

Mathematical modelling for bidirectional motor-mediated motility in a fungal
model system

Submitted by Congping Lin to the University of Exeter
as a thesis for the degree of
Doctor of Philosophy
in July 2012

This thesis is available for library use on the understanding that it is copyright
material and that no quotation from the thesis may be published without proper
acknowledgement.

I certify that all material in this thesis which is not my own work has been
identified and that no material has previously been submitted and approved for
the award of a degree by this or any other University.

Signature:

This page is intentionally left blank.

Abstract

In *Ustilago maydis* hyphae, bidirectional transport of early endosomes (EEs) occurs on microtubules (MTs) that have plus and minus ends. The transport is powered by kinesin-3 towards the plus ends of MTs and dynein towards the minus ends. Experiments show an accumulation of dynein at the MT plus end.

To investigate the mechanism of this accumulation, I consider two extended asymmetric simple exclusion principle (ASEP) models for the bidirectional transport of dynein in this thesis. In the simpler two-lane model, collision between opposite-directed motors is excluded whereas the more sophisticated 13-lane model takes into account that the MT usually consists of thirteen protofilaments. The presence of multi protofilaments allows dynein to avoid collision with kinesin by changing protofilaments, a behaviour that has been experimentally described. Both models are supplied by quantitative data obtained in *U. maydis* by live cell imaging and suggest that the stochastic behaviour of dynein can account for half of dynein motors in the accumulation at the MT plus end. Moreover, for the two-lane model, by using a mean field approximation, I give an analytical approximation for the accumulation size which shows linear dependence on the flux. In contrast, this dependence is nonlinear in the 13-lane model and appears to be associated with a phase transition leading to a “pulsing state”.

Accompanied experimental studies have shown that *U. maydis* contains a complex MT array and that kinesin-3 moves early endosomes along antipolar MT bundles. In order to better understand the bidirectional EE motility, I extend the two-lane ASEP to model bidirectional transport along an antipolar MT bundle. In this model, the MTs are coupled at minus ends where organelles can switch MTs on which they move. By a mean-field approximation and numerical simulations, I investigate how the switching affects phases of density profiles as well as the type of motor that dominates the active transport in the bundle.

Contents

Contents	4
List of Figures	7
List of Tables	9
Acknowledgement	11
Nomenclature	11
1 Biological background	12
1.1 Bidirectional transport	12
1.1.1 Microtubules	13
1.1.2 Molecular motors	13
1.1.3 Mechanisms of bidirectional transport	15
1.2 Endosome motility in the fungal model system - <i>Ustilago maydis</i> . . .	17
1.3 Summary of biological background	20
1.4 Thesis overview	20
2 Stochastic lattice models for intracellular transport	23
2.1 Asymmetric simple exclusion process	24
2.1.1 Model definition	25
2.1.2 Properties of ASEP in steady state	26
2.2 Generalizations of ASEP	27
2.3 Numerical methods	31
3 Queueing induced by bidirectional motor motion near the end of a microtubule	34
3.1 Modelling bidirectional motor motion	35
3.1.1 Assumptions for the model	35
3.1.2 A discrete model for motor motion	37
3.2 Mean field analysis of equilibrium states	38
3.2.1 Asymptotic form of the shock solution	40

3.3	Quantitative estimates for queue size	42
3.3.1	Tip size from simulations	44
3.4	Queueing models at the tip	46
3.4.1	Queueing at the tip as an $M/M/\infty$ -process	46
3.4.2	Other queueing models at the tip	48
3.5	Discussion	48
4	Bidirectional transport and pulsing states in a multi-lane ASEP model	50
4.1	Introduction	50
4.2	A multi-lane model for bidirectional transport	52
4.2.1	A simple two-lane model	55
4.2.2	A homogeneous thirteen-lane model	56
4.3	Influence of collisions and lane-changes on transport properties	57
4.3.1	Mean field approximation and cross-lane diffusion	57
4.3.2	A phase transition in the tip accumulation	60
4.3.3	Influence of lane-changes on the tip accumulation	61
4.3.4	Measures of bidirectional transport efficiency	63
4.4	Critical behaviour and pulsing states	67
4.4.1	Pulsing states in the system	68
4.4.2	System size effects	69
4.4.3	A simple model with a critical injection rate	72
4.5	Discussion	74
5	A model for motor-mediated bidirectional transport on an antipolar microtubule bundle	76
5.1	Introduction	76
5.2	A lattice model with antipolar bundling	78
5.3	Spatial distribution of particles and mean-field analysis	82
5.3.1	Spatial distribution in the unipolar section	84
5.3.2	Spatial distribution along the entire bundle	85
5.4	Dominance of particles in the transport	92
5.4.1	Dominance in occupancy	92
5.4.2	Dominance in current	94
5.5	Discussions	96
6	Conclusion and outlook	98
6.1	Conclusions	98
6.2	Future studies	100
6.2.1	Outlook for organelle transport in <i>Ustilago maydis</i>	100

6.2.2 Outlook for modelling intracellular transport	101
A Appendix: a stochastic mechanism in the formation of dynein accumulation	103
B Appendix: mean field approximation for the multi-lane model	134
C Appendix: an example of program codes	137
References	150