Publishable executive summary

The “Active biomimetic systems” studied in this STREP are built up from two types of molecular machines, growing filaments and stepping motor proteins. Growing filaments generate pushing forces; stepping motor proteins exert pulling forces. The first objective of this STREP, which started on May 1, 2005, is to elucidate these force generation mechanisms and to obtain a systematic understanding of the corresponding molecular processes.

Because of its small size, a single molecular machine generates rather small forces and is easily perturbed by thermal noise. In order to have some appreciable ‘impact’ onto their surroundings, these molecular machines have to act in groups. Therefore, the second objective of this STREP is to study and clarify the cooperative behavior of small and large groups of molecular machines.

The third objective, which applies both to the single motor properties and to the cooperative behavior of many motors, is to control and to vary the system properties in a reliable and systematic manner. Thus, the different projects in this STREP have the common target to control and maximize the generated forces, to control and optimize the transport properties, and to vary the architecture of the filament/motor assemblies in a controlled manner.

The research activities performed in this STREP are organized in six workpackages which were all active during this reporting period, May 1, 2006 until April 30, 2007.

In the first workpackage about ``Force generation by actin filaments", propulsion of a liposome or vesicle via a meshwork of branched filaments has been achieved. The observed movement of the liposome gives important clues to the molecular attachment of the filaments to the liposome. On the basis of the new data, several possible models for this attachment can be ruled out. Once the vesicle is continuously propelled, it attains a peculiar asymmetric shape from which one can deduce the forces generated by the filaments onto the vesicle membrane.

In the second workpackage about ``Force generation by microtubules", bundles of microtubules have been shown to generate an increased force that is roughly proportional to the number of filaments in the bundle. In addition, collective transitions to a shrinking state have been observed. A theoretical study on the force generation by crosslinked bundles has also been completed. In the next step, the effect of crosslinkers on growing bundles will be elucidated experimentally.

In the third workpackage about ``Force generation by stepping motors", the pulling of membrane tubes via groups of molecular motors has been further investigated both experimentally and theoretically. It has been found that all motors form a continuous cluster at the tip share the force. In addition, a new motility assay has been established in which the molecular motor dynamin acts as a molecular ``cutter" of membrane tubes.

Dynamin has been shown to be rotating motor which cuts the membrane tube by wrapping around it in a helix-like fashion.

In the fourth workpackage about ``Transport by stepping motors'', a general theory for the free energy transduction of stepping motors has been developed. This theory describes all available single molecule data for kinesin in a quantitative manner. One important aspect of the new theory is that the motor can switch between different motor cycles or pathways. This ``gearbox'' has important consequences for all aspects of motor transport including the dependence of the motor's run length on various control parameters. The latter quantity has been determined, both experimentally and theoretically, for cargo particles that are pulled by several motors. A detailed comparison between experiment and theory shows that the cooperative transport of cargo leads to a run length distribution with a ``fat'' tail.

In the fifth workpackage about ``Self-organization in actin-based system'', networks of actin filaments have been constructed using myosin minifilaments as dynamic crosslinkers. The concentration of ATP can be used to control the activity of the myosin motors. For high ATP concentrations, the myosins induce mutual sliding of actin filaments; for low ATP concentrations, the myosins act as static crosslinkers that form complex architectures of these filaments. Further progress has been made in the assembly of contractile bundles of actin/myosin bundles between two beads. The contractile forces generated by these bundles have been measured by optical tweezers.
This architecture represents an important step towards the construction of ``nanomuscles''.

In the sixth workpackage about ``Self-organization in microtubule-based systems'', an improved gliding assays for microtubules has been constructed. In a conventional assay, the molecular motors are immobilized on a solid substrate in a random fashion. In the improved assay developed here, the motors are anchored to a well-defined pattern of nanodots. The nanodots are so small that only one motor is located on each dot. The separation of the dots can be varied from a few nanometers to hundreds of nanometers with nanometer precision. In this way, the number of motors that pull on a single microtubule can be varied systematically over a wide range. As one increases the density of the motors or of the microtubules, the filaments have a strong tendency to form a nematic phase.

This STREP involves the following partners:

Max Planck Institute of Colloids and Interfaces, Potsdam, Germany (coordinator)
FOM Institute for Atomic and Molecular Physics, Amsterdam, Netherlands
BASF-AG, Ludwigshafen, Germany
Curie Institute, Paris, France
European Molecular Biology Laboratory (EMBL), Heidelberg, Germany
Fritz Lipmann Institute, Jena, Germany
Enzymology and structural biochemistry Lab., CNRS, Gif-sur-Yvette, France
Politecnico of Milano, Milano, Italy
University of Heidelberg, Heidelberg, Germany

University of Leipzig, Leipzig, Germany
Institute of Chemistry of the Chinese Academy of Sciences, Beijing, China