3rd Wolfgang Pauli International Workshop on:

Mathematical Modelling of Actin-Based Motility

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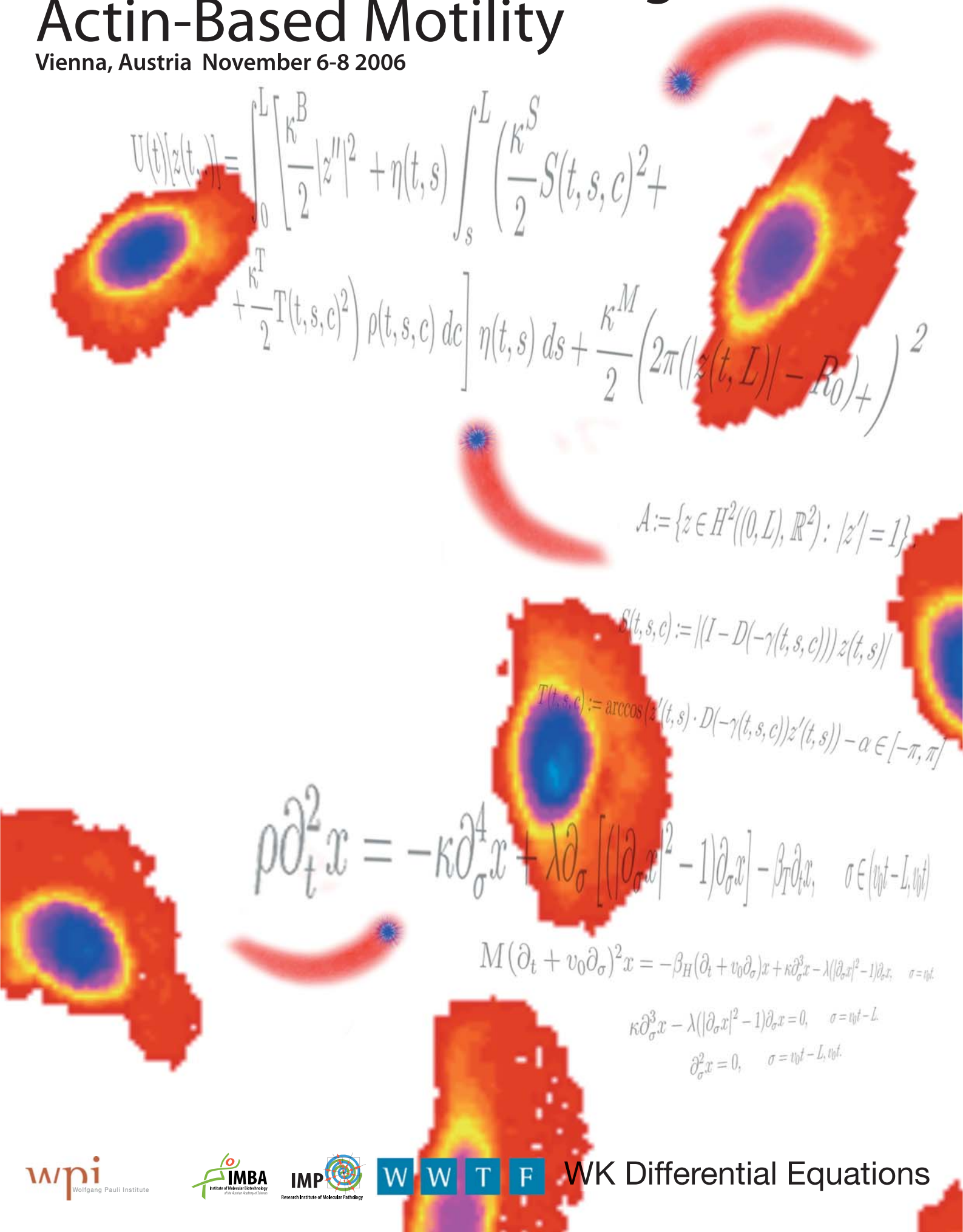

wpi Wolfgang Pauli Institute

IMBA Institute of Molecular Biotechnology of the Austrian Academy of Sciences

IMP Research Institute of Molecular Pathology

WWTF WK Differential Equations

NIR GOV

The Weizmann Institute of Science, Israel

Membrane fluctuations driven by actin and myosin: waves and quantized division

We present a model which couples the membrane with the protrusive forces of actin polymerization and contractile forces of molecular motors, such as myosin. The actin polymerization at the membrane is activated by freely diffusing membrane proteins, that may have a distinct spontaneous curvature. Molecular motors are recruited to the polymerizing actin filaments, from a constant reservoir, and produce a contractile force. All the forces and variables are treated in the linear limit, which allows us to derive analytic solutions. Our results show that for concave membrane proteins the myosin activity gives rise to propagating membrane waves similar to those observed on different cells. For convex membrane proteins the myosin activity gives rise to an unstable contraction, which yields a length-"quantization" of the mitosis process.

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Developing mathematical models, algorithms and programming tools for analysis of actin-based motility

Joint work with
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The actin cytoskeleton is a dynamic meshwork of proteanous filaments that is disposed beneath the plasma membrane. Actin monomers self-assemble into filaments to generate forces and movements during cell morphogenesis and movement. However, the high supra-molecular and organisational complexity of the cell cytoskeleton renders it difficult to study actin-based movement in a cellular environment. Therefore, a-cellular assays are currently used to unravel how controlled actin polymerisation contributes to cell movement. Several biophysical models were proposed for the mechanisms by which actin filament assembly generates force that is translated into the movement [1-3]. Among those, stochastic simulations have considerable potential to assess the dynamic processes in the cell regulatory system. Results obtained with this approach are often in closer approximations to the molecular reality than those yielded by classical analytical models based on a set of differential equations. However, so fare, no comprehensive and systematic comparative study or evaluation of modelling approaches used in cytoskeleton research is available.

Our work aimed at developing an advanced computer-simulation approach, based on stochastic and analytical modelling algorithms, for the simulation and analysis of the actin filament formation and its effect on small-bodies (beads, bacteria) motility in terms of forces and velocities.

Our approach combined stochastic simulations of the biochemical reactions, mechanical filament-filament interactions and force-filed constrains. The biochemical reactions were simulated using the modified Gillespie's method with the discrete time introduced. The mechanical model, including filament-filament and filament-bead (or bacteria) interactions, viscous friction and Brownian effects were realized to simulate the forces in the considered systems. The simulation models and computation algorithms were developed as the C++ classes and integrated in the standalone executable software package.

We developed a simulation model of a simplified biochemical network that reproduced an actin-polymerization process in a limited volume of a cell. The model generated 8 first-order chemical reactions, linked with a 3D spatial model of the system, including filaments and other solid bodies (beads or bacteria). The homogeneity of the concentrations in the volume was validated via Monte Carlo simulation of diffusion. The preliminary results of our simulations, in particular some selected biochemical parameters, like the rate of actin-polymerization and the actin-monomer diffusion constant, are in good agreement with those published elsewhere and with the results of FRAP experiments carried out in our lab on some selected actin-polymerization systems.

References:

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[2] Paluch, E., Piel, M., Prost, J., Bornens, M. and Sykes, C., Biophys J (2005) 89, 724-33.
[3] Alberts J. B. and Odell, G. M., PLoS Biol (2004) 2, p. e412.