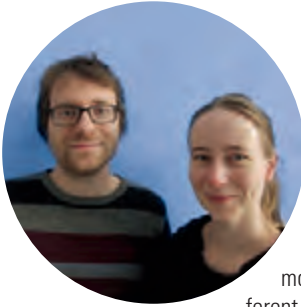# Cargo Transport by Teams of Molecular Motors: Elastic Coupling and Interference Regimes

Florian Berger 06.11.1981
2008: Diploma, Physics,
(University of Stuttgart)
Thesis: Optimization in Driven Systems
2012: PhD, Physics, (MPI of Colloids and
Interfaces, Potsdam) Thesis: Different
Modes of Cooperative Transport by
Molecular Motors
Since 2012: Postdoc
(MPI of Colloids and Interfaces,
Potsdam)

Corina Keller 27.10.1977
2009: Diploma, Physics,
(Humboldt University Berlin)
Thesis: Coupled Molecular Motors
2013: PhD, Physics, (MPI of Colloids and
Interfaces, Potsdam) Thesis: Coupled
Molecular Motors: Network Representa-
tion and Dynamics of Kinesin Motor Pairs
Since 2013: Postdoc
(MPI of Colloids and Interfaces,
Potsdam)

Active transport by molecular motors is ubiqui-
tous in all eukaryotic cells. These motor pro-
teins convert chemical energy into mechani-
cal work which enables them to transport
cargoes such as RNAs, protein complexes or
organelles. Such intracellular transport is often
driven cooperatively by several molecular
motors, which may belong to the same or to dif-
ferent motor species like kinesin, dynein or myosin.
These motors step stochastically along filaments, from which
they unbind after a finite run length. Understanding how these
motors interact and how their movements are coordinated
and regulated is a central and challenging problem of cellular
transport [1]. To establish a general theoretical framework for
elucidating and analysing such transport processes, we re-
cently introduced two complementary approaches: (i) a detail-
ed enzymatic chemo-mechanical description that starts from
the nucleotide states of the single motors [2] and (ii) a coarse-
grained description considering the single motor as a stochas-
tic stepper [3,4]. Such theoretical approaches integrate the
well-established properties of individual motors into a predic-
tive theory for cooperative transport.

Network Representation of Motor Pairs

Cargo transport by two coupled molecular motors is studied
using a chemomechanical network for the complete transport
system and analyzing the trajectories generated by this net-
work. The theoretical description starts from the different
nucleotide states of a single motor supplemented by chemi-
cal and mechanical transitions between these states. As an
instructive example, we focus on kinesin-1, for which a
detailed chemomechanical network has been developed pre-
viously [5]. The motor pair system considered here consists of
two kinesin motors, a leading and a trailing motor, which are
attached to the same cargo and walk on the same filament.
Each motor can unbind from and rebind to the filament indi-
vidually. As a consequence, the cargo is actively pulled by
either one or two motors. A mechanical step of one of the
motors during a 2-motor run leads to an elastic interaction
force between the two motors described by the extension of
a linear spring. The state space of the elastically coupled
motor pair is characterized by three variables, the chemical
states i_{le} and i_{tr} of the leading and trailing motor and of the
extension ΔL of the motor-motor separation [2]. The resulting
network has a layer structure as shown in **Fig. 1**, where each
layer corresponds to a constant value of ΔL. Any 1-motor run
occurs on one of the boundary lines of the network and may
be terminated either by unbinding of the active motor which

leads to the unbound motor pair state, or by the rebinding of
the inactive motor and a subsequent 2-motor run. Mechani-
cal steps during 2-motor runs lead to transitions between
neighbouring ΔL-layers. Even though this motor pair network
has a complex structure, it involves, apart from the single
motor parameters, only two additional parameters, the cou-
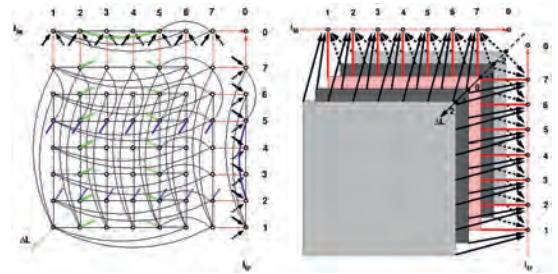pling parameter K and the single motor rebinding rate π_{si}.

Fig. 1: State space of a motor pair described by the individual motor
states i_{le} and i_{tr} and the extension ΔL of the motor-motor separation.
(left) Detailed description of the layer with $\Delta L=0$ and (right) stack of
five ΔL-layers.

Activity States and Motor Pair Parameters

In stochastic simulations, we studied the trajectories gener-
ated from the chemomechanical network of the motor pair as
a function of the single motor rebinding rate π_{si} and the elas-
tic coupling parameter K [2]. In experimental studies, the val-
ues of these two parameters are usually not known but have
to be determined in a consistent manner. Our theory shows
that one can determine these two parameters by measuring
the average run times during 1- and 2-motor runs of cargo
trajectories. Alternatively, individual motor trajectories and
the properties of the ΔL-distribution can be used to deduce
the two unknown parameters. Which activity state is domi-
nant during a motor pair walk also depends on these two
parameters. The corresponding activity diagram in **Fig. 2**
shows the crossover line which separates the parameter
regime, in which 1-motor runs dominate the cargo run, from
the regime, in which 2-motor runs are more likely. From indi-
vidual motor trajectories, one can deduce the distribution of
the extension ΔL of the motor-motor separation during 2-
motor runs as shown in **Fig. 2**. Within the studied range for
the coupling parameter, the number of accessible ΔL values
varies by one order of magnitude. The maximal values of ΔL
observed in the simulations determines the size of the net-
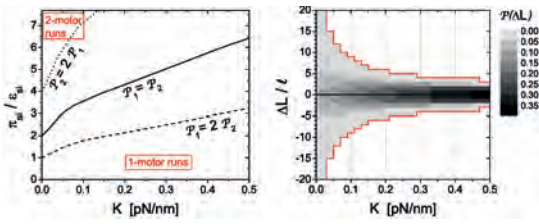work in **Fig. 1**.

Fig. 2: (left) Activity regimes of a motor pair as a function of elastic coupling parameter K and single motor rebinding rate π_{si}. (right) Probability distribution $P(\Delta L)$ for the extension ΔL of the motor-motor separation as a function of the coupling parameter K.

Distinct Transport Regimes for Elastically Coupled Motors

The case of cargo transport by two identical motors involves an elastic coupling between the motors that can reduce the motors' velocity and/or the binding time to the filament. We show that this elastic coupling leads, in general, to four distinct transport regimes characterized by the motor pair's average velocity v_2 and its average binding time t_2, during which the two motors remain simultaneously bound to the filament [3]. Both quantities depend on the single motor dynamics and on the strength K of their elastic coupling. Thus, strongly coupled and/or fast motors can quickly build up a large strain force that pulls one of the motors from the filament, while weakly coupled and/or slow motors may unbind spontaneously before reaching such a large force. The motor pair dynamics are governed by the interplay of three different forces: the stall force F_s, which corresponds to the maximal force that a single motor can generate, the detachment force F_d, which is the typical force that one motor can sustain for an extended period of time, and the scale F_K for the elastic strain forces between the two motors.

Using a continuous-time Markov process to describe the single motors as stochastic steppers, we calculate the average binding time t_2 and the velocity v_2 for two active motors and identify four different transport regimes, see **Fig. 3**. We estimate the crossover lines between these regimes from time scale arguments for the strain force generation which, in addition, allows us to obtain an intuitive understanding of the mutual motor-motor interference.

We apply our framework to predict the behavior of different pairs of molecular motors based on typical parameters from single motor experiments. In addition to a weak coupling regime, kinesin and dynein motors are found to exhibit a strong coupling and an enhanced unbinding regime, whereas myosin motors are predicted to attain a reduced velocity regime. All of these regimes can be explored experimentally by varying the elastic coupling parameter K. Our theory is consistent with the available experimental data for a kinesin-1 and myosin V.
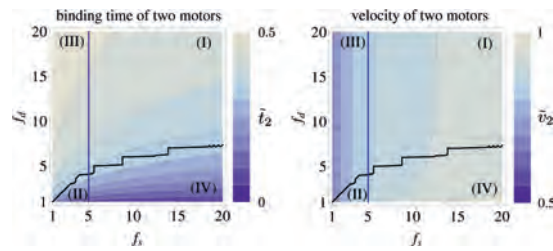

Fig. 3: (left) Average binding time and (right) velocity of a cargo pulled by two active motors in units of the single motor binding time and single motor velocity, respectively. Both quantities are displayed in a colored contour plot as functions of the rescaled single motor stall force $f_s=F_s/F_K$ and the rescaled detachment force $f_d=F_d/F_K$, where the force scale $F_K=K/2l$ is the elastic strain force between the motors per motor step with step size l. The solid blue line separates the region with and without a reduced velocity, whereas the solid black line separates the region of spontaneous and force-induced unbinding. These lines define four distinct transport regimes: (I) weak coupling with essentially unchanged velocity and binding time; (II) strong coupling with both reduced binding time and reduced velocity; (III) reduced velocity with no effect on the binding time and (IV) enhanced unbinding with no effect on the velocity.

F. Berger, C. Keller, S. Klumpp, R. Lipowsky
florian.berger@mpikg.mpg.de.
corina.keller@mpikg.mpg.de

References:
[1] Berger, F., Keller, C., Müller, M. J. I., Klumpp, S., Lipowsky, R., Co-operative transport molecular motors, Biochem. Soc. Trans., **39**, 1211-1215 (2011).
[2] Keller, C., Berger, F., Liepelt, S., Lipowsky, R., Network complexity and parametric simplicity for cargo transport by two molecular motors, J. Stat. Phys., **150**, 205-234 (2013).
[3] Berger, F., Keller, C., Klumpp, S., Lipowsky, R., Distinct transport regimes of two elastically coupled molecular motors, Phys. Rev. Lett., **108**, 208101 (2012).
[4] Berger, F., Keller, C., Lipowsky, R., Klumpp, S., Elastic coupling effects in cooperative transport by a pair of molecular motors, Cell. Mol. Bioeng., 6, 48-64 (2013).
[5] Liepelt, S., Lipowsky, R., Kinesin's network of chemomechanical motor cycles, Phys. Rev. Lett., **98**, 258102 (2007).