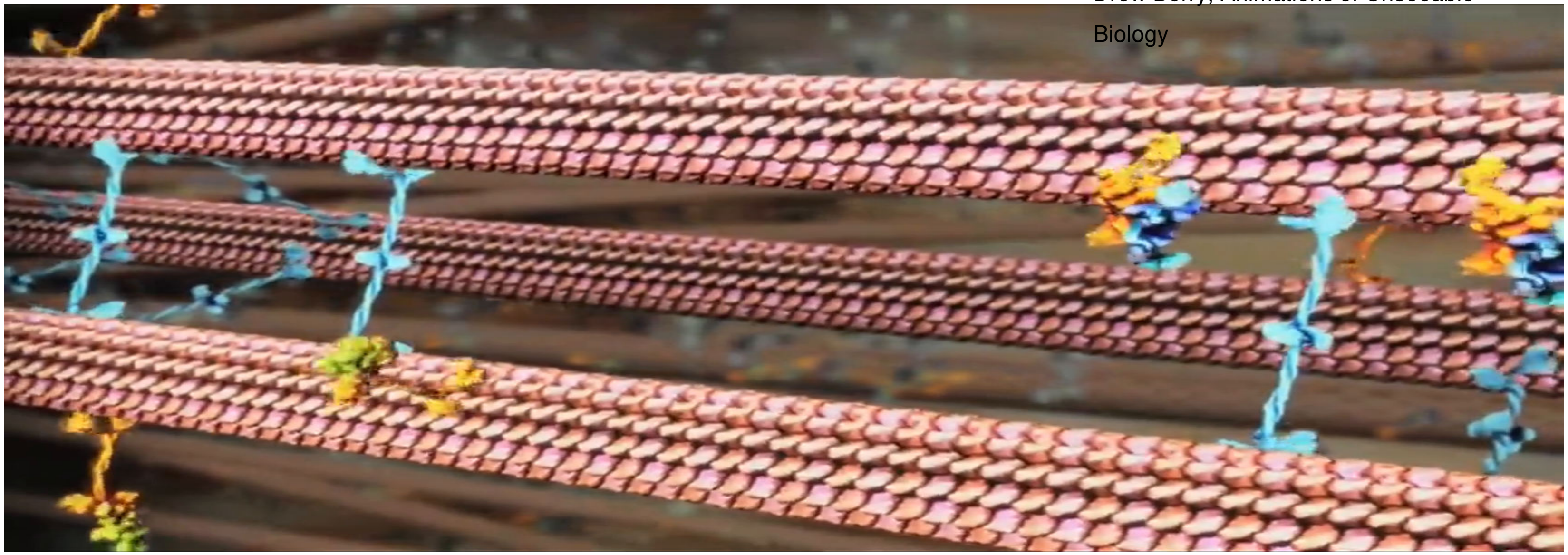
Drew Berry, Animations of Unseeable Biology



The Dynein Catch Bond

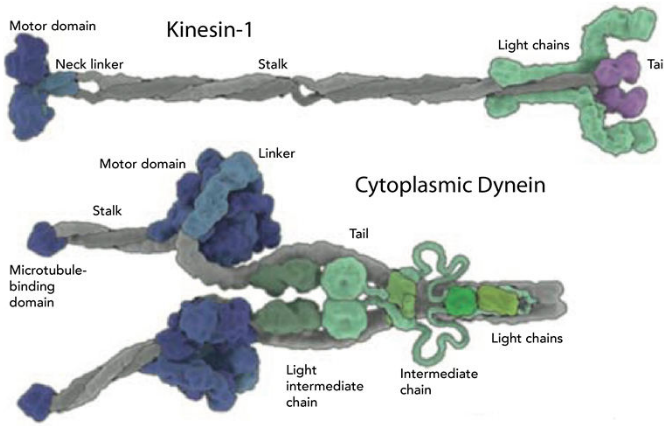
Implications for Cooperative Transport

Mithun Kumar Mitra

Department of physics IIT Bombay

Indian Statistical Physics Community Meeting 2017

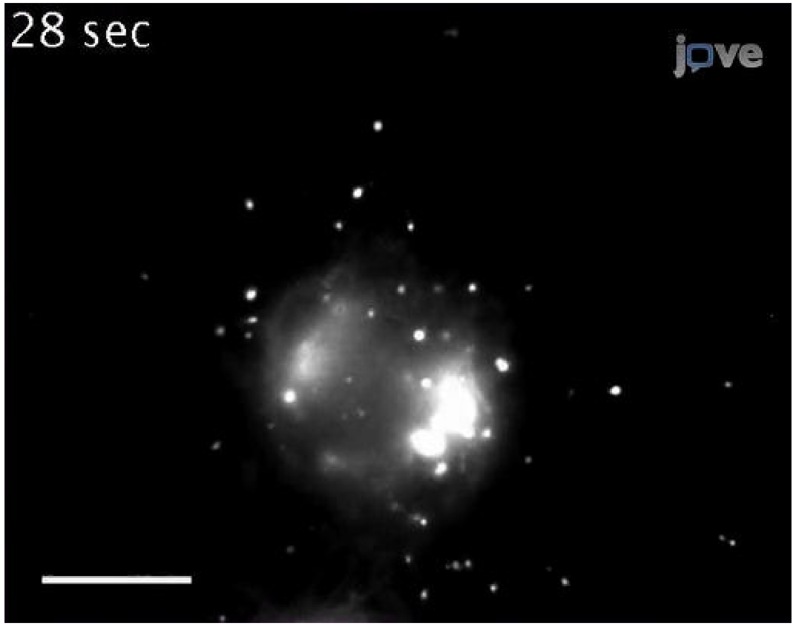
Catch Bond In Dynein



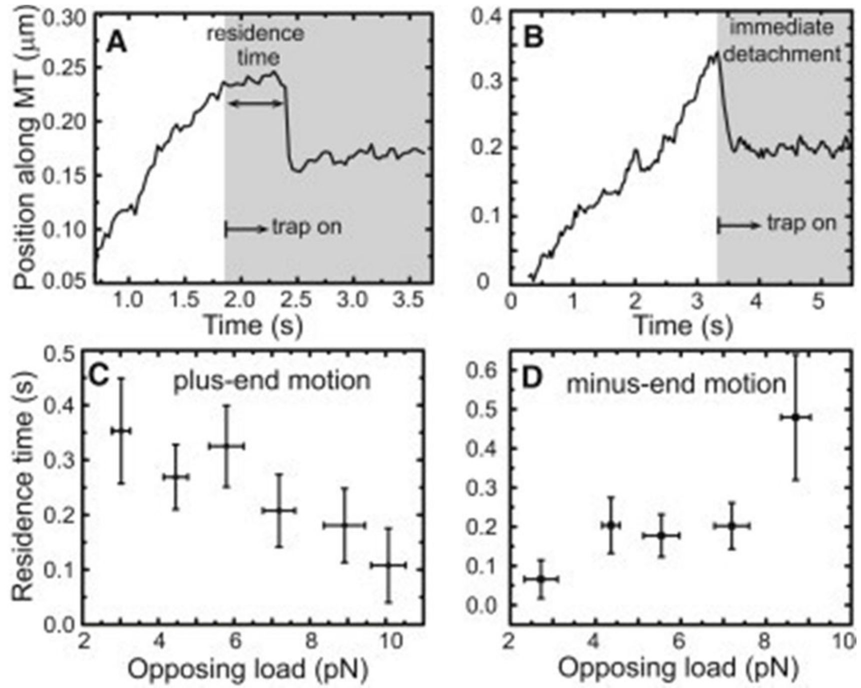
Carter J. Cell Sci. (2013)

Kinesin: Postive directed motors

Dynein: Negative directed motors



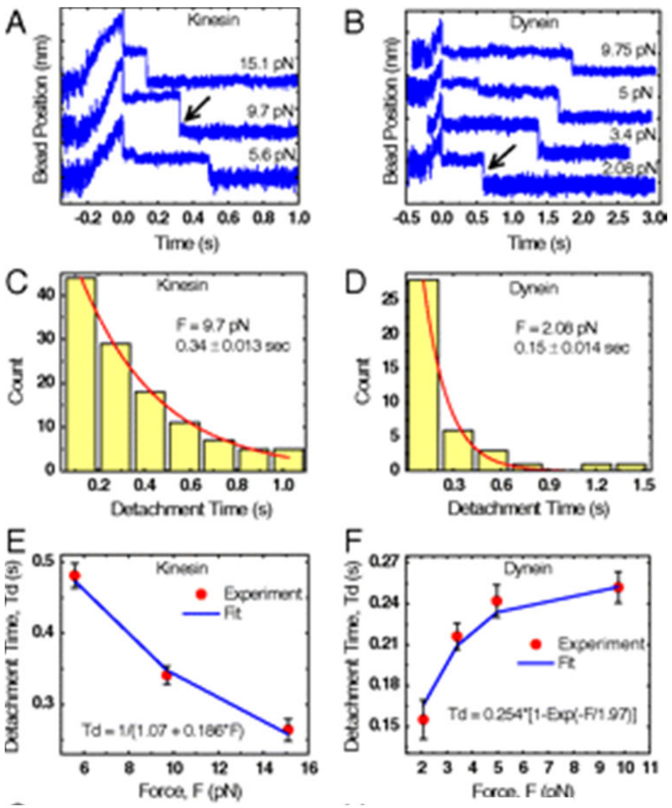
Lu et. al. J. Vis. Exp. 81, 50838 (2013)



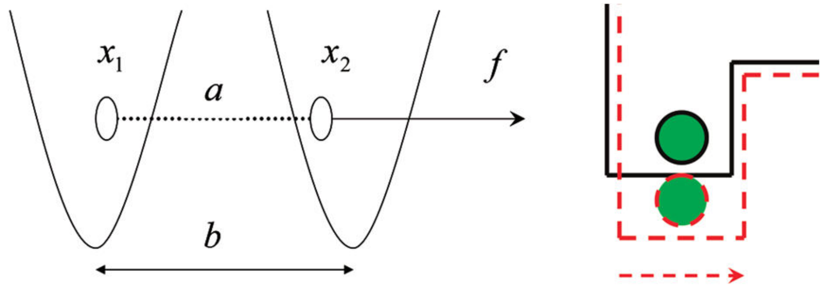
Leidel et. al. Biophys J. 2012

Rai et. al. Cell 2013

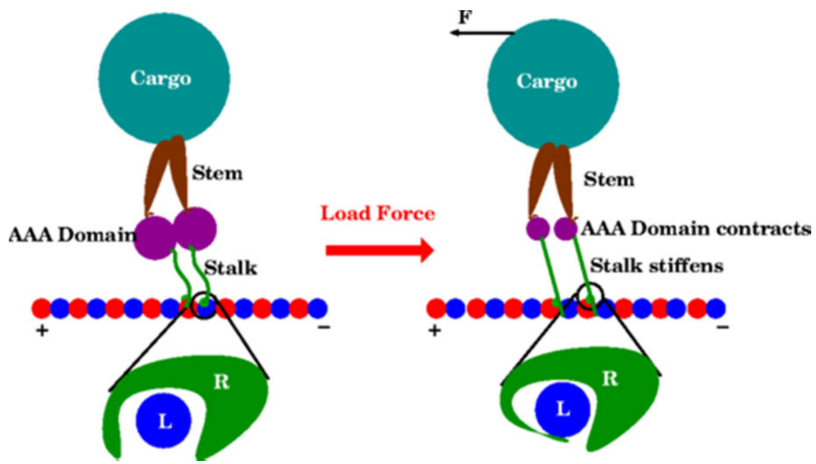
Single Dynein Unbinding Rate



Kunwar et. al. PNAS 2011



Prezhdo & Pereverzev, Acc. Chem. Res. 2008

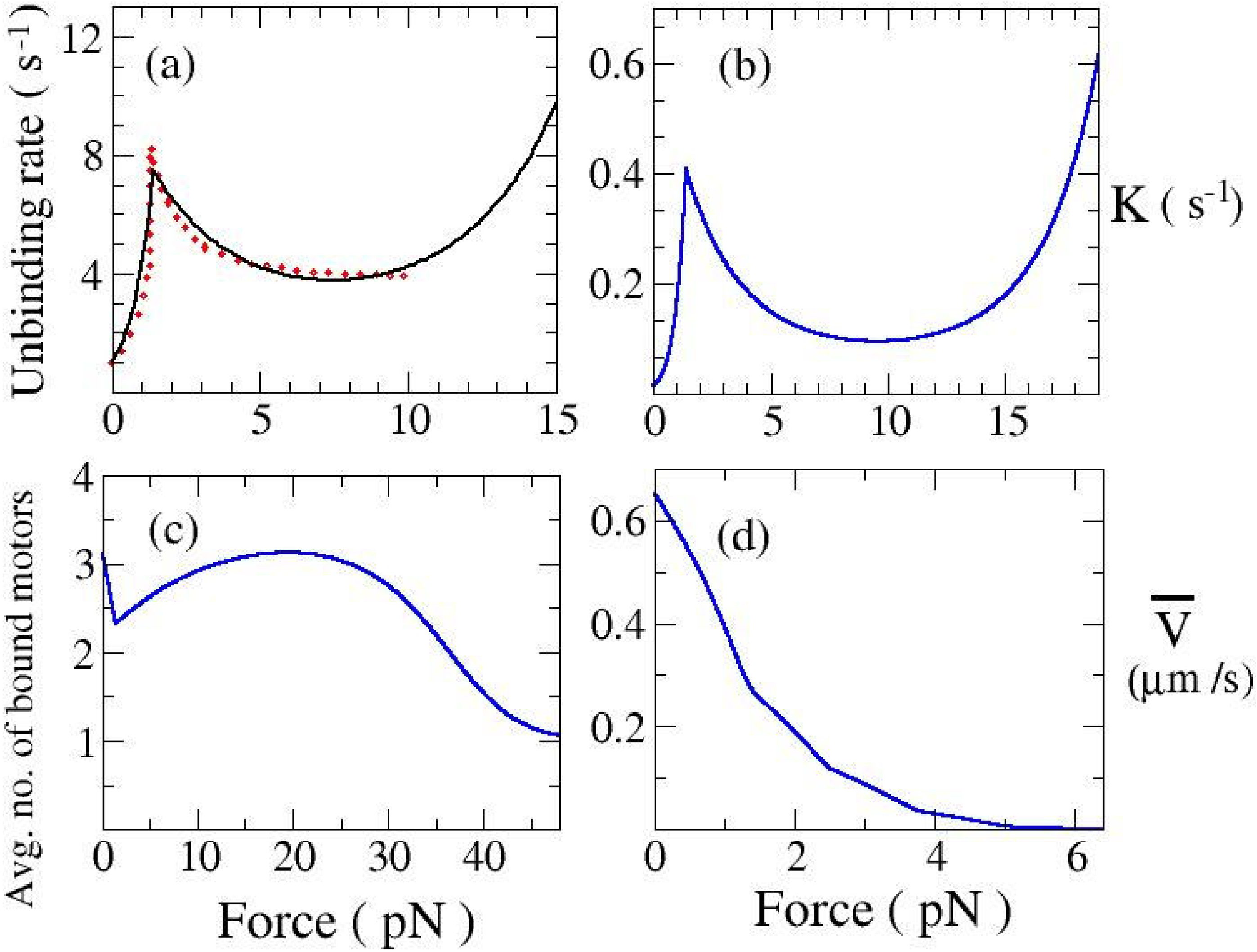


Nair et. al. PRE 2016

$$\epsilon(f)=\epsilon_0 \exp[-E_d(f)+f/f_d]$$

$$E_d(f)=\Theta(f-f_m)\alpha[1-\exp(-f/f_0)]$$

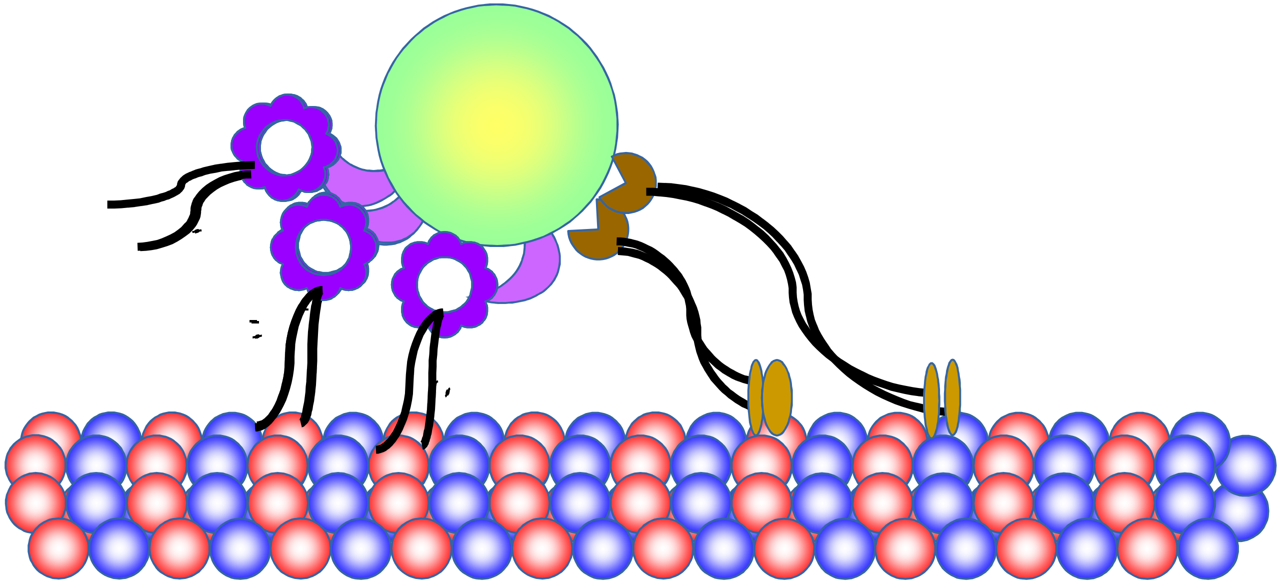
Comparison with experiments



$\alpha=68, f_0=40.7\,pN, f_m=1.4\,pN, f_s=1.25\,pN, \epsilon_0=1\,s^{-1}\ \ \pi_{ad}=1.6\,s^{-1}, v_0=0.65\,\mu m\,s^{-1}$

Bidirectional Transport

Mean Field: Equal load sharing between motors



$$\frac{\partial}{\partial t} p(n_+, n_-, t) = p(n_+ + 1, n_-, t)\,\varepsilon_+(n_+ + 1, n_-) + p(n_+, n_- + 1, t)\,\varepsilon_-(n_+, n_- + 1)$$

$$+\, p(n_+ - 1, n_-, t)\,\pi_+(n_+ - 1, n_-) + p(n_+, n_- - 1, t)\,\pi_-(n_+, n_- - 1)$$

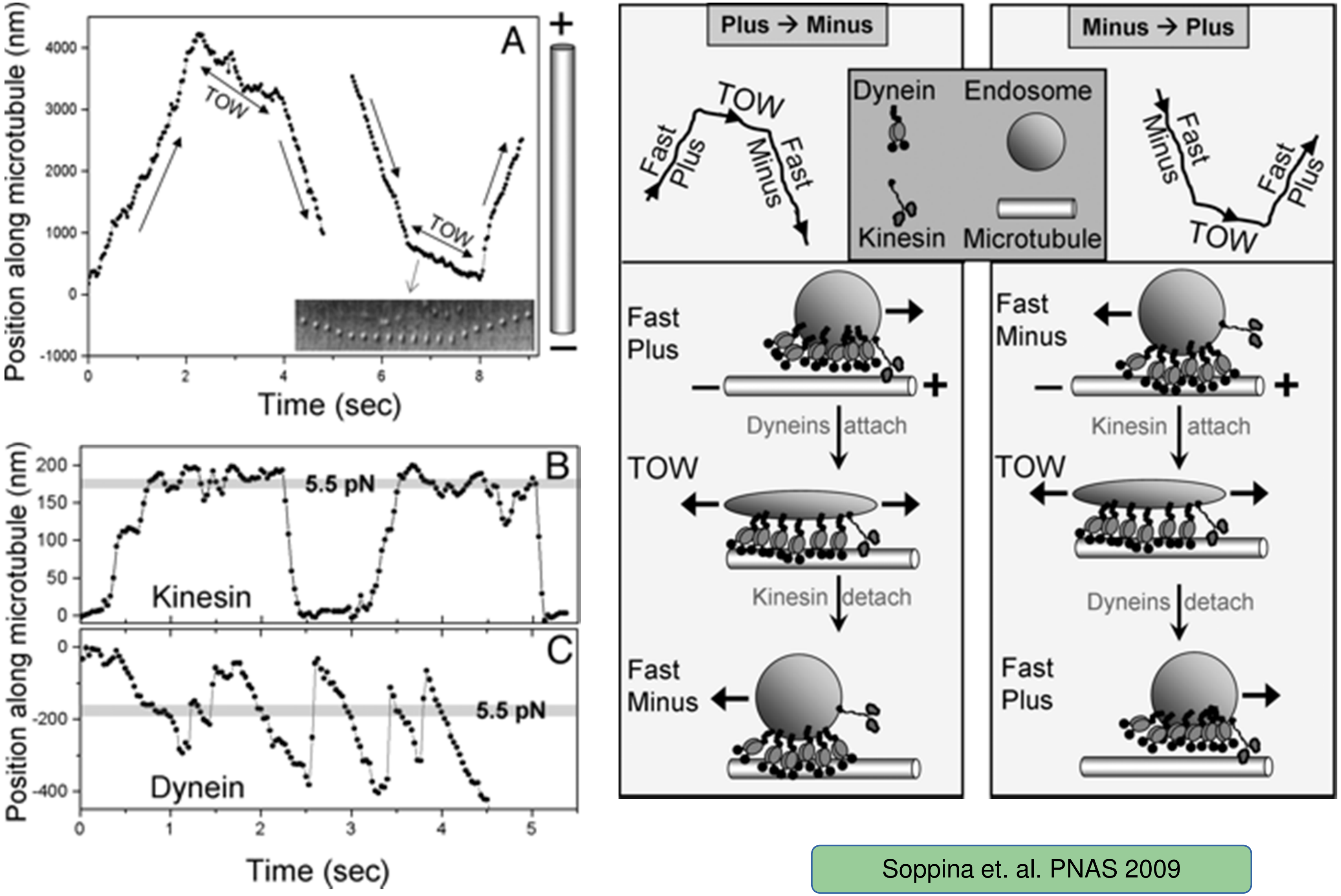
$$-\, p(n_+, n_-, t)\left[\pi_+(n_+, n_-) + \pi_-(n_+, n_-) + \varepsilon_+(n_+, n_-) + \varepsilon_-(n_+, n_-)\right]$$

Binding rate $\pi_n = (N - n)\pi_{ad}$

Velocity Model $v_n(F) = v_0(1 - F/n f_s)$

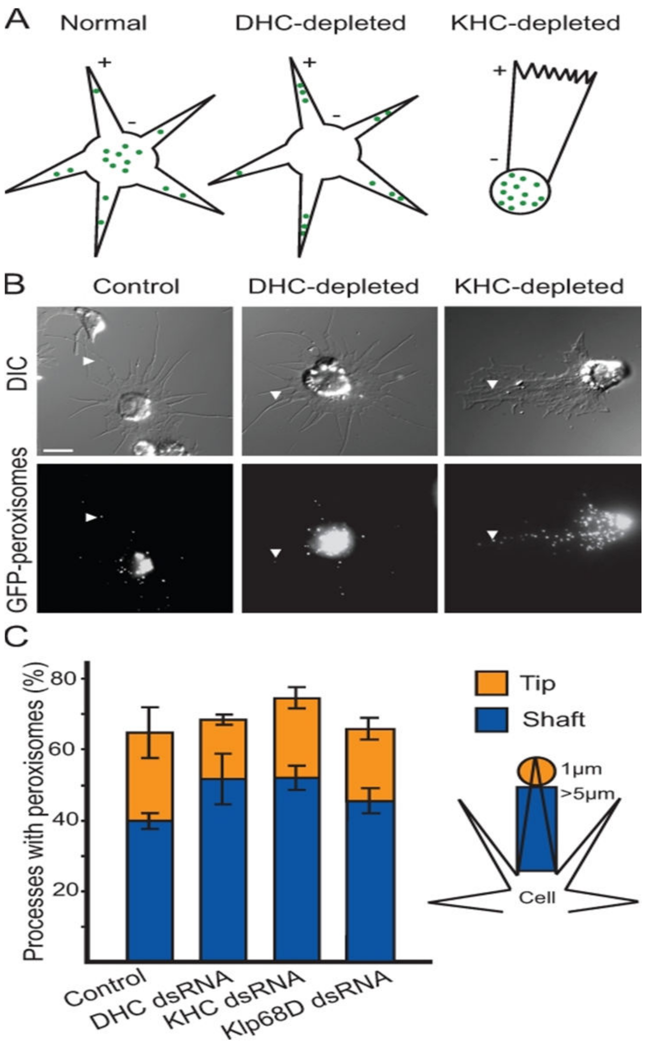
Muller et. al. PNAS 2005

Tug-of-war Hypothesis

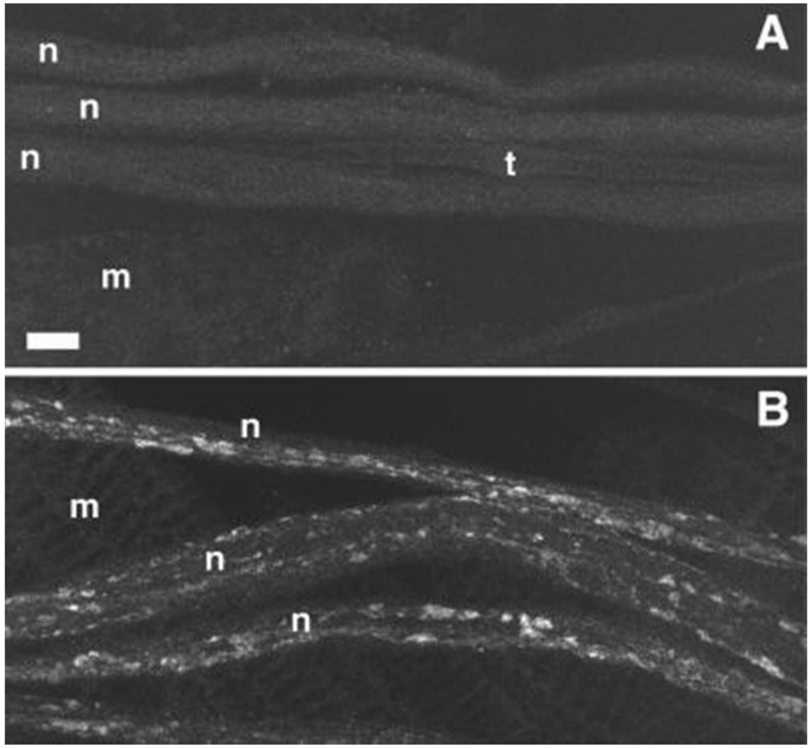


Soppina et. al. PNAS 2009

Paradox of co-dependence



Ally et. al. J. Cell Biol. 2009



Martin et. al. Mol. Biol. Cell 1999

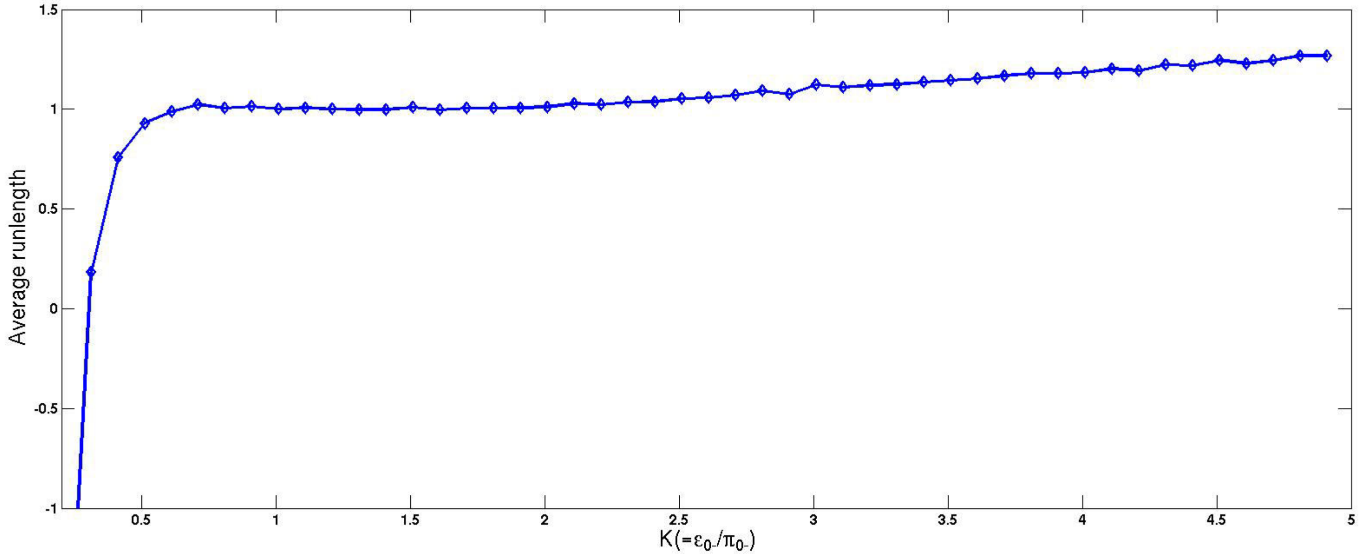
Processivity - I

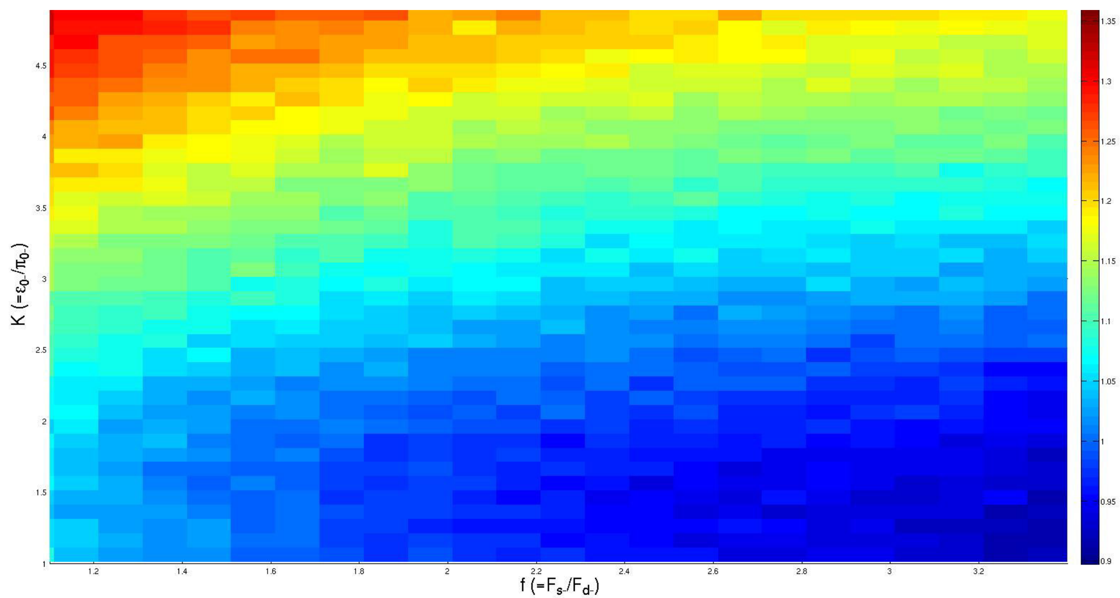
4 Kinesins
4 Dyneins

$F_{d+}=3.0\ pN$
$F_{s+}=6.0\ pN$
$\pi_{0+}=5\,s^{-1}$
$\epsilon_{0+}=5\,s^{-1}$
$v_{f+}=0.65\,\mu m\,s^{-1}$

$F_{d-}=0.67\ pN$
$\pi_{0-}=10\,s^{-1}$
$v_{f-}=0.65\,\mu m\,s^{-1}$
$\alpha=20\,k_B T$
$F_m=1.4\ pN$
$F_0=7.0\ pN$

$v_B=1\,nm/s$





Processivity - II

4 Kinesins
4 Dyneins

$F_{d+} = 3.0\, pN$

$F_{s+} = 6.0\, pN$

$\pi_{0+} = 5\, s^{-1}$

$\epsilon_{0+} = 5\, s^{-1}$

$v_{f+} = 0.65\, \mu m\, s^{-1}$

$F_{d-} = 0.67\, pN$

$\pi_{0-} = 1\, s^{-1}$

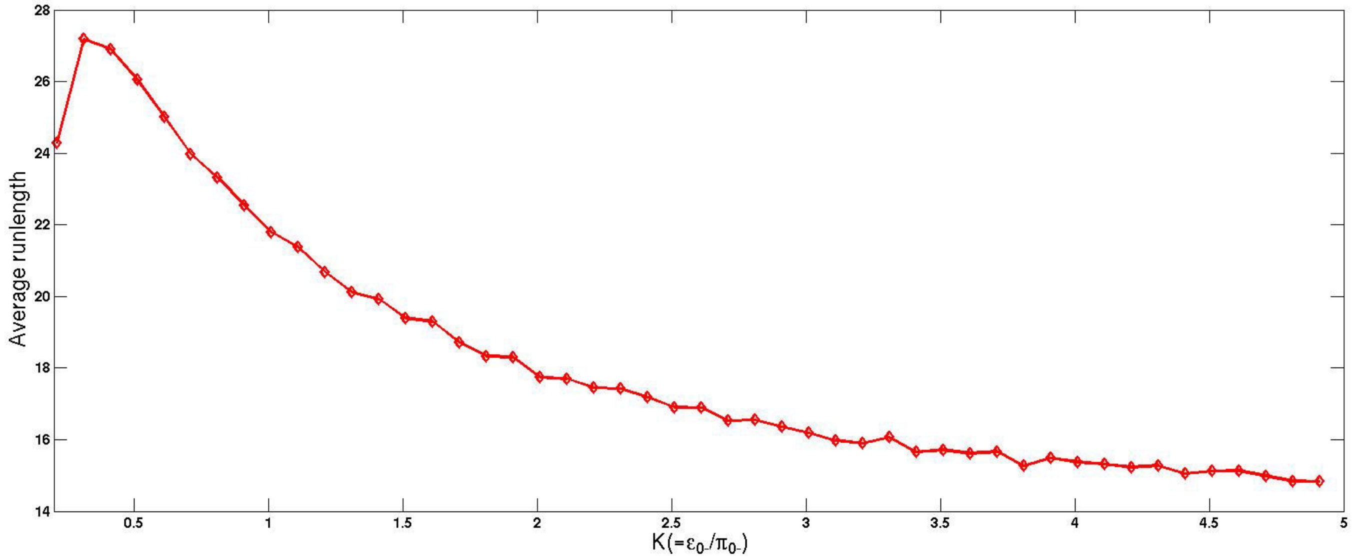
$v_{f-} = 0.65\, \mu m\, s^{-1}$

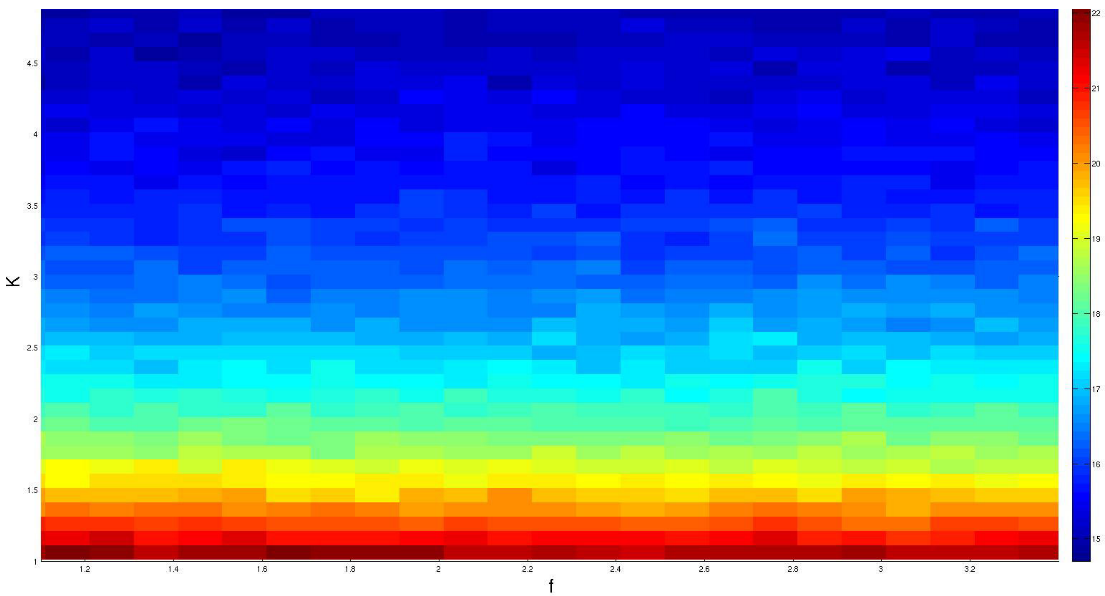
$\alpha = 20\, k_B T$

$F_m = 1.4\, pN$

$F_0 = 7.0\, pN$

$v_B = 1\, nm/s$





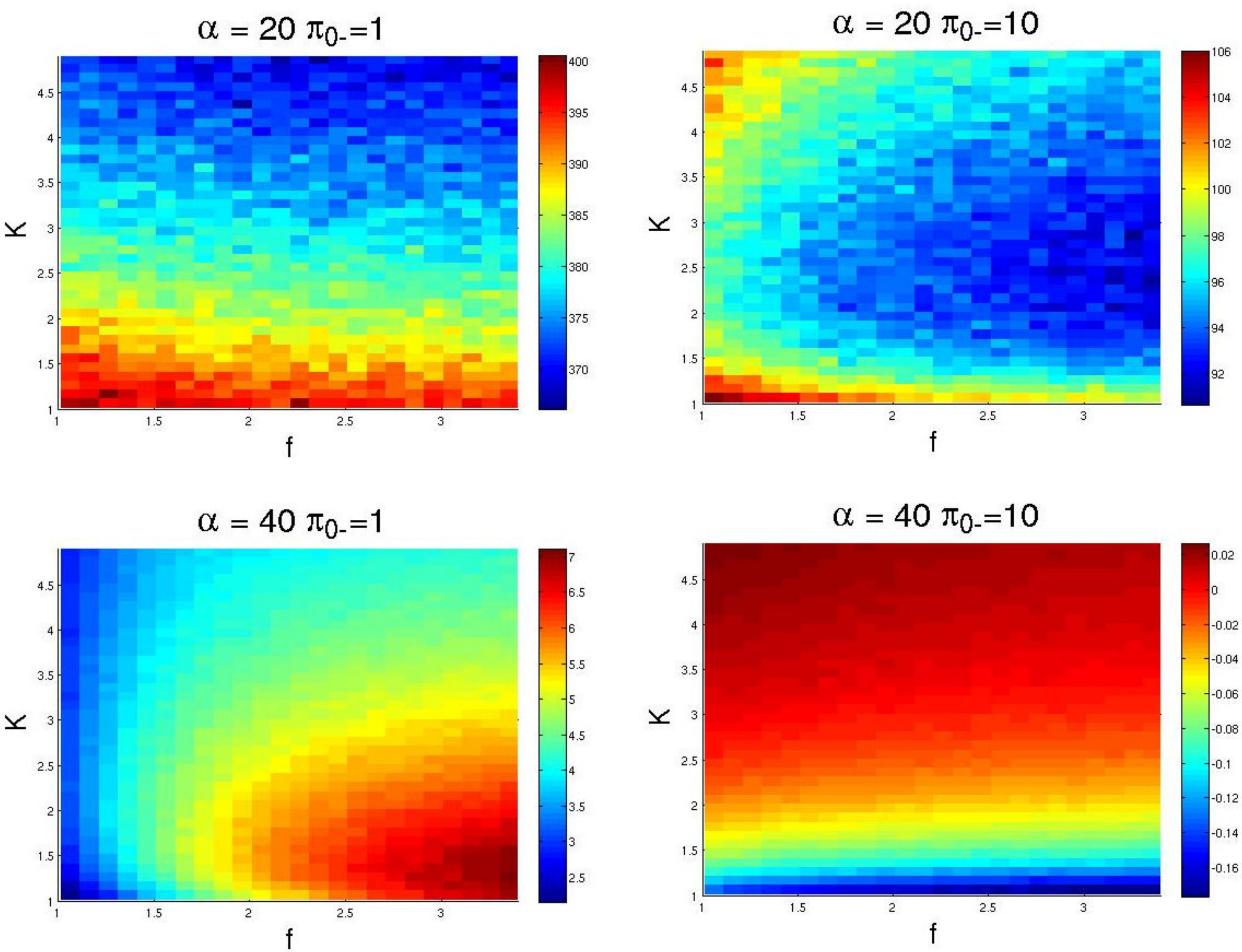
Processivity - Iii

6 Kinesins
2 Dyneins

$F_{d+}=3.0\,pN$
$F_{s+}=6.0\,pN$
$\pi_{0+}=5\,s^{-1}$
$\epsilon_{0+}=5\,s^{-1}$
$v_{f+}=0.65\,\mu m\,s^{-1}$

$F_{d-}=0.67\,pN$
$v_{f-}=0.65\,\mu m\,s^{-1}$
$F_m=1.4\,pN$
$F_0=7.0\,pN$

$v_B=1\,nm/s$



Processivity - IV

2 Kinesins
6 Dyneins

$F_{d+}=3.0\,pN$

$F_{s+}=6.0\,pN$

$\pi_{0+}=5\,s^{-1}$

$\epsilon_{0+}=5\,s^{-1}$

$v_{f+}=0.65\,\mu m\,s^{-1}$

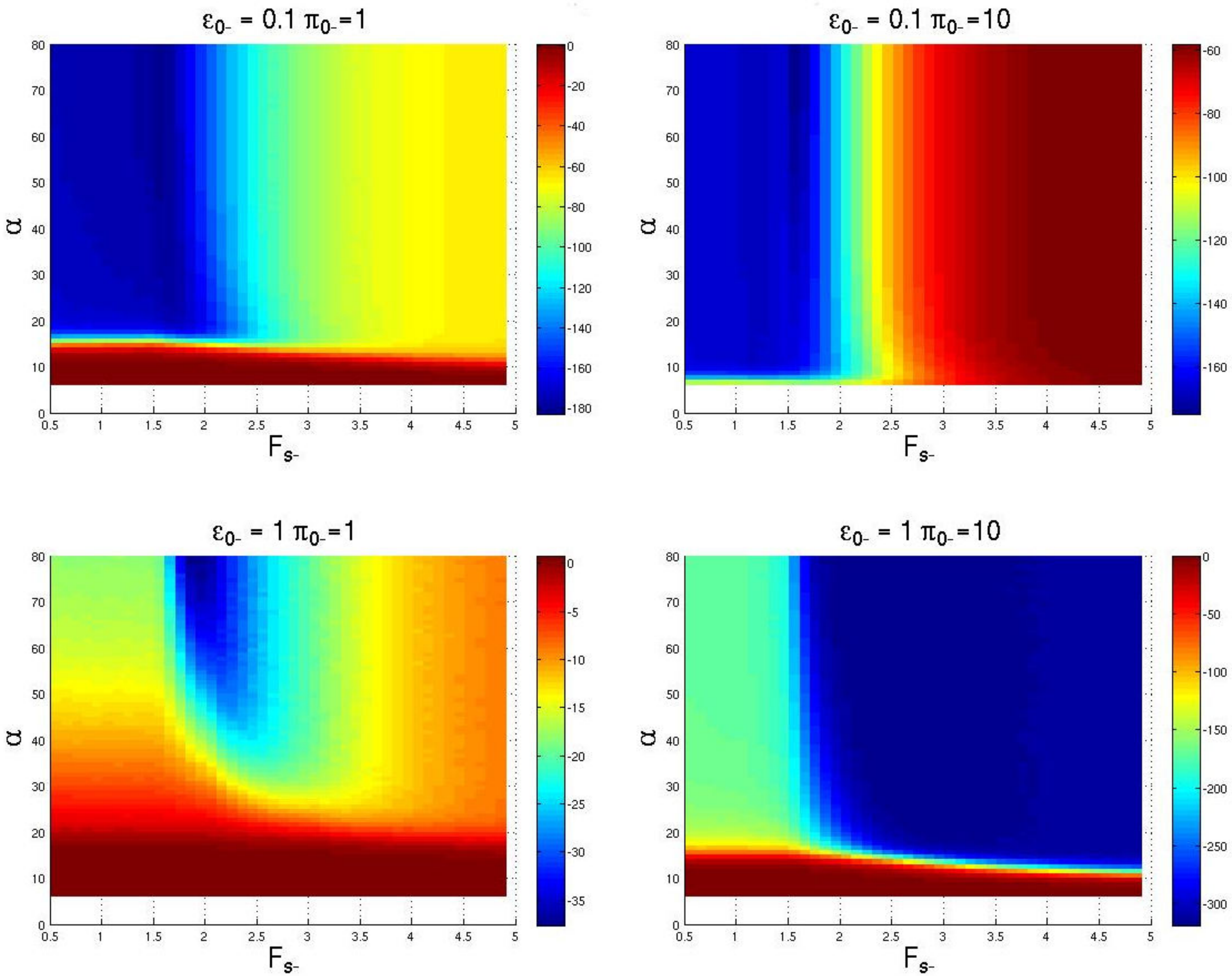
$F_{d-}=0.67\,pN$

$v_{f-}=0.65\,\mu m\,s^{-1}$

$F_{m}=1.4\,pN$

$F_{0}=7.0\,pN$

$v_{B}=1\,nm/s$



Conclusions

- Unidirectional transport by catch-bonded dynein motors shows non-monotonic velocity profiles with force
- Bidirectional transport by kinesin and catch-bonded dynein can exhibit both tug-of-war and co-dependent transport characteristics in appropriate regimes
- Pause times and switch times show interesting behaviour in the presence of a catch bond

Perspectives

- Stochastic load sharing of motors
- Incorporating the dynein chemo-mechanical cycle
- Incorporating multiple step-sizes in dynein

Collaborators

- Sudipto Muhuri, Pune University
- Abhishek Chaudhuri, IISER Mohali
- Sameep Chandel, IISER Mohali
- Anil Nair, Pune University
- Supriyo Naskar, IIT Bombay
- Palka Puri, IIT Bombay

Effect of catch bonding on transport of cellular cargo by dynein motors
Anil Nair et. al. PRE **94**, 032403 (2016)

Financial Support: IIT Bombay Seed Grant, Ramanujan Fellowship DST

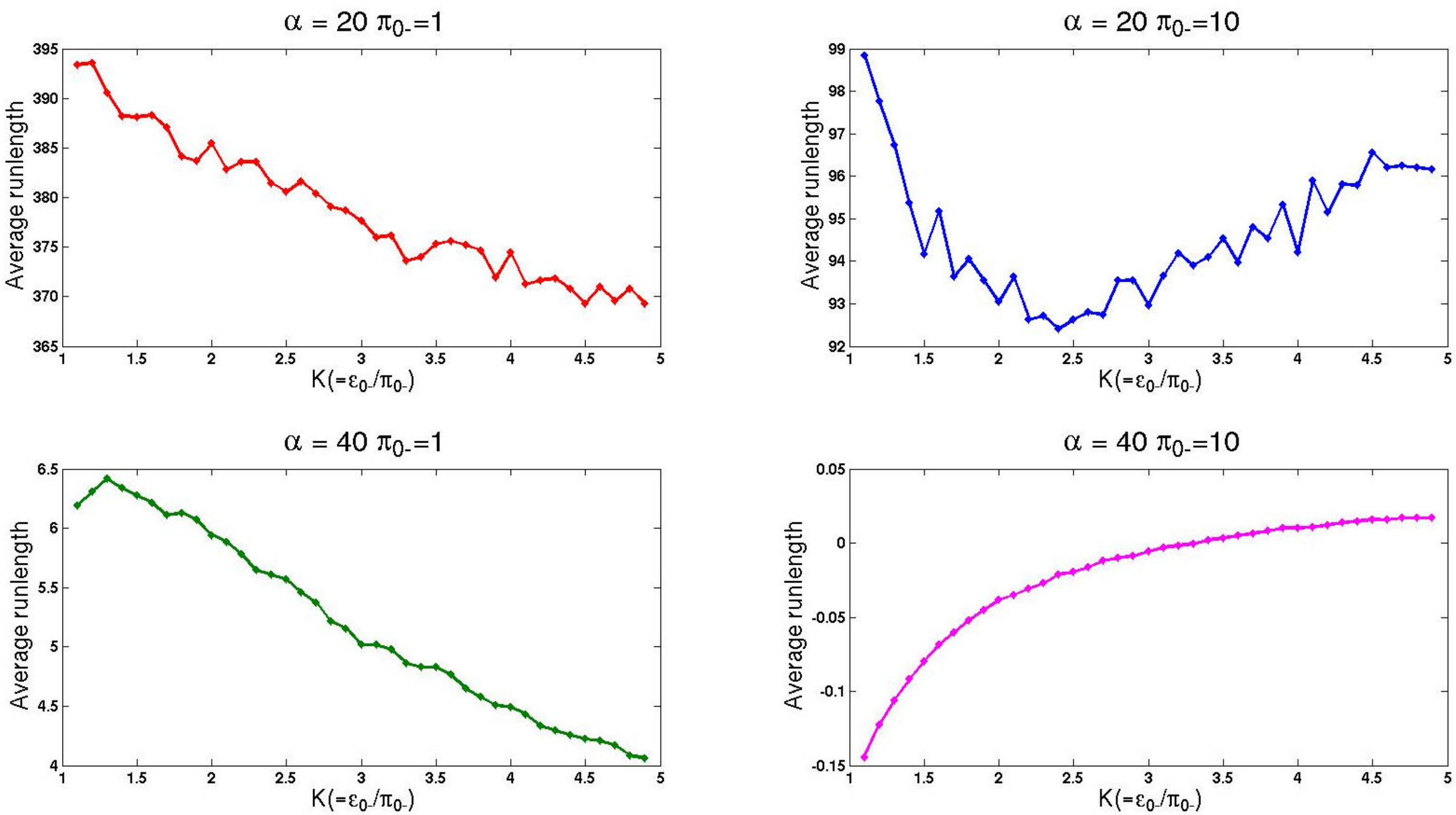
Processivity - IV

6 Kinesins
2 Dyneins

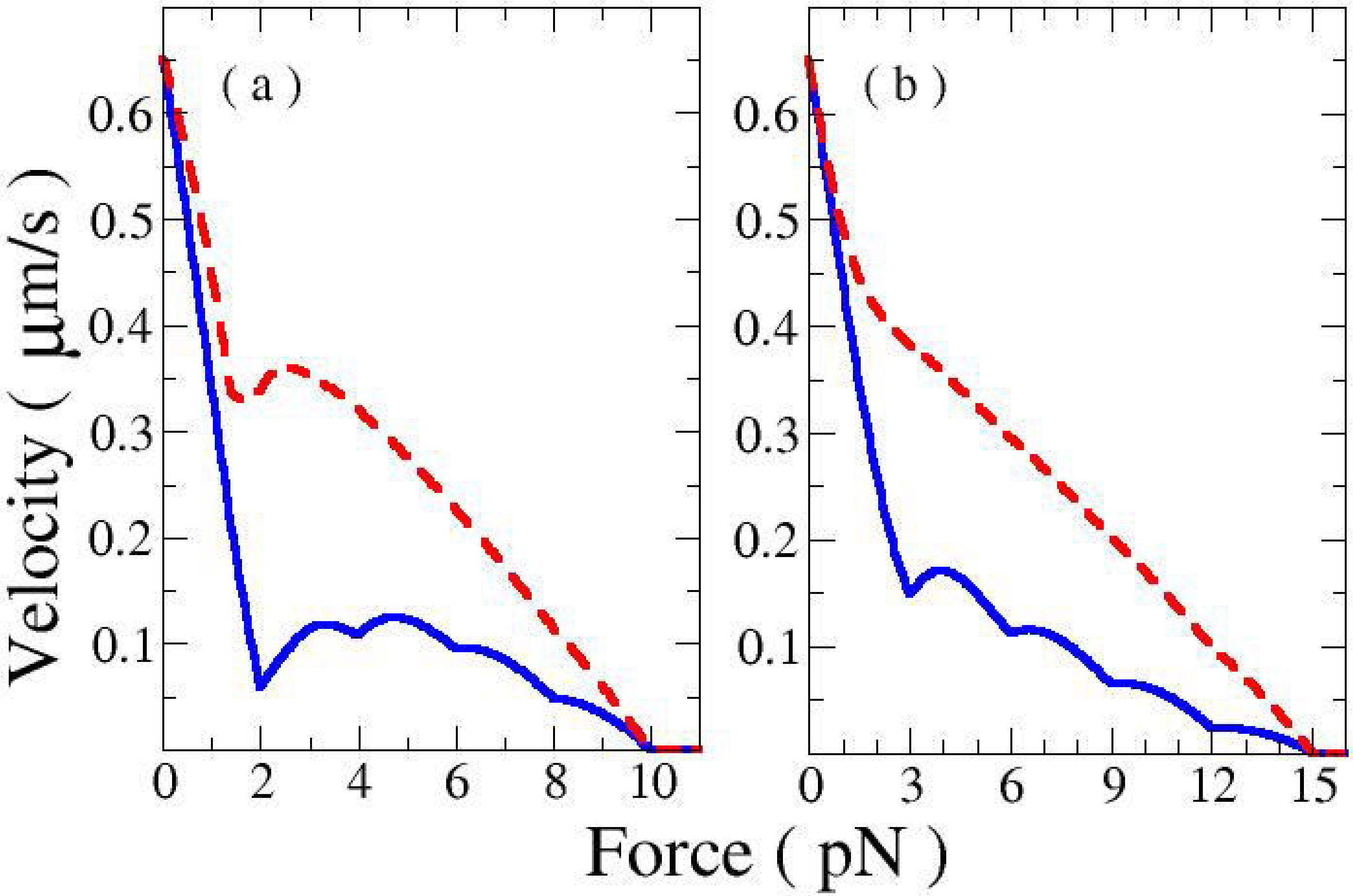
$F_{d+}=3.0\ pN$
$F_{s+}=6.0\ pN$
$\pi_{0+}=5\,s^{-1}$
$\epsilon_{0+}=5\,s^{-1}$
$v_{f+}=0.65\,\mu m\,s^{-1}$

$F_{d-}=0.67\ pN$
$v_{f-}=0.65\,\mu m\,s^{-1}$
$F_{s-}=1.675\ pN$
$F_m=1.4\ pN$
$F_0=7.0\ pN$

$v_B=1\,nm/s$



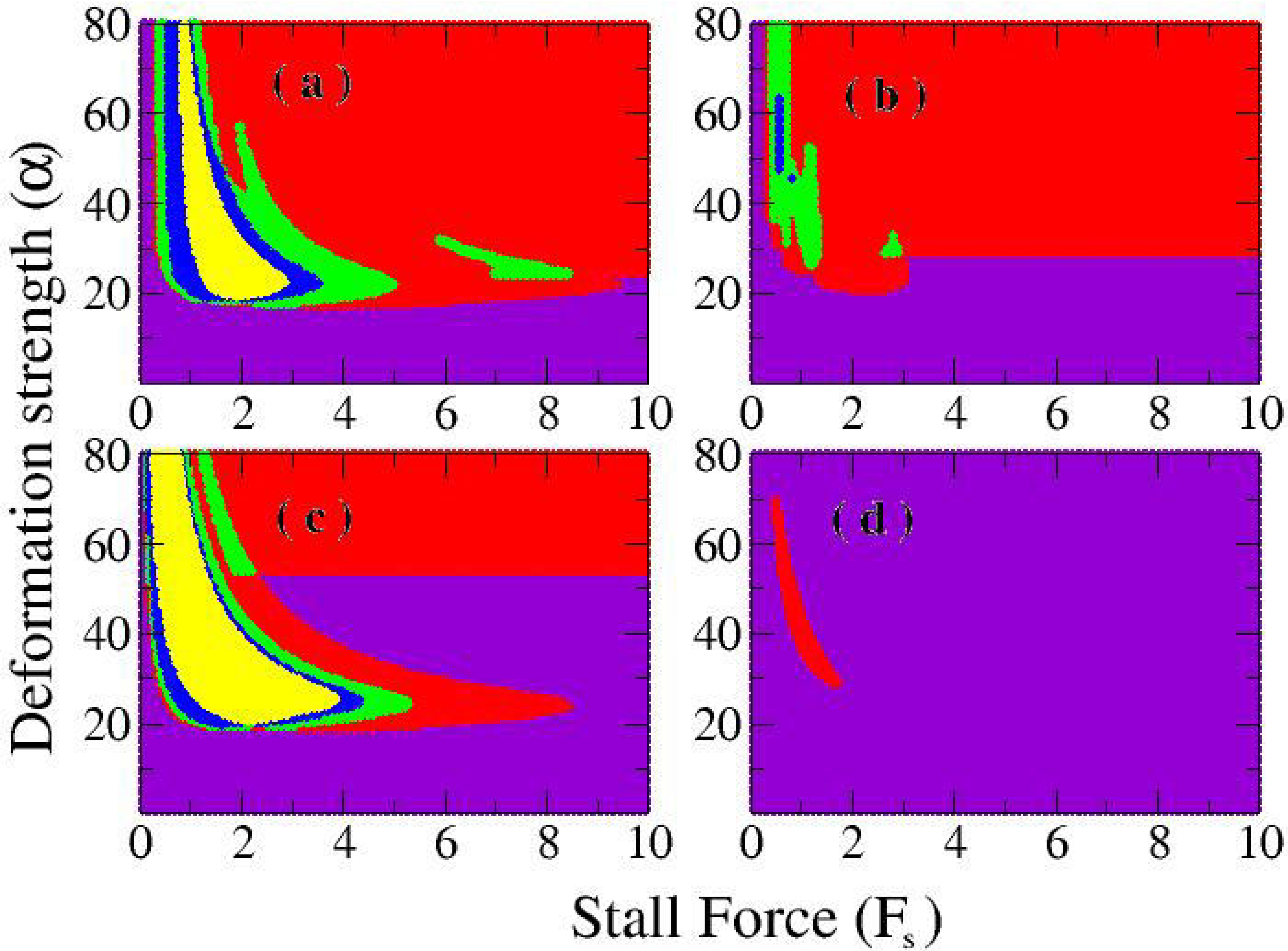
Velocity Profiles



$N=5, \alpha=35, f_0=7\ pN, f_m=1.4\ pN, f_s=2\ pN, f_d=0.67\ pN, \epsilon_0=1\ s^{-1}, v_0=0.65\ \mu m\ s^{-1}$

$\pi_{ad}=0.1/1.0\ s^{-1}$

Velocity diagram



$$N=5, f_0=7\,pN, f_m=1.4\,pN, f_d=0.67\,pN, \epsilon_0=1\,s^{-1}, v_0=0.65\,\mu m\,s^{-1}$$
$$\pi_{ad}=0.1/1.0\,s^{-1}$$