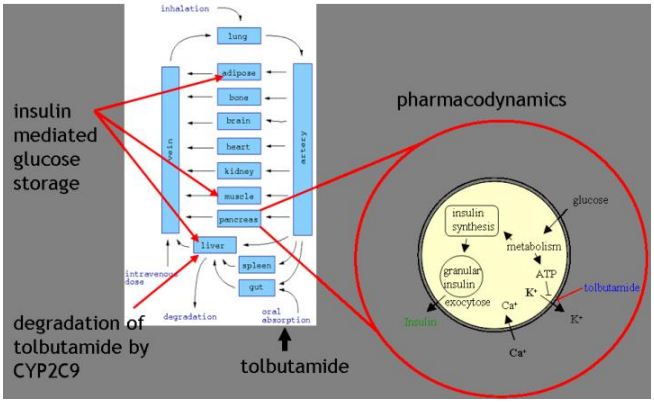
Junior Research Group "Computational Physiology"

Free University of Berlin and DFG Research Center MATHEON, Berlin, Germany

The junior research group (JRG) is active in the field of mathematical modelling and numerical analysis of multiscale problems for stochastic and deterministic systems, with a strong focus on applications to life sciences. The current projects are on conformation dynamics, hybrid modelling and pharmacokinetics.



Conformation dynamics: There are many problems in physics, biology, medicine, where the length and time scales of interest remain entirely beyond the computational capacity currently available, and will remain out of reach in the foreseeable future. As a consequence, there is an increasing need for simplified, reduced descriptions. Reduced models may provide insight and numerical simulations for larger length scales and longer time scales, but of course at the cost of discarding some level of detail. Instead of simply neglecting some degrees of freedom, one is rather interested in reduced models that incorporate into their dynamical behaviour the effective influence of the neglected coordinates. In this context, the JRG aims at developing mathematical tools and numerical algorithms for the identification and efficient simulation of reduced model systems. In cooperation with the Bio Computing Group (FU Berlin) and the Molecular Dynamics Group (ZIB) we developed novel mathematical techniques for the identification of metastable behaviour in Markovian systems, in particular in application to the conformation dynamics of drug-like molecules.

Hybrid modelling: Simulation of signal pathways and gene-regulatory networks often requires a stochastic formulation of the reaction kinetics in order to correctly capture the influence of small numbers of molecules and relevant fluctuations. On the other hand, metabolic networks with large numbers of molecules and continuously occurring reaction are successfully modelled by the deterministic formulation of chemical reaction kinetics (based on the law of mass action). Aiming at more detailed cellular systems consisting of gene-regulatory networks and signalling pathways coupled to metabolic networks, the aim of the project is to devise adaptive numerical schemes for the simulation of coupled stochastic and deterministic models of biochemical reaction systems and its mathematical justification. Moreover, we are interested in the efficient solution of the chemical master equation. Within this project, we cooperate with experimentally working groups at the Free University of Berlin (Microbiology) and the EMBL (Heidelberg), as well as with theoretical oriented groups at the Max Planck Institute for Molecular Genetics (Berlin) and CERMICS & INRIA (Paris).

Pharmacokinetics: Pharmacokinetics is the study of the drug/xenobiotic-organism interaction, in particular the investigation of absorption, distribution, metabolism, excretion and toxicological (ADMETox) processes. In the past decade, considerable progress was made with the use of computational approaches, in particular in the early stage of the drug discovery process. As a result, modelling and simulation is possible prior to any in vivo experiments. Studying ADMETox profiles is used to identify and understand the physiological mechanisms that are most relevant from the point of view of pharmacokinetics. The JRG aims at designing generic physiologically based pharmacokinetic models coupled to metabolic and regulatory pathways on a mechanistic basis in order to analyze effect-related biomarkers (see figure). A second topic is the design of models and efficient mathematical techniques to capture the effects of natural variability on the kinetics. In cooperation with Computing in Technology (CiT), the JRG develops a modular, application-specific and user-friendly virtual lab for modelling and simulation in

pharmacokinetics/dynamics. We moreover cooperate with the Federal Institute for Risk Assessment (BfR) Berlin, pharmaceutical companies, and the Charite Berlin.

The JRG is supported within the DFG Research Center MATHEON "Mathematics for key technologies: Modeling, simulation, and optimization of real-world processes" (www.matheon.de). It is involved in the International Max Planck Research School "Computational Biology and Scientific Computing", Berlin, and the COST B25 action. At the time, a postdoc, two PhD students and four Master students work within the group. For further details please visit URL
http://compphysiol.mi.fu-berlin.de.

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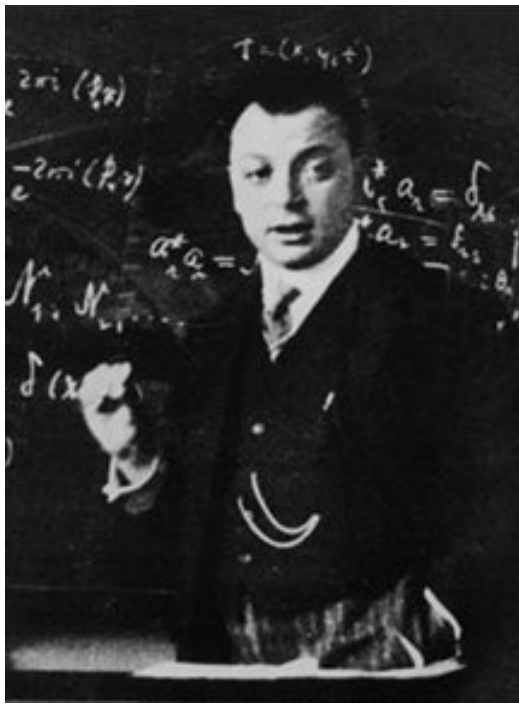

Wolfgang Pauli
Mathematical physicist (1900 – 1958)
Wien, Hamburg, Kopenhagen, Zürich, Princeton