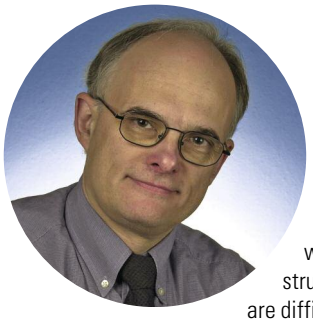
Research in the Department of Theory & Bio-Systems

Das Leben besteht in der Bewegung.
Aristoteles



Reinhard Lipowsky 11.11.1953
1978: Diploma, Physics, (University of Heidelberg)
1982: PhD (Dr. rer. nat.), Physics (University of Munich)
1979-1984: Teaching Associate (University of Munich)
1984-1986: Research Associate (Cornell University)
1986-1988: Group leader (FZ Jülich)
1987: Habilitation, Theoretical Physics (University of Munich)
Thesis: Critical behavior of interfaces: Wetting, surface melting and related phenomena
1989-1990: Associate Professorship (University of Munich)
1990-1993: Full Professorship (University of Cologne), Director of the Division "Theory II" (FZ Jülich)
Since Nov 1993: Director (Max Planck Institute of Colloids and Interfaces, Potsdam)

The main objective of our research activities is to understand the hidden dimensions of self-organization in biomimetic and biological systems. The molecular building blocks of these systems join "by themselves" and form a variety of supermolecular assemblies, which then interact to produce even larger structures and networks. Since these processes are difficult to observe experimentally on the relevant length and time scales, theory and computer simulations are essential in order to integrate different experimental results into a coherent and unified framework. The department is also responsible for the International Max Planck Research School on "Biomimetic Systems".

The associates of the department form several research groups. At present, the research group leaders and topics are:

· *Rumiana Dimova:* Biophysics Lab;
· *Volker Knecht:* Molecular Dynamics;
· *Thomas Weikl:* Proteins and Membranes;
· *Mark Santer:* Carbohydrates and Polysaccharides;
· *Christian Seidel:* Polymers and Polyelectrolytes;
· *Angelo Valleriani:* Stochastic Processes;
· *Stefan Klumpp:* Regulation of Bioprocesses.

The main results of these research groups are described in separate reports on the following pages. These reports are related to four main topics: Polymers and proteins, carbohydrates, membranes and vesicles, as well as complex systems. Both carbohydrates and complex systems represent relatively new research fields in the department.

As far as membranes and vesicles are concerned, two particularly interesting results are about the cooperative binding of membrane-anchored receptors, see **Fig. 1** and separate report by *T. Weikl*, and the formation of membrane nanotubes induced by aqueous phase separation, see **Fig. 2** and my separate report.

Other topics that are only partially covered in the subsequent reports include the multiscale motility of molecular motors and the dynamics of filaments. In the following, I will briefly summarize our recent results on these topics.

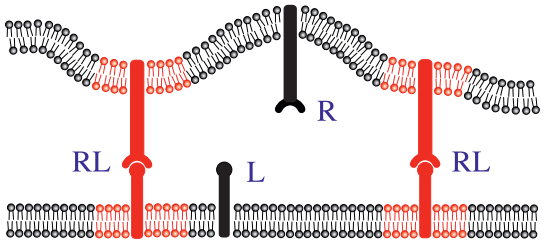


Figure 1: Cooperative binding of membrane-anchored receptors (R) and ligands (L). Binding requires that R and L are located opposite to each other and that the separation of the corresponding membrane segments matches the length of the RL-complexes.

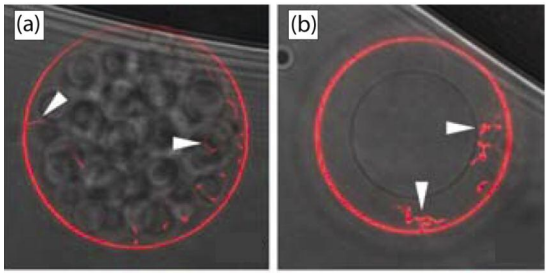


Figure 2: Membrane nanotubes within a lipid vesicle as indicated by the white arrows (a) during and (b) after aqueous phase separation within the vesicle. The fluorescently labeled membrane (red) forms both the large vesicle (outer circle), which has a diameter of about 40 µm, and the thin nanotubes, which have a thickness below optical resolution.

Motility of Molecular Motors.
We have focused on a particular class of molecular motors, namely motors that step along cytoskeletal filaments. Such stepping motors are essential for intracellular transport within eukaryotic cells as well as for their locomotion and division. All stepping motors have a similar molecular architecture with two identical motor domains, both of which are able to hydrolyze ATP into ADP and inorganic phosphate (Pi) as well as to dock onto the cytoskeletal filaments. In the last couple of years, we studied the multiscale motility of these motors on three different levels: conformational changes of motor proteins; free energy transduction by single motors; and cargo transport by motor teams.

Conformational Changes of Motor Proteins.
When viewed with atomistic resolution, each motor domain of kinesin contains several subdomains: the nucleotide binding pocket, the microtubule binding site, and the neck linker, see **Fig. 3**. After ATP has been bound to the empty nucleotide binding pocket, it is hydrolyzed into ADP and Pi, both of which are successively released from the pocket. We have studied the associated conformational changes by atomistic Molecular Dynamics simulations, which revealed a certain allosteric coupling between the different subdomains (*A. Krukau, V. Knecht*).

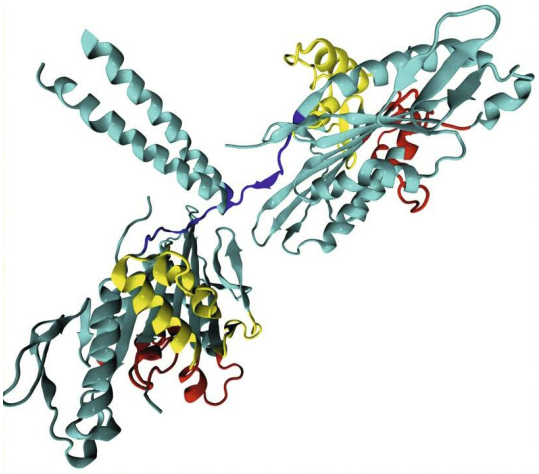


Figure 3: Two motor domains of kinesin (ribbon representation). Each motor domain contains a nucleotide binding pocket (red), a microtubule binding site (yellow), and a neck linker (blue). The „crosstalk" between these different subdomains depends on the occupancy of the nucleotide binding pocket (empty, ATP, or ADP).

Free Energy Transduction by Single Motors.
Since each motor domain can exhibit three different nucleotide states, a dimeric motor with two such domains can attain nine such states. These states are connected by chemical and mechanical transitions and form a chemomechanical network with a large number of motor cycles. Such a representation has been used to integrate many experimental data for two different stepping motors, namely for kinesin in contact with microtubules (*S. Liepelt, A. Valleriani*) and for myosin V that walks along actin filaments (*V. Bierbaum*). Both kinesin and myosin V are characterized by a competition between several motor cycles.

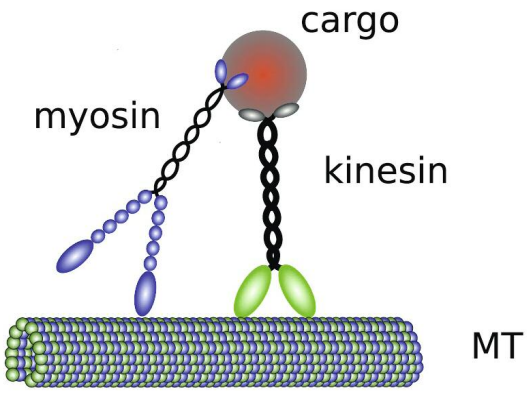


Figure 4: Cargo transport by the microtubule-based motor kinesin is enhanced by the actin-based motor myosin V. The latter motor binds to microtubules (MT) as well and then diffuses along these filaments. Vice versa, kinesin can bind to and diffuse along actin filaments. In this way, the two types of motors can transport the same cargo along both microtubules and actin filaments.

Cargo Transport by Motor Teams.
The transport of cargo within eukaryotic cells is performed by teams of molecular motors. Because each motor unbinds from the filament after a certain number of steps, the number of actively pulling motors varies with time. The case of two kinesins has been theoretically studied using two different representations of their state space (*C. Keller, F. Berger, S. Klumpp, S. Liepelt*). In some cases, cargo transport by one team of motors is enhanced by another team of motors that do not move in a directed manner but only diffuse along the filaments. One example is kinesin-driven cargo transport along microtubules that can be enhanced by the actin-based motor myosin V, see **Fig. 4** (*F. Berger, M.J.I. Müller*).

Depolymerization of Actin Filaments.
As mentioned, actin filaments provide the tracks for molecular motors such as myosin V. In addition, the polymerization and depolymerization of these filaments plays an essential role for many cellular processes such as cell division, locomotion, and adhesion. Quite recently, the depolymerization of single filaments was observed to be interrupted for extended periods of time. The interruptions are not coupled to ATP hydrolysis but arise from random modifications of actin protomers (*T. Niedermayer*).

For additional information about research at the Department of Theory & Bio-Systems, see subsequent reports and *www.mpikg.mpg.de/th/*

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Director, Department of Theory & Bio-Systems