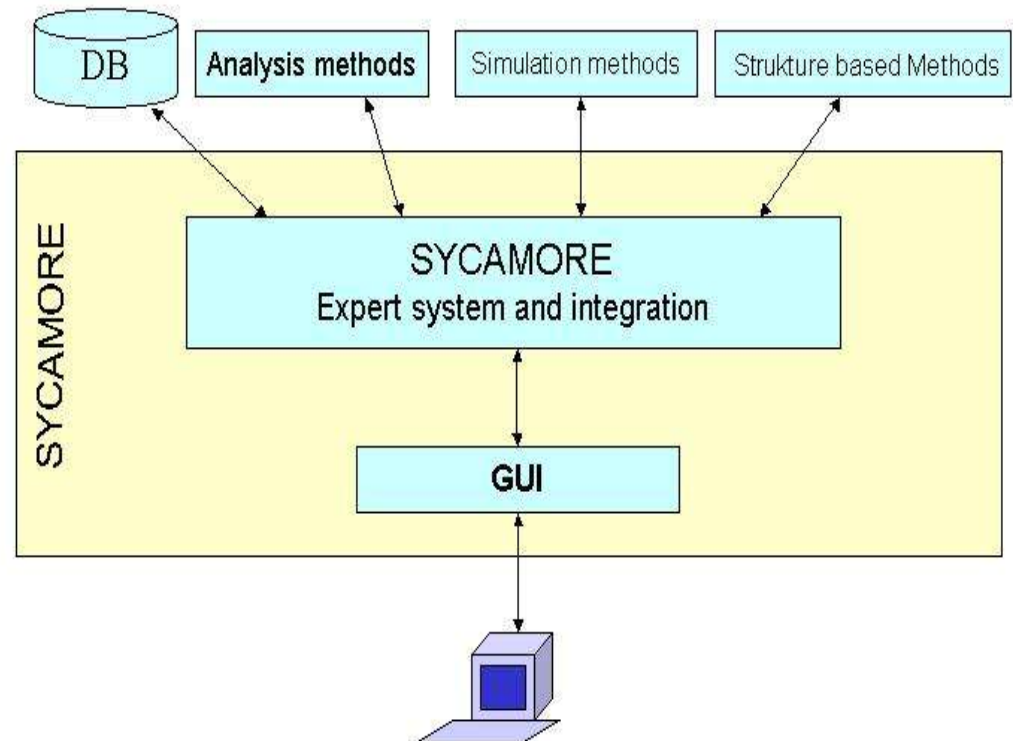
- ❑ Unified methodology for the kinetic modeling of complex cellular networks encompassing metabolic, signal transduction and genetic sub-structures with a focus on network representation and complexity reduction.
- ❑ Novel methods for the analysis of complex networks based on systems theory regarding structural properties, network decomposition, identification of model structures, and others.
- ❑ New and / or improved computer tools for standardized modeling and simulation, including model and data storage.
- ❑ Integration of experimentation and modeling with respect to efficient experimental design and real-time control of biological processes.

Coordination of activities

- ❑ `Division of labor` between the platform partners and joint projects in key areas (e.g. complexity reduction, ...).
- ❑ Modeling and analysis of disjointed, yet connected cellular subnetworks in signal transduction, gene expression and metabolism.
- ❑ Progress meetings of the platform partners every 6 months.
- ❑ Annual international workshop `Modeling and simulation of complex biological systems` open to all researchers within the BMBF initiative.
- ❑ Internal web portal for modeling and bioinformatics

Systems biology Computational Analysis and Modelling Research Environment

- ❑ Build a suite of methods and tools to facilitate the integration of experimental and computational approaches.
- ❑ Support the user in the choice of appropriate computational tools to tackle a specific problem.



I. Evaluate and integrate existing methods

II. Develop new methods

- ❑ Complexity reduction of big models
- ❑ Hybrid simulation methods
- ❑ Structure based methods to compute kinetic constants
- ❑ Sensitivity analysis of higher order
- ❑ Semi-automatic generation of models from databases

III. Apply tools to selected sub-systems of the hepatocyte



Kinetic modeling of complex cellular networks with special focus on hepatocytes

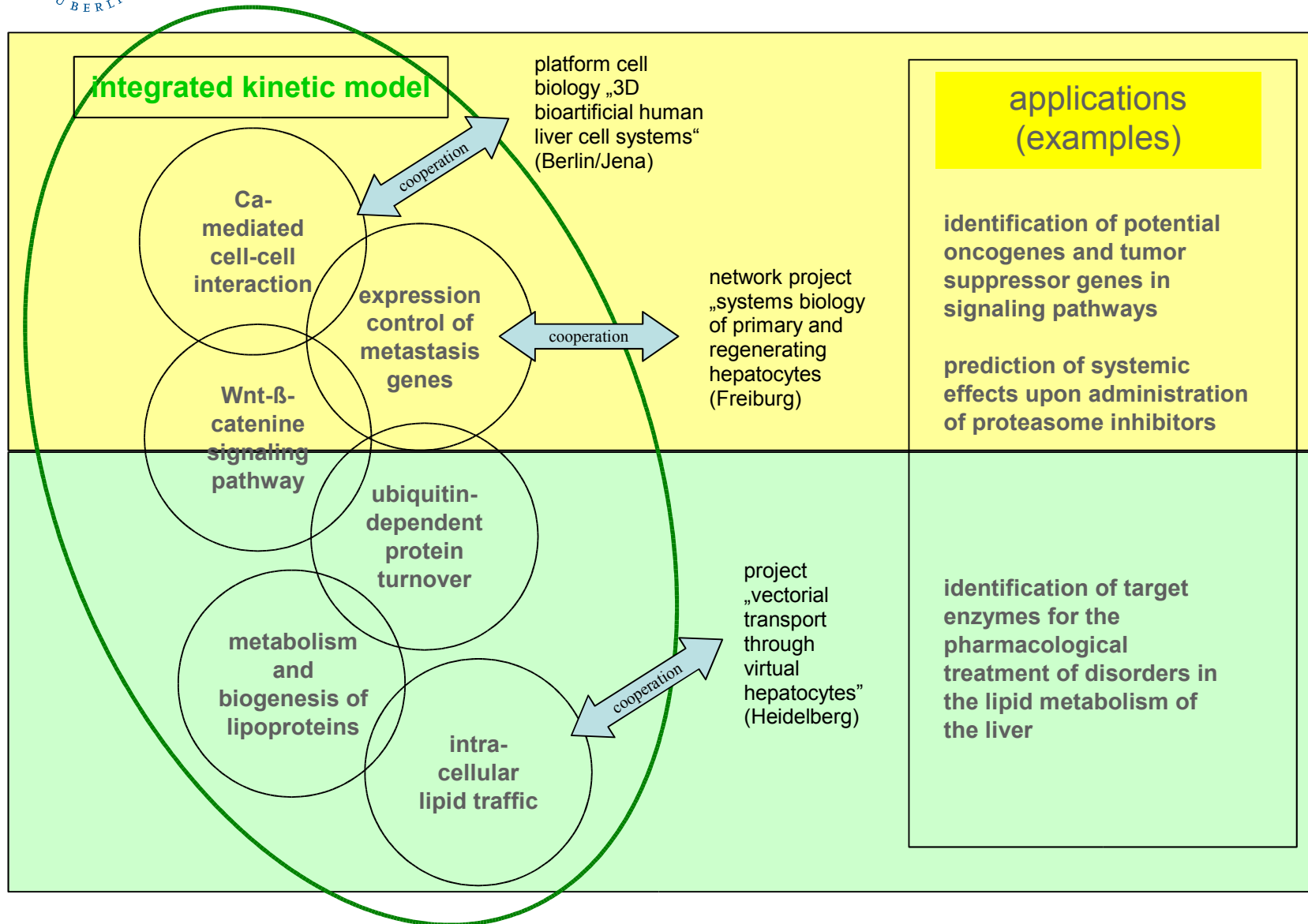
I. Methods and tools

- ❑ Generalized control theory of cellular networks based on the well-established concept of metabolic control theory (Heinrich/Kacser).
- ❑ Standards for the formal and graphical representation of cellular networks.
- ❑ Theoretical framework for identification and evaluation of potential interfaces between various types of cellular networks.
- ❑ Inter-active software modules for computer simulations of hepatocyte-relevant kinetic models.

II. Modeling of selected sub-networks



Kinetic modeling of selected sub-networks: successive development of an integrated model



interfaces between the various modules of the integrative cell model



Characterization of complex signaling and regulatory processes in hepatocytes using modeling and systems theory analysis

I. Methods and tools

- ❑ Modeling concepts for regulatory networks
- ❑ Visualization of models and simulations in ProMoT
- ❑ Structural analysis of signal transduction networks
- ❑ Software sensors for process control

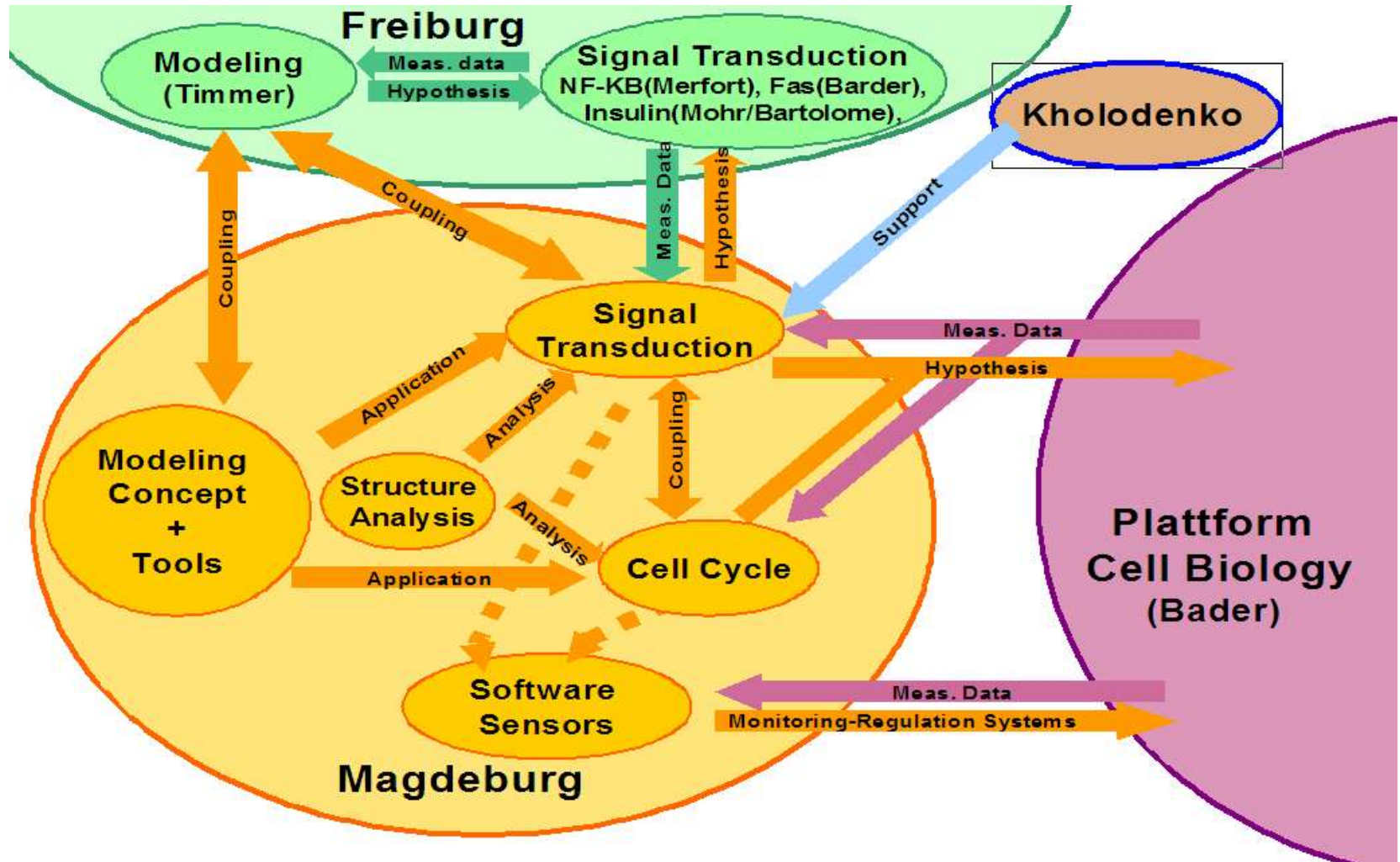
II. Model-based analysis of selected sub-networks

- ❑ Mitogenic and apoptotic signaling pathways
- ❑ Signal integration in proliferation control

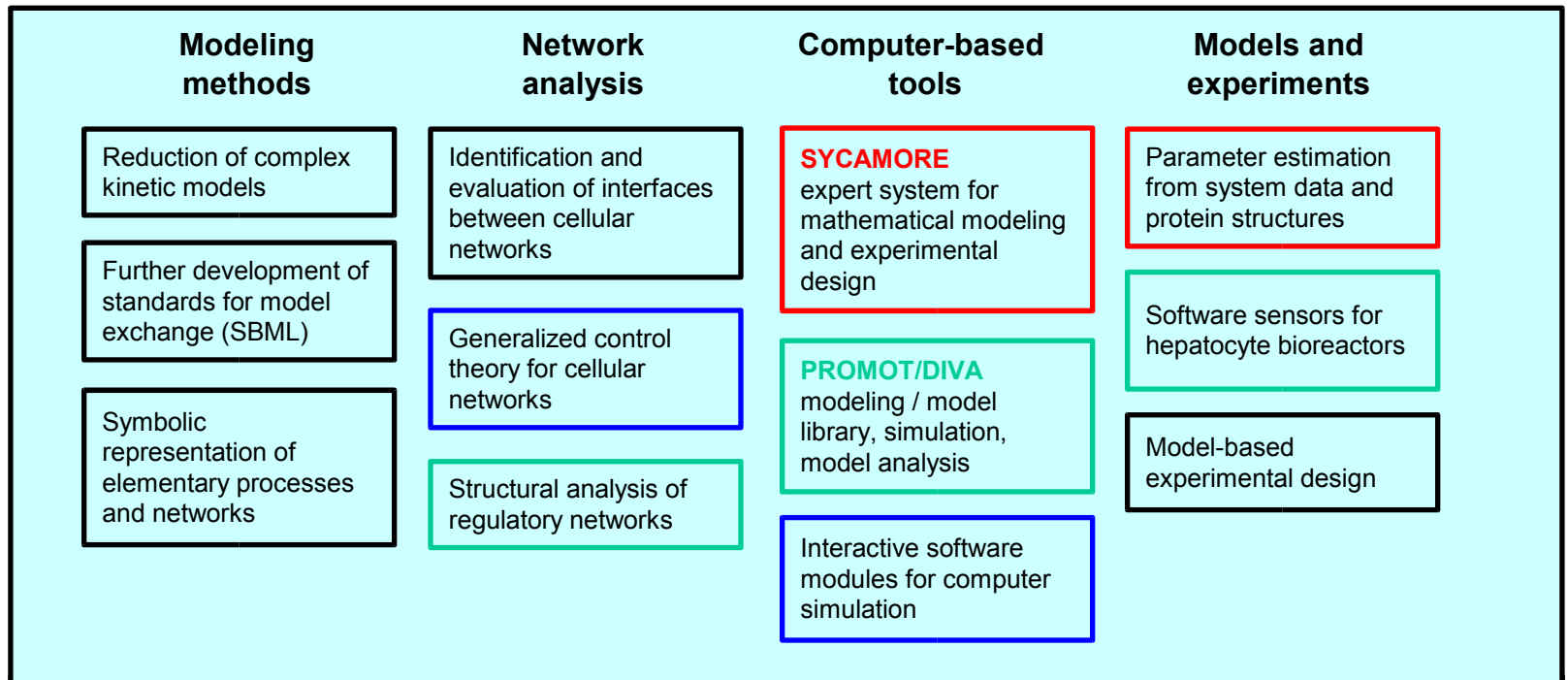


MAX-PLANCK-GESELLSCHAFT

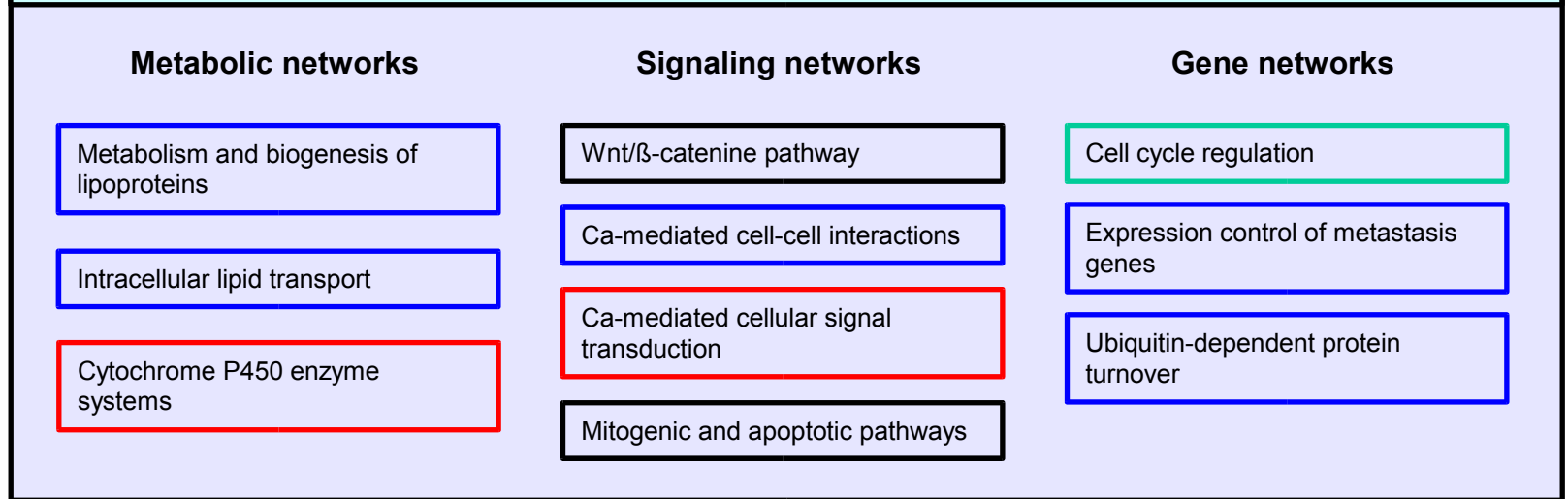
Characterization of complex signaling and regulatory processes in hepatocytes using modeling and systems theory analysis



Methods and tools



Cellular systems



Heidelberg

Magdeburg

Berlin

All groups