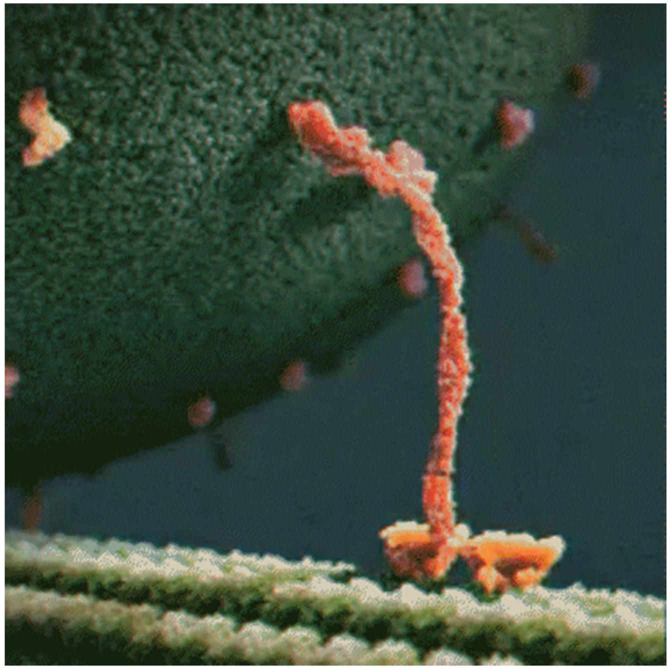
# The Dynein Catch Bond

## Implications for Cooperative Transport

**Mithun Kumar Mitra**
Department of physics IIT Bombay

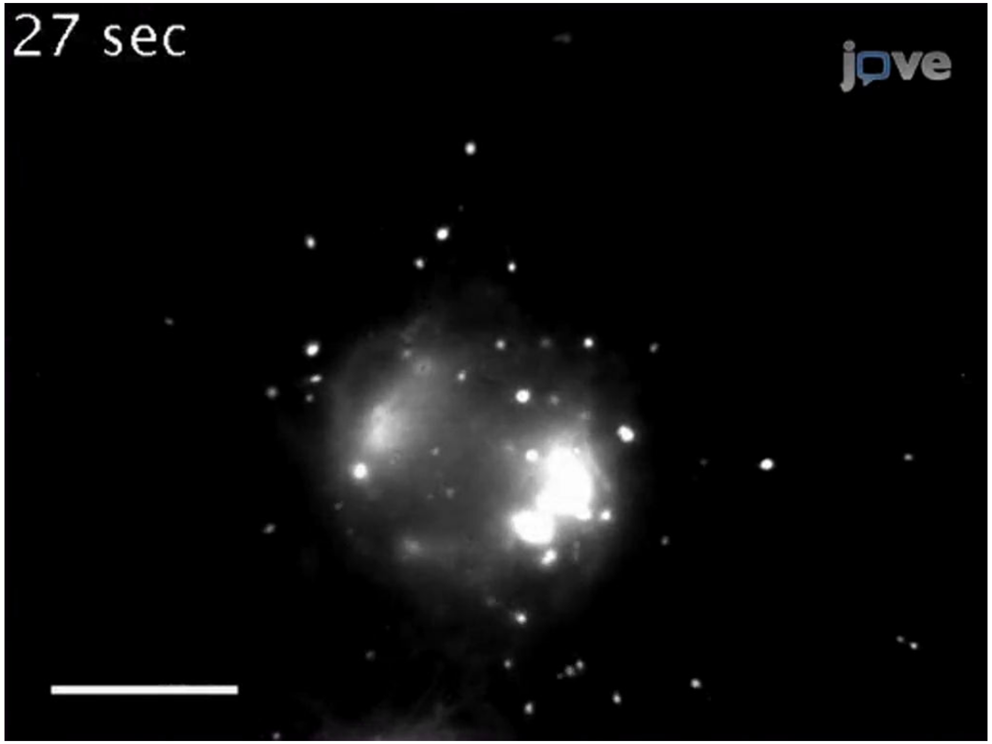
**Collective dynamics of FILAMENTS, 2017**

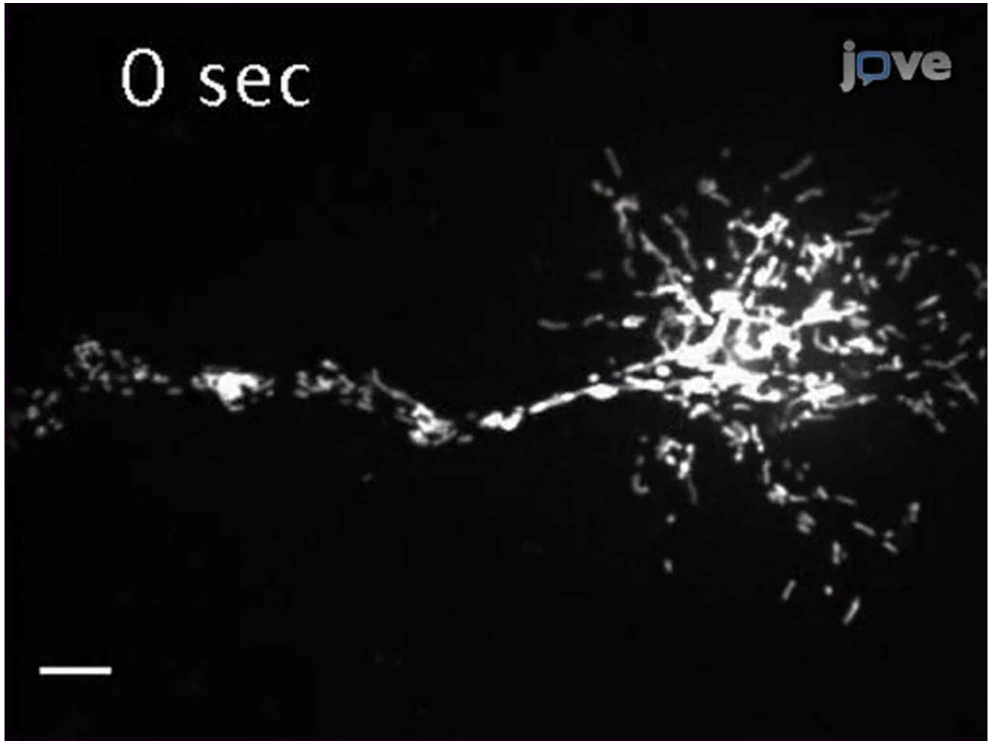


Kinesins walk towards the plus end of MT

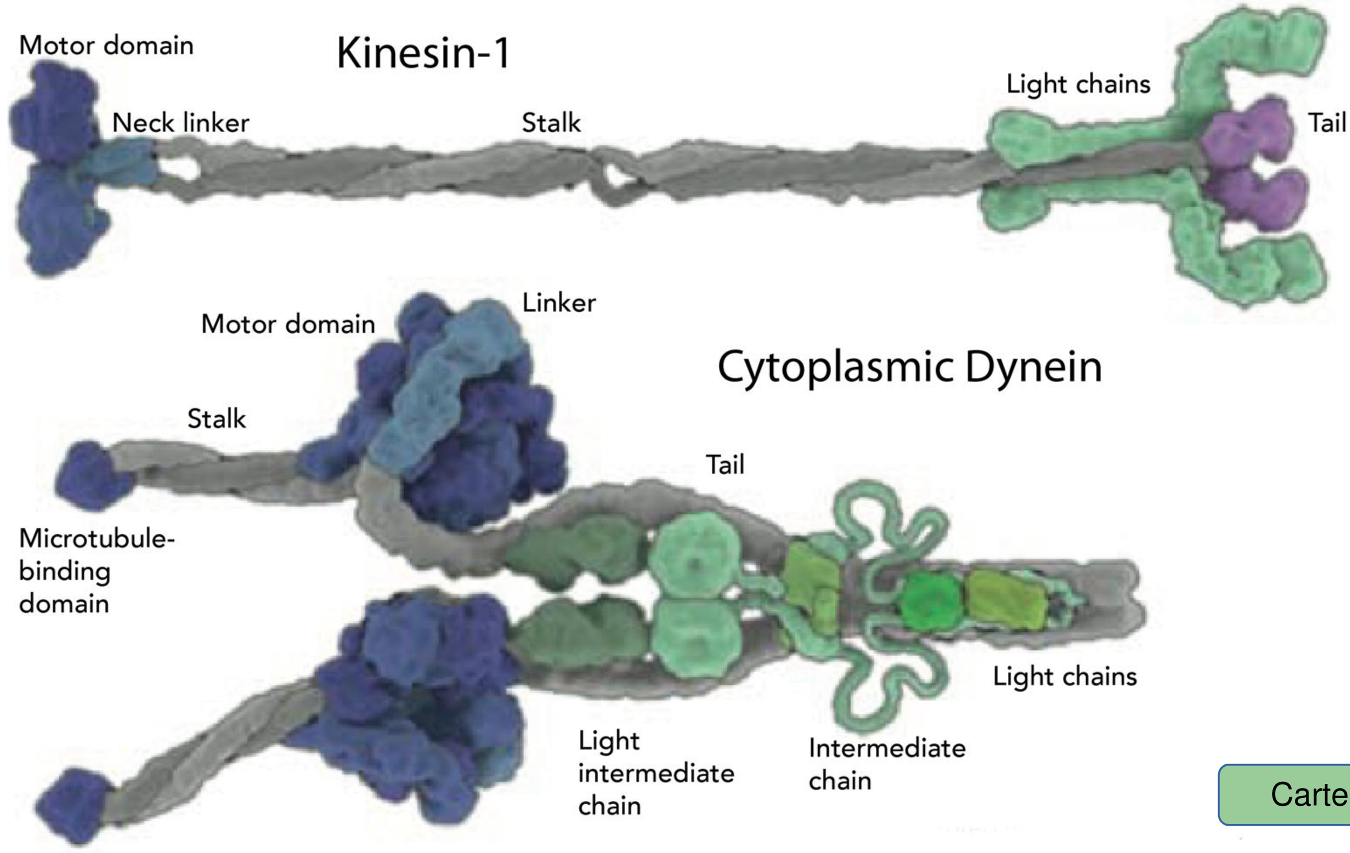
Dyneins walk towards the minus end of MT

Most cargo bound to both species

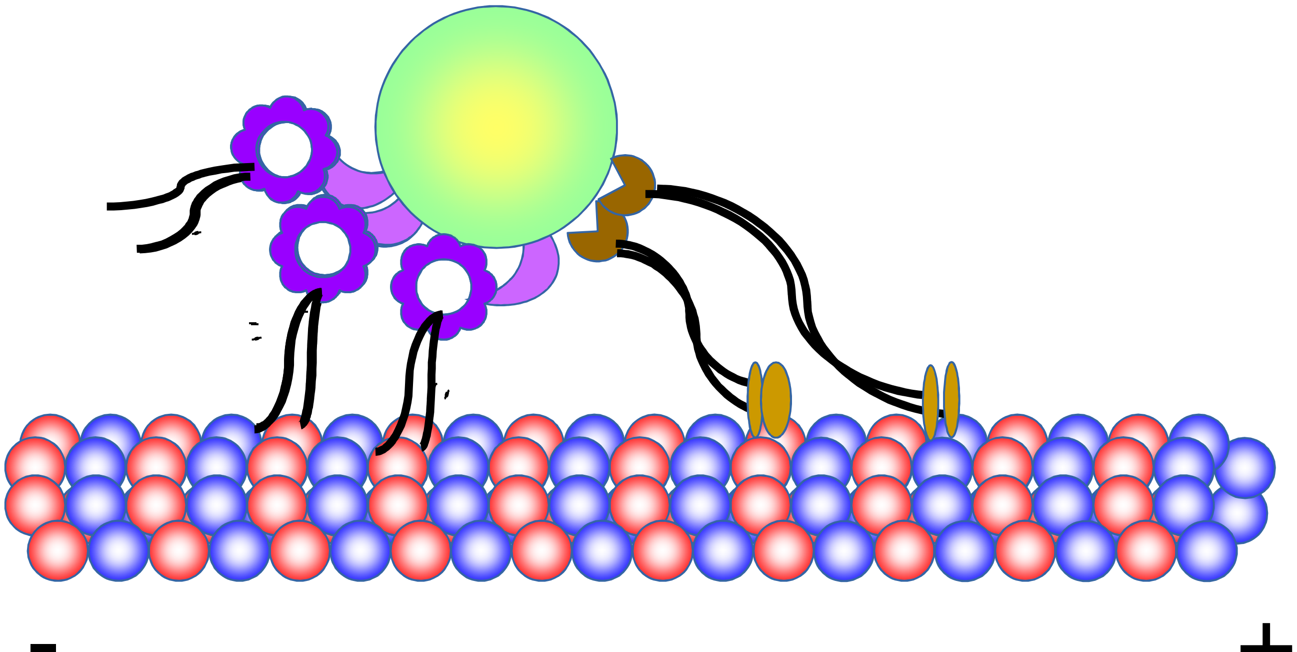


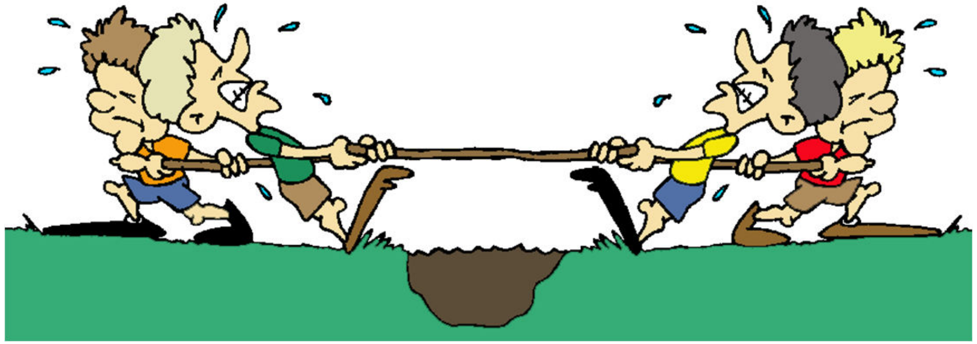




Lu et. al. J. Vis. Exp. 81, 50838 (2013)




Carter J. Cell Sci. (2013)





# Motor tug-of-war

PNAS

## Tug-of-war as a cooperative mechanism for bidirectional cargo transport by molecular motors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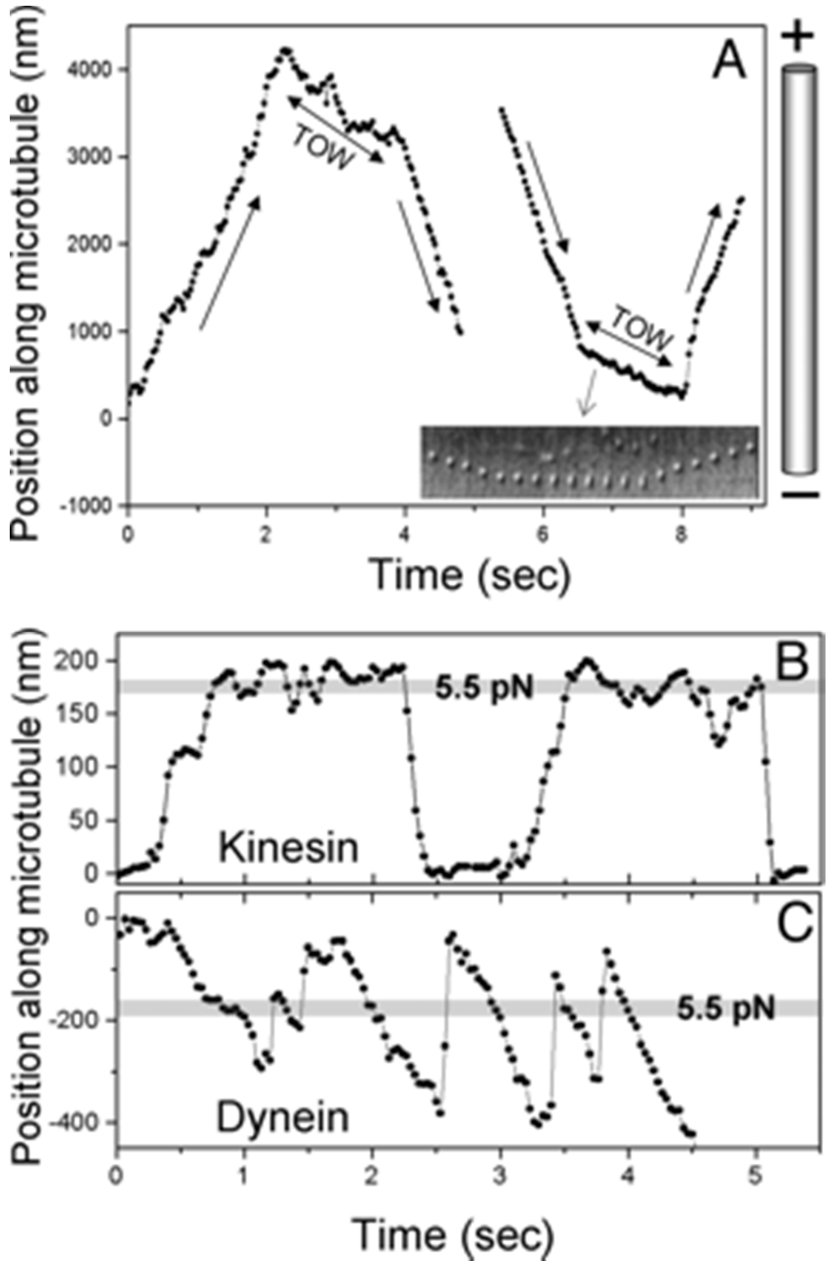
**Intracellular transport is based on molecular motors that pull cargos along cytoskeletal filaments. One motor species always moves in one direction, e.g., conventional kinesin moves to the**

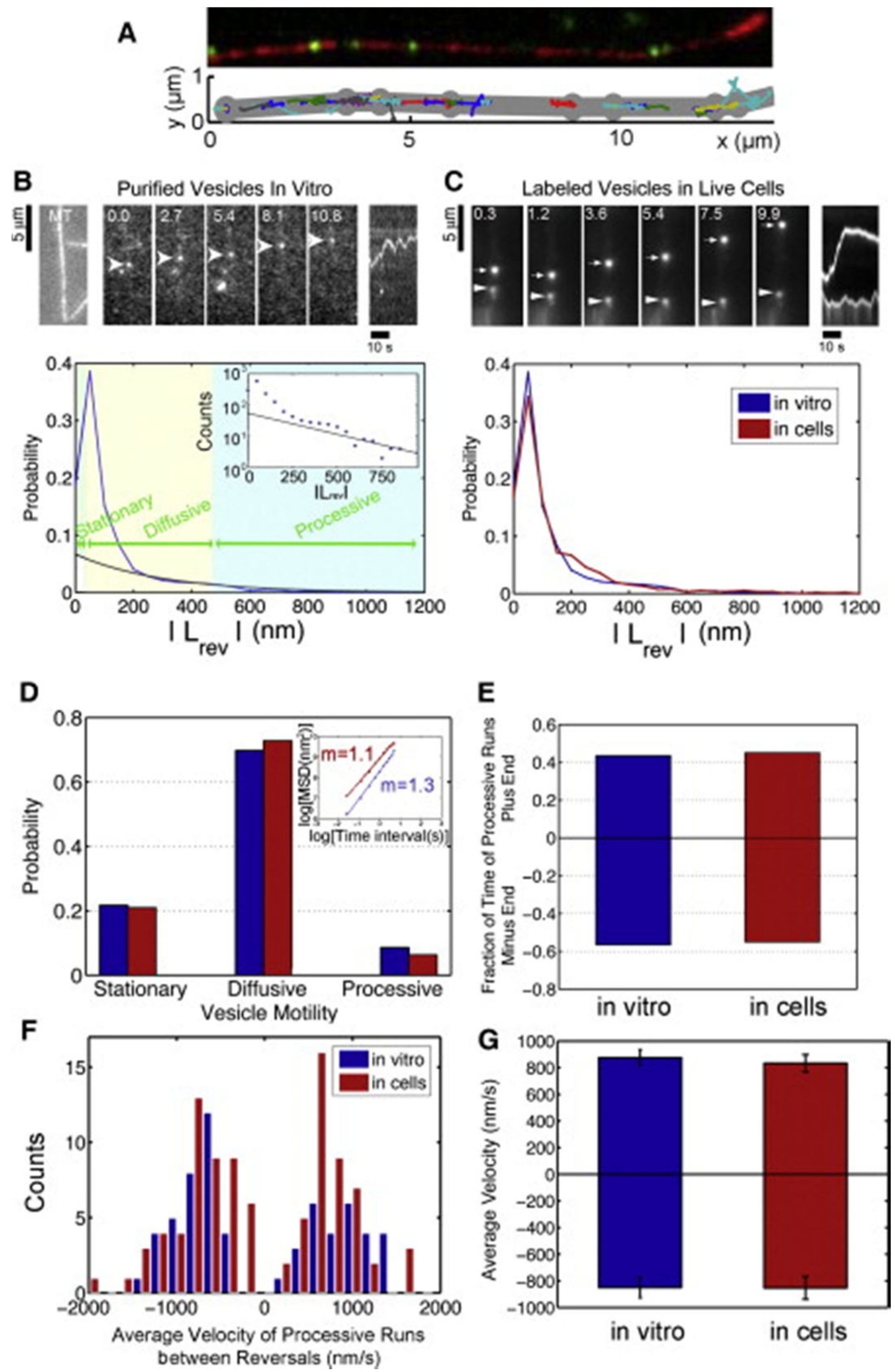

rectional transport, as briefly reviewed in the following paragraphs, has led many authors to reject a tug-of-war scenario and search for a coordination complex. However, as shown in this

## Stepping, strain gating, and an unexpected force-velocity curve for multiple-motor based transport

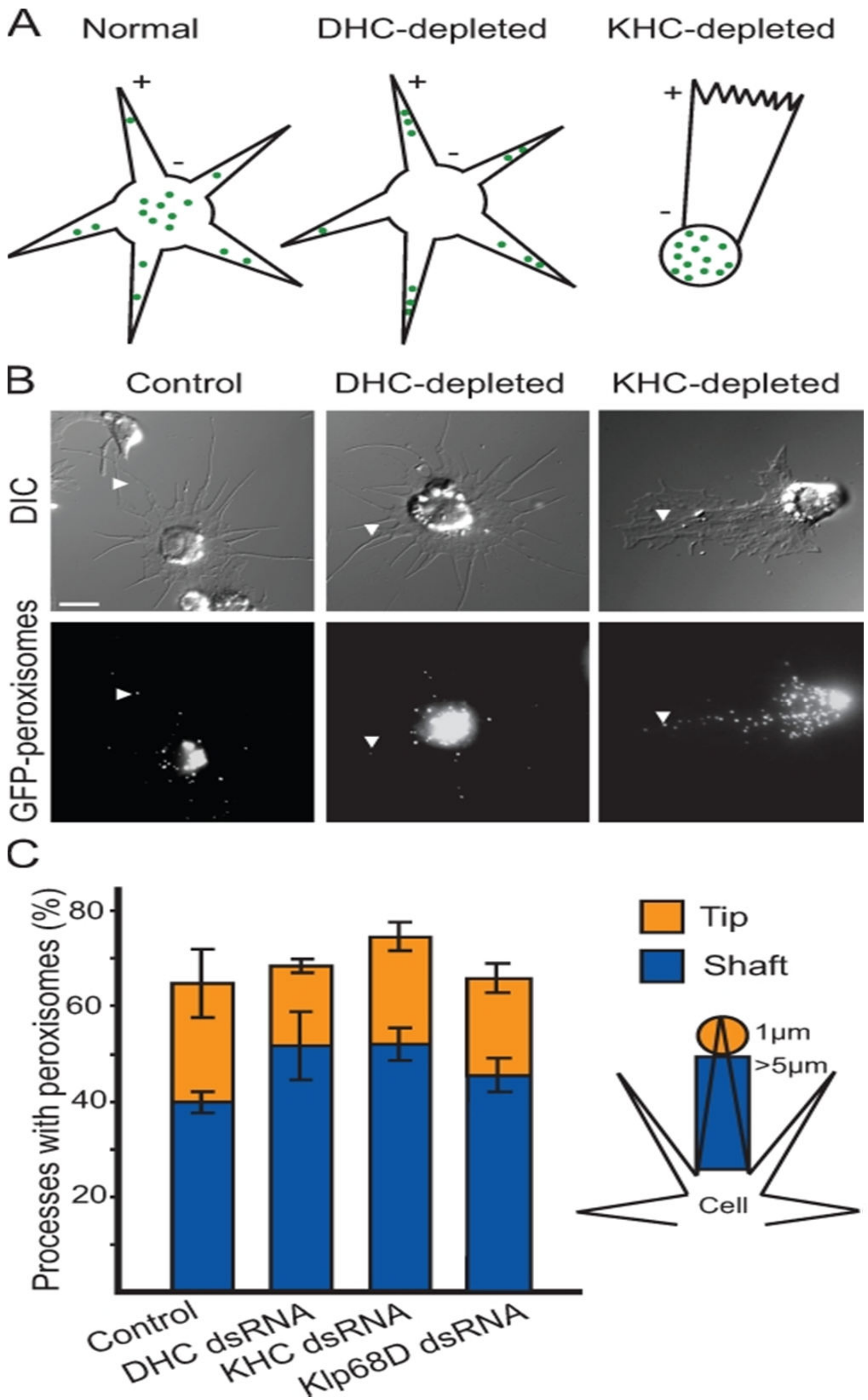

**Ambarish Kunwar**, **Michael Vershinin**, **Jing Xu**, and **Steven P. Gross**
Department of Developmental and Cell Biology, University of California Irvine, Irvine, CA -92697, USA



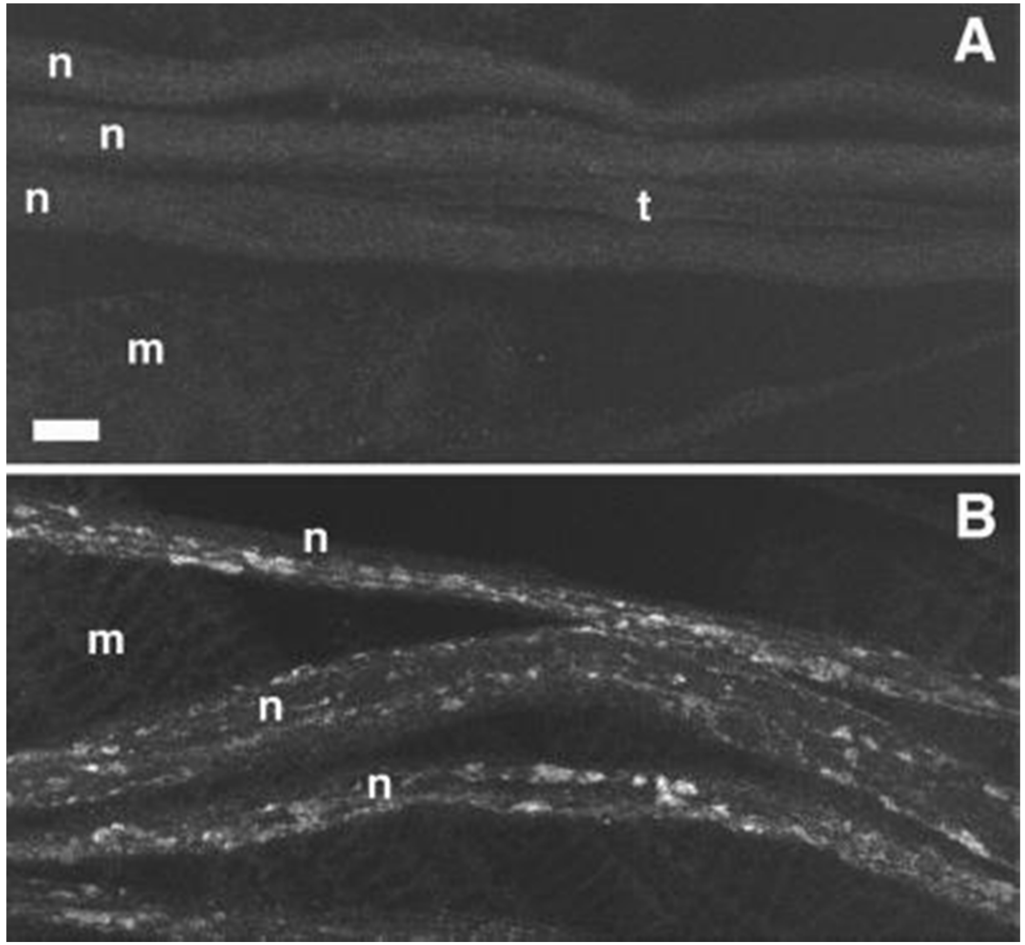

Soppina et. al. PNAS 2009




Hendricks et. al. Curr. Biol. 2010




Ally et. al. J. Cell Biol. 2009

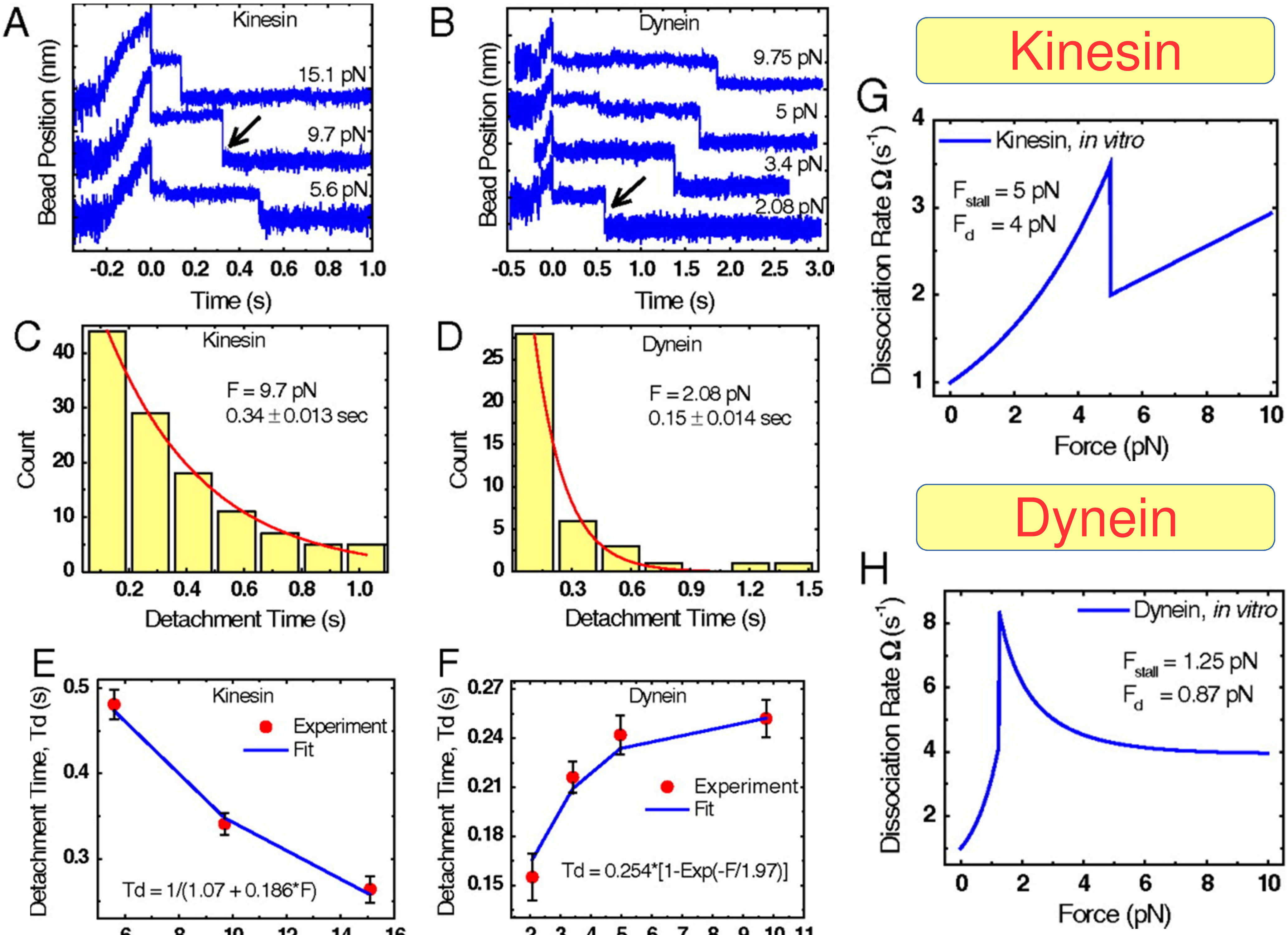



Martin et. al. Mol. Biol. Cell 1999

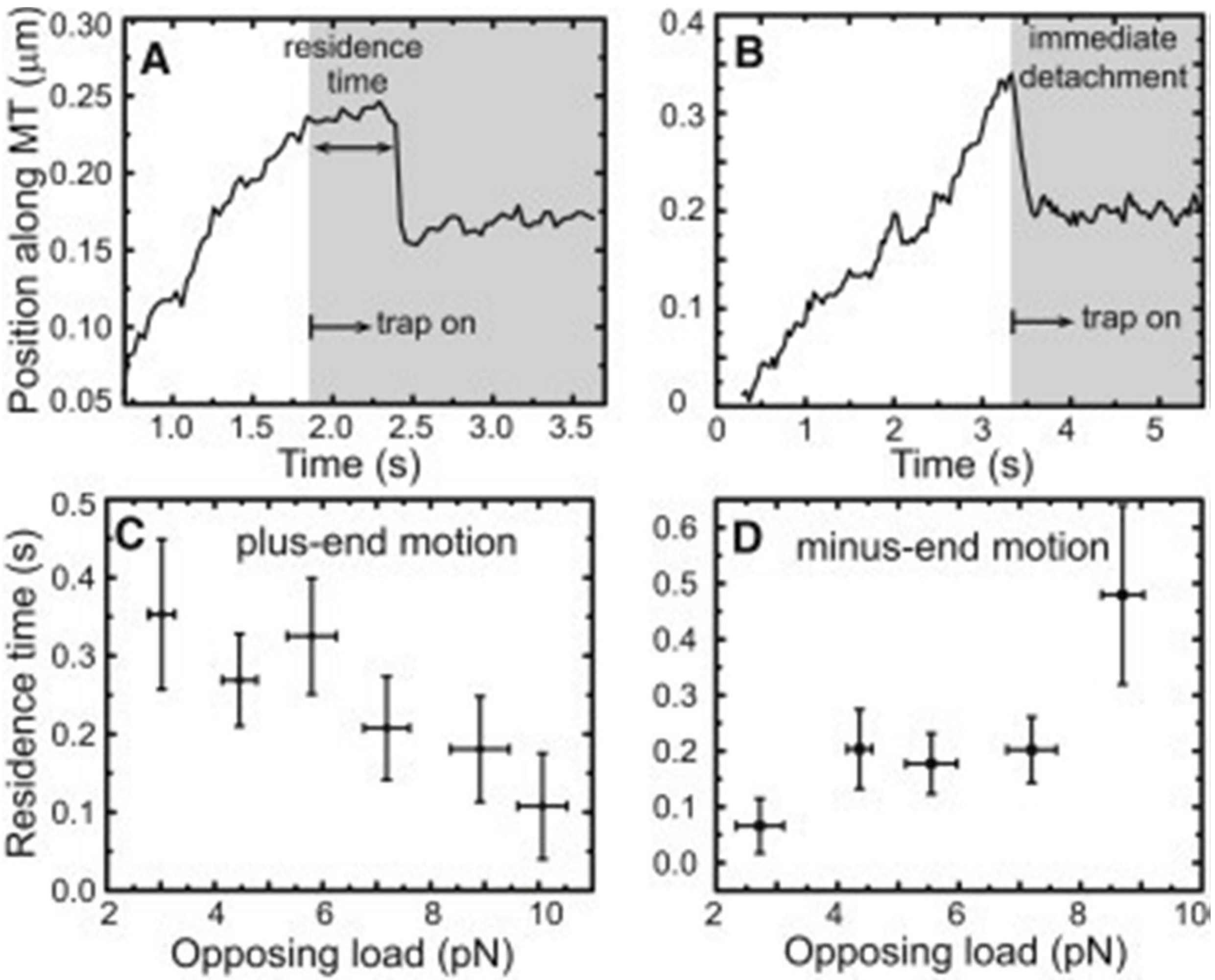
# Bidirectional cargo transport: moving beyond tug of war

*William O. Hancock*

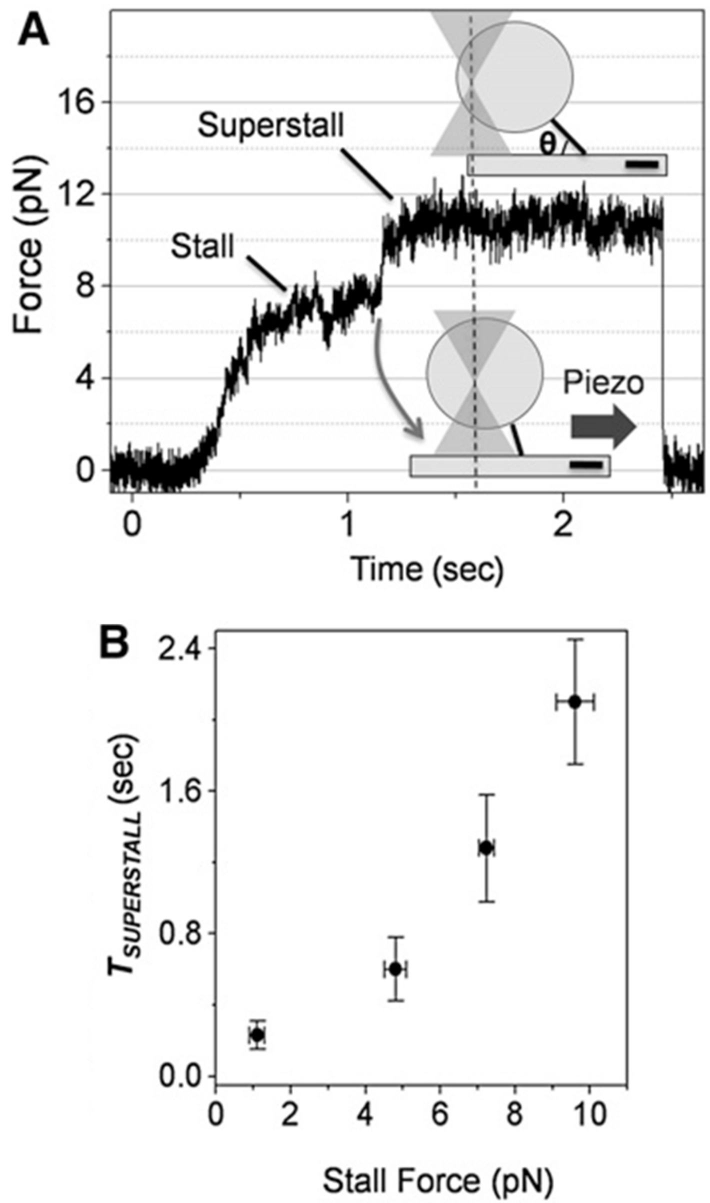
Abstract | Vesicles, organelles and other intracellular cargo are transported by kinesin and




Kunwar et. al. PNAS 2011

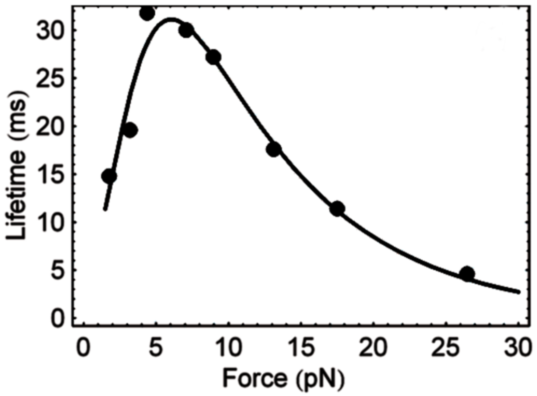



Leidel et. al. Biophys J. 2012



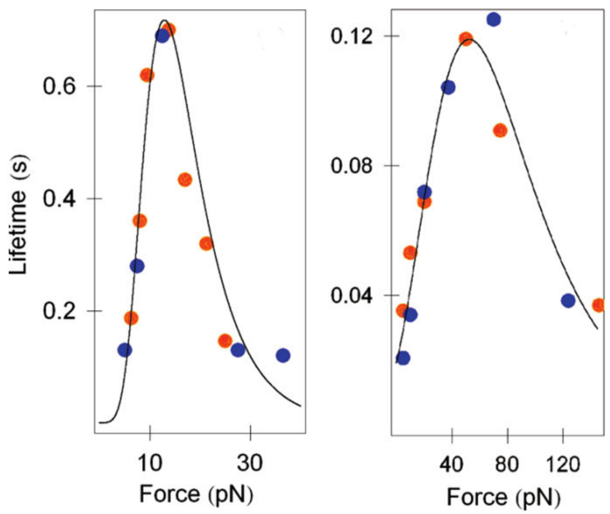

Rai et. al. Cell 2013

Receptor-Ligand lifetimes under force
(P/L Selectin with monomeric/dimeric PSGL-1)

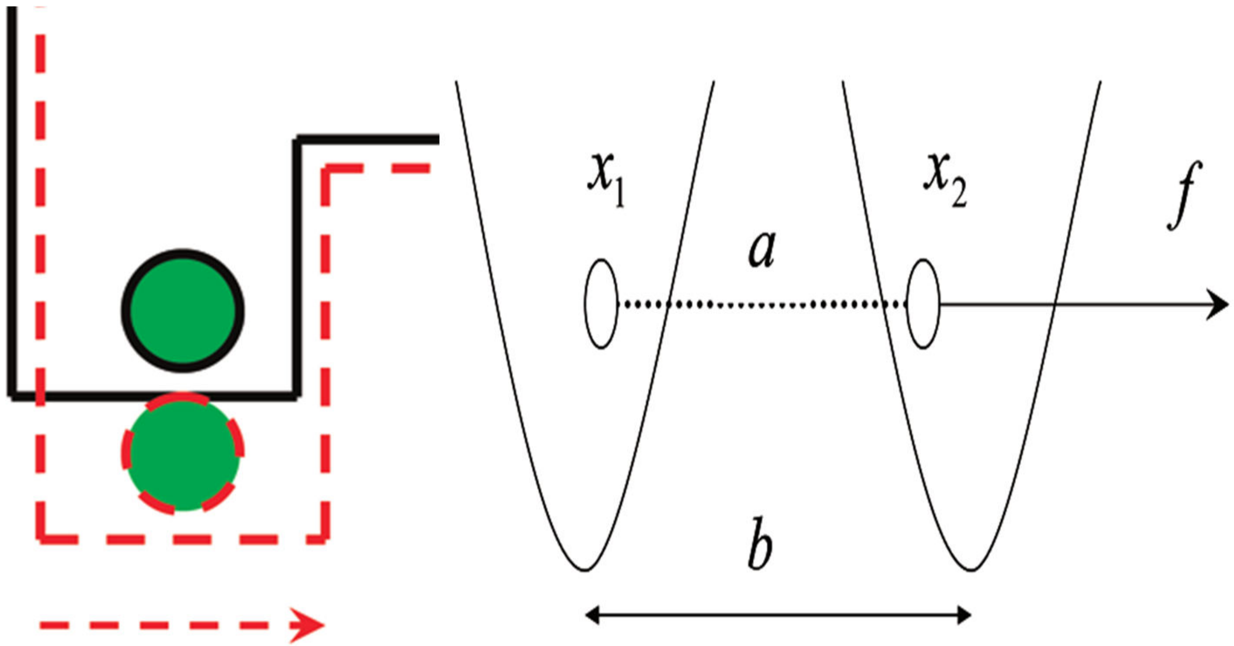



Prezhdo & Pereverzev, Acc. Chem. Res. 2008

Lifetime of Actin-Myosin complex




Pereverzev & Prezhdo, PRE 2006



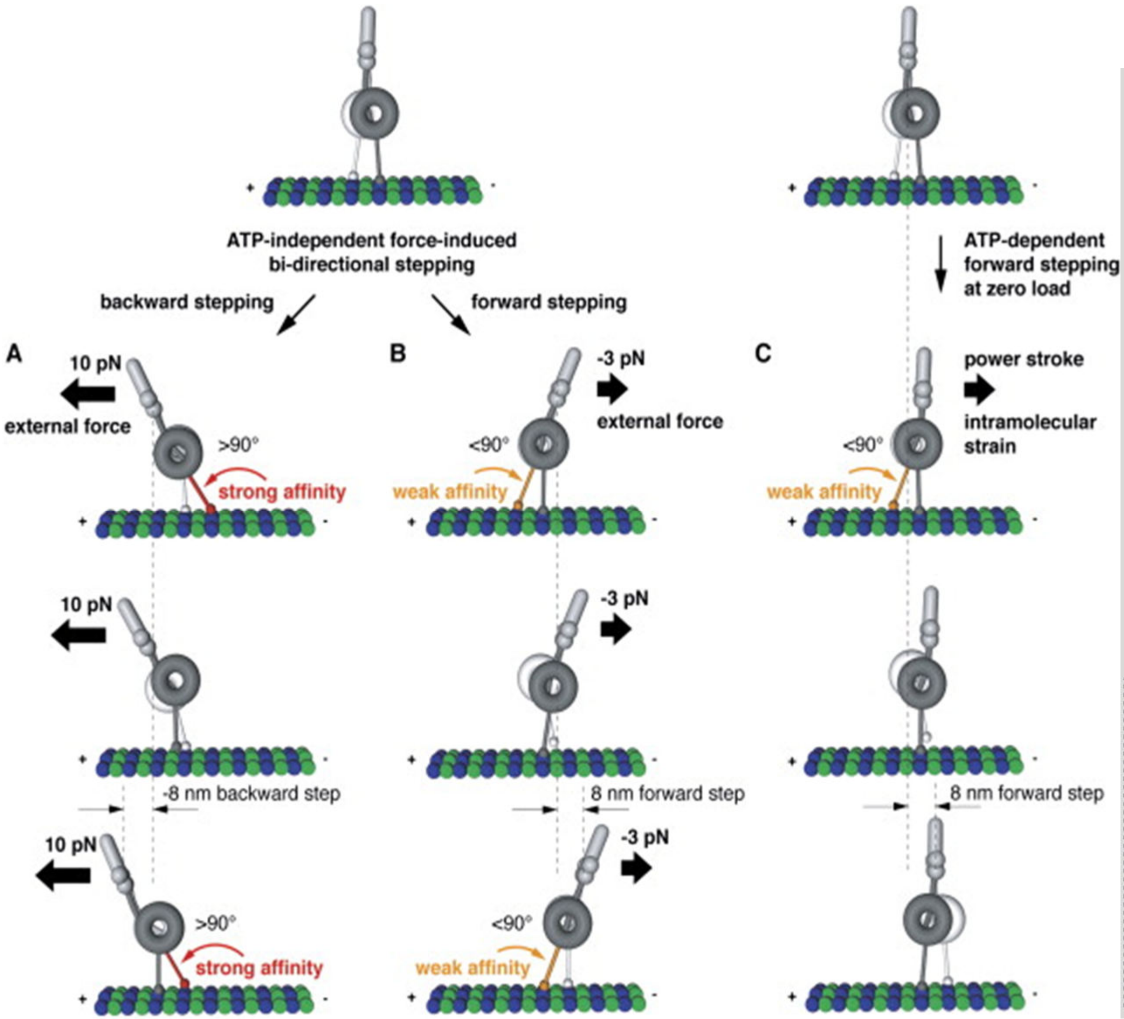

Prezhdo & Pereverzev, Acc. Chem. Res. 2008

$$\varepsilon(F) = \varepsilon_0 \exp\left[\frac{F}{F_d} - E_d(F)\right]$$

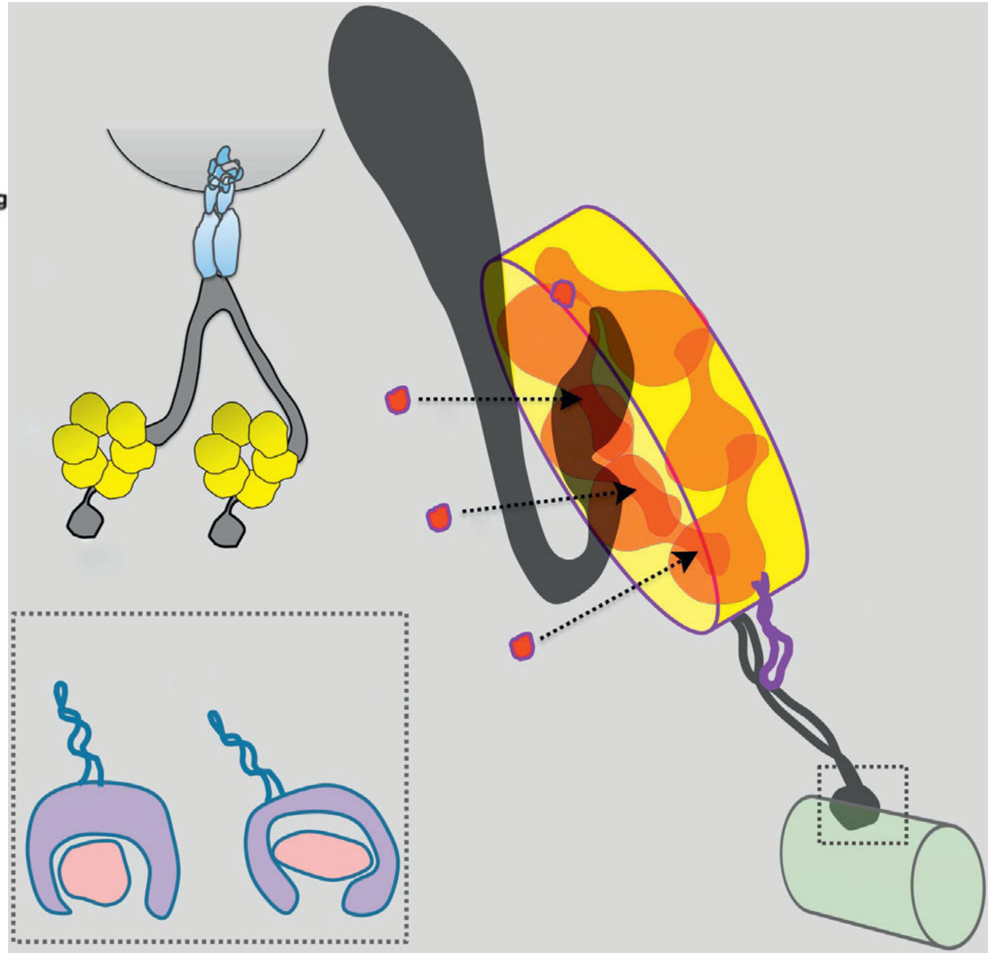
$$E_d(F) = \alpha\left[1 - \exp(-F/F_0)\right]$$

Catch bond strength

Catch bond Force Scale

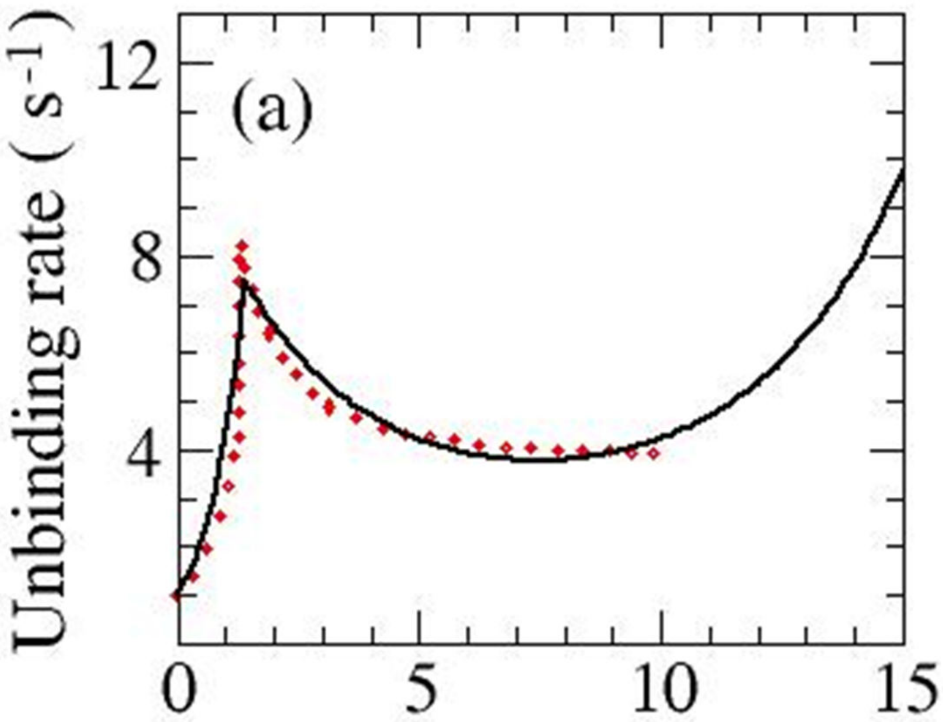



Gennerich et. al. Cell 2007



Mallik et. al. Trends Cell Bio. 2013

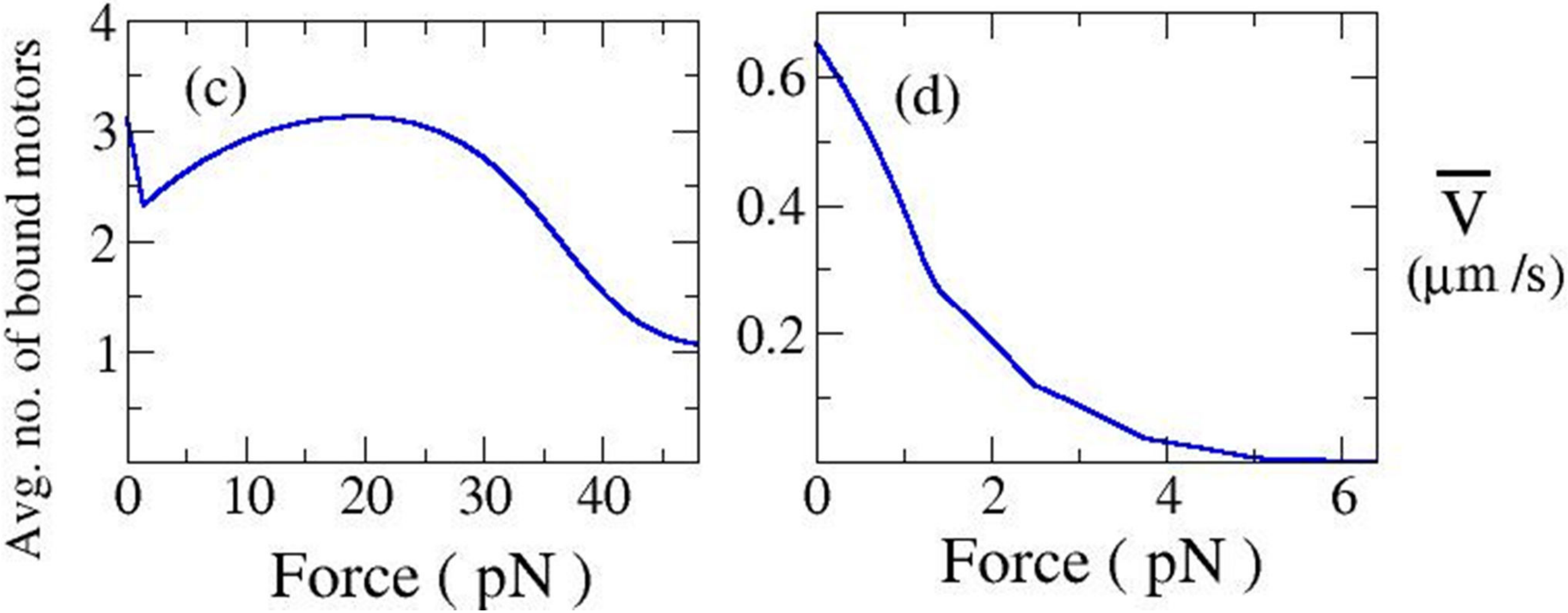
$$E_d(F) = \Theta(F - F_s)\,\alpha\left[1 - \exp\left(-(F - F_s)/F_0\right)\right]$$

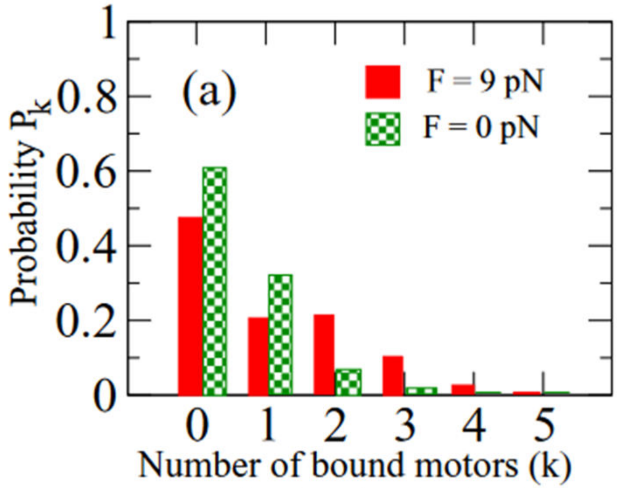


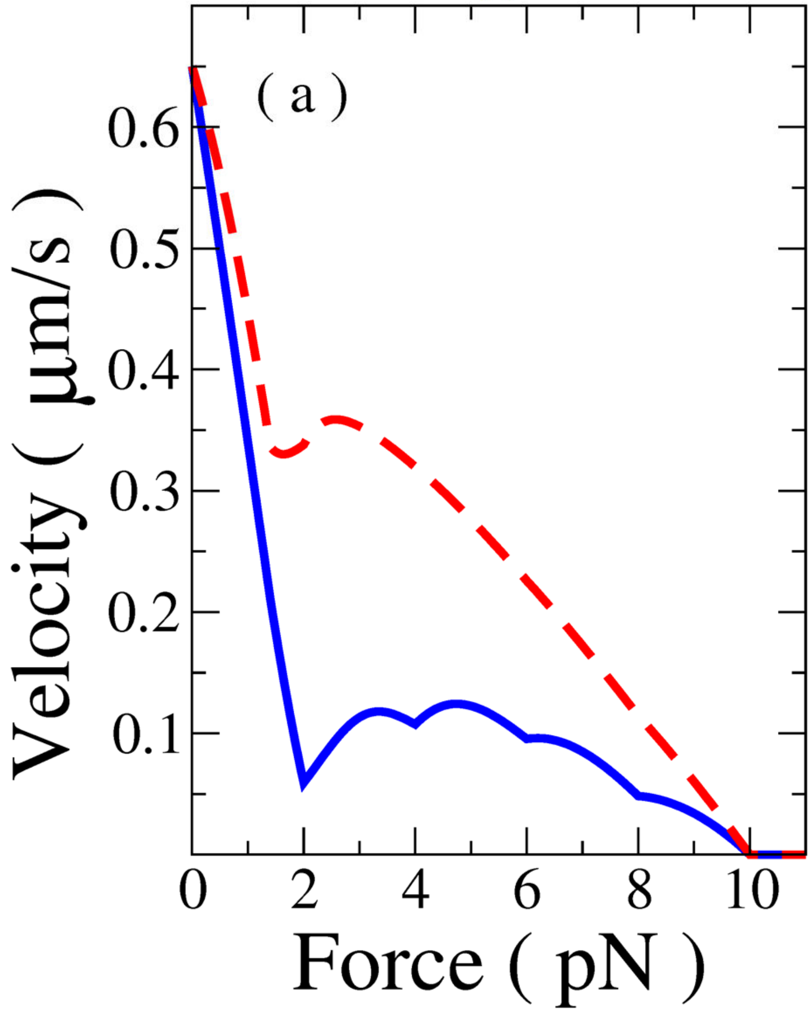

$$\alpha = 68\, k_B T$$

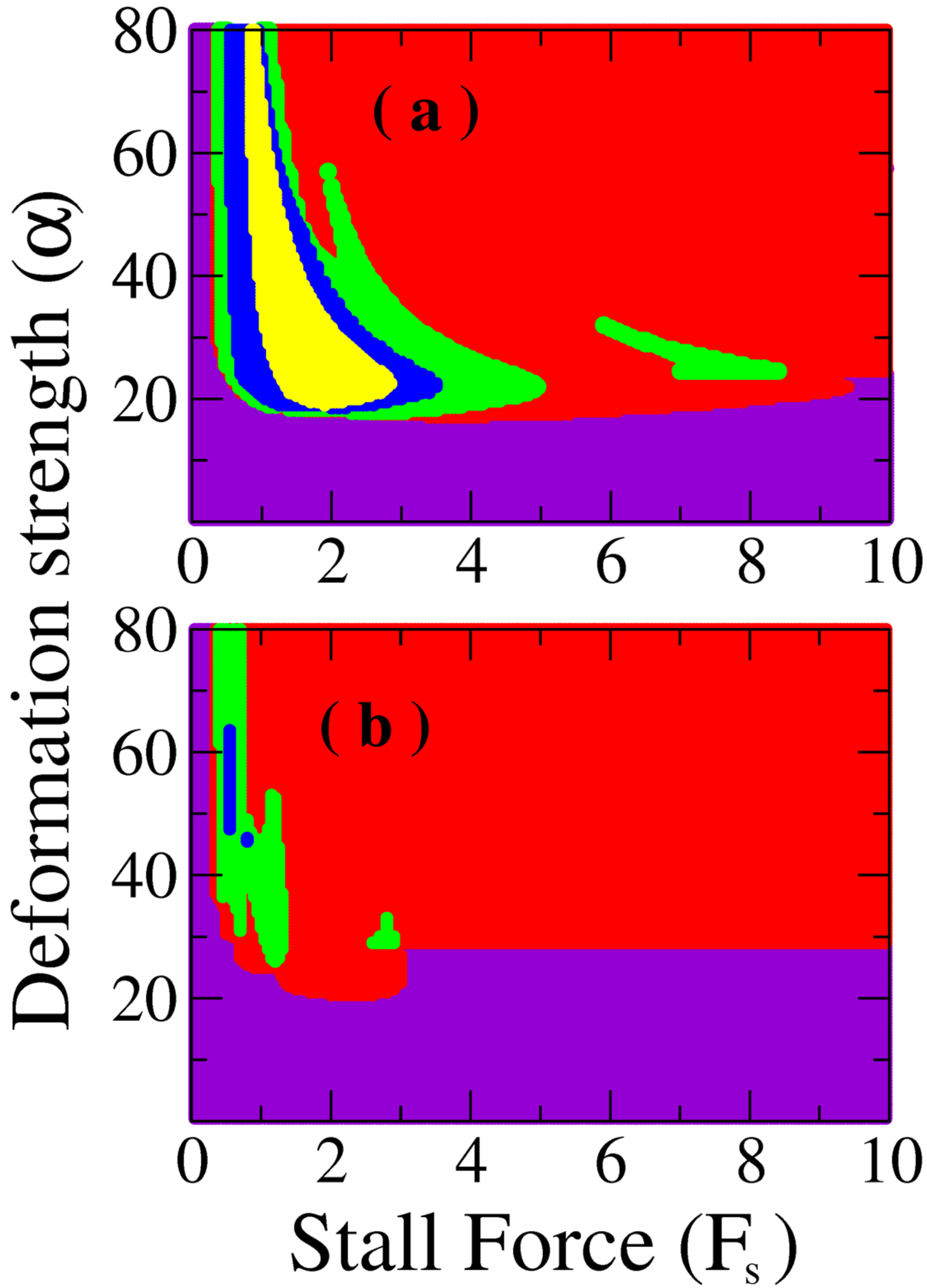
$$F_0 = 40\, pN$$

Nair et. al. PRE 2016



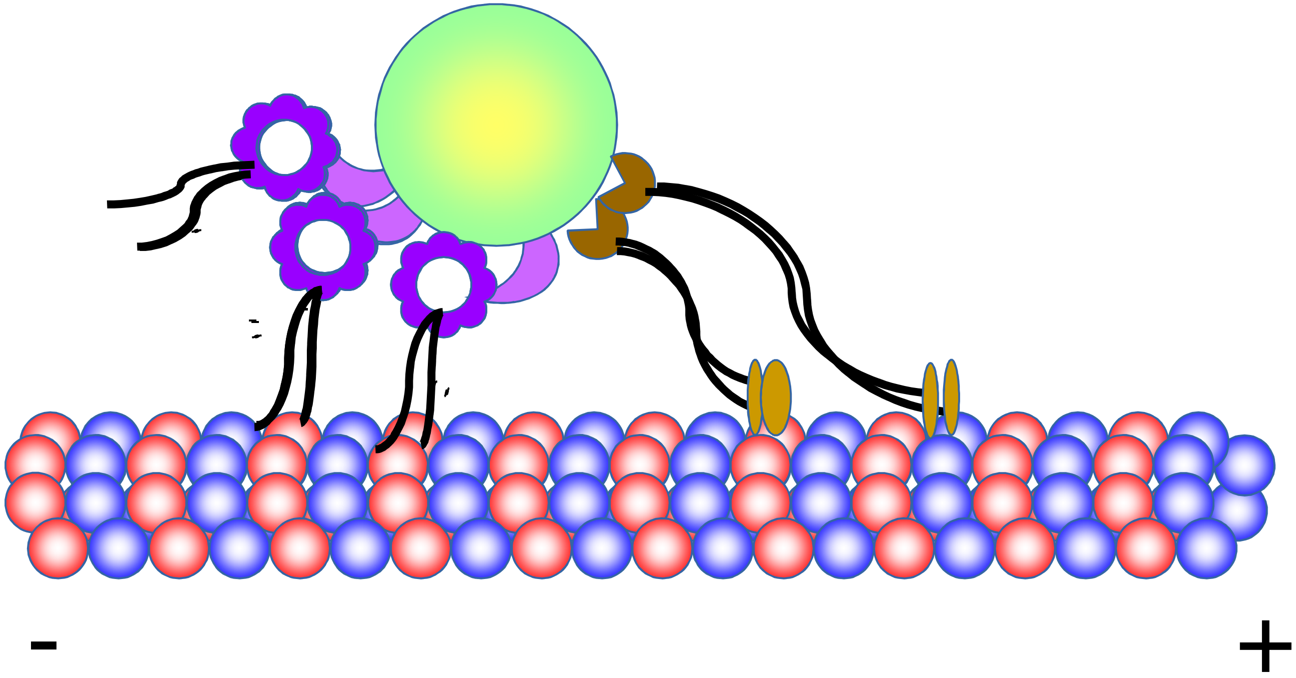



Nair et. al. PRE 2016

## Mean Field: Equal load sharing between motors




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

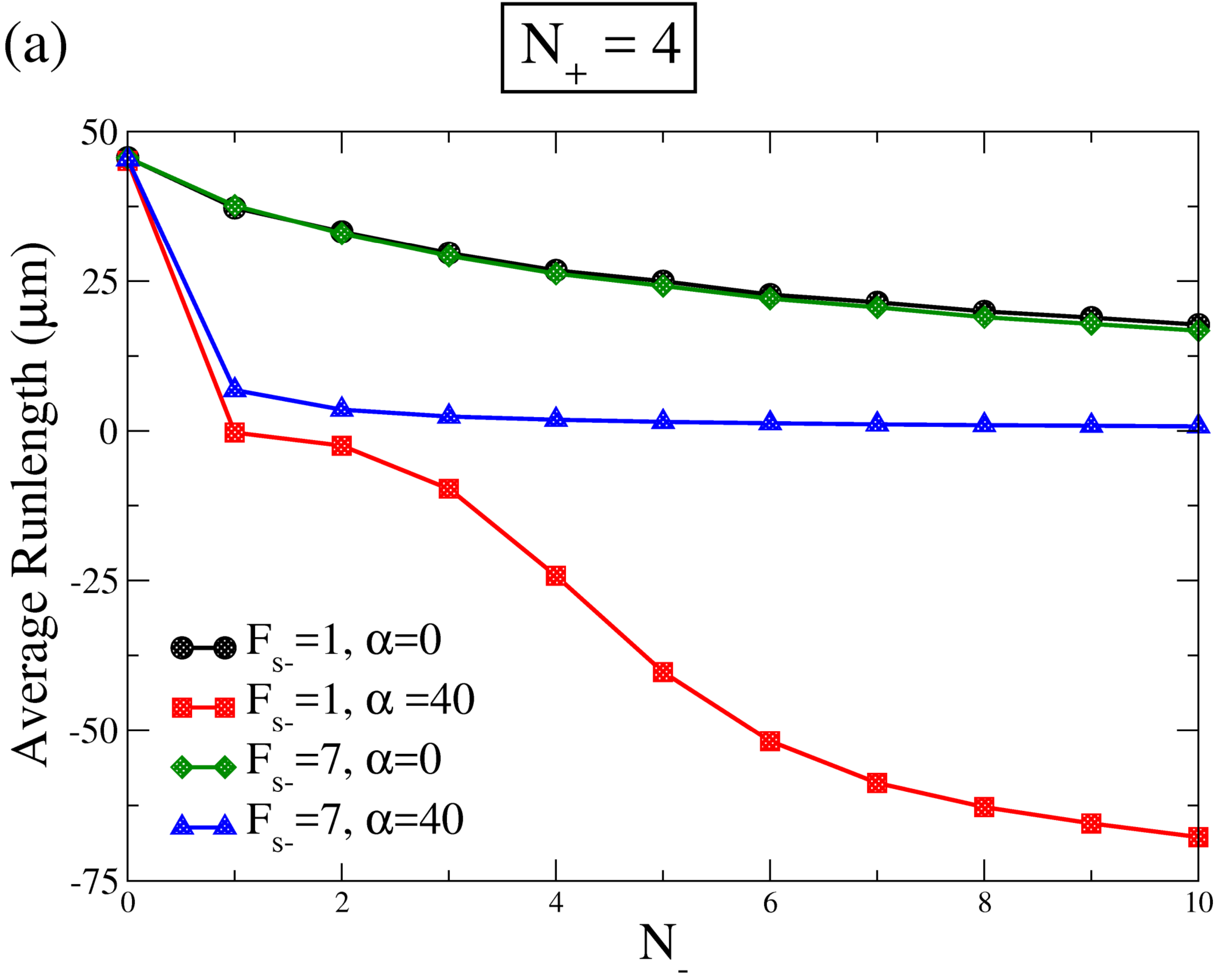
$$+ p(n_+ - 1, n_-, t)\,\pi_+(n_+ - 1, n_-) + p(n_+, n_- - 1, t)\,\pi_-(n_+, n_- - 1)$$

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

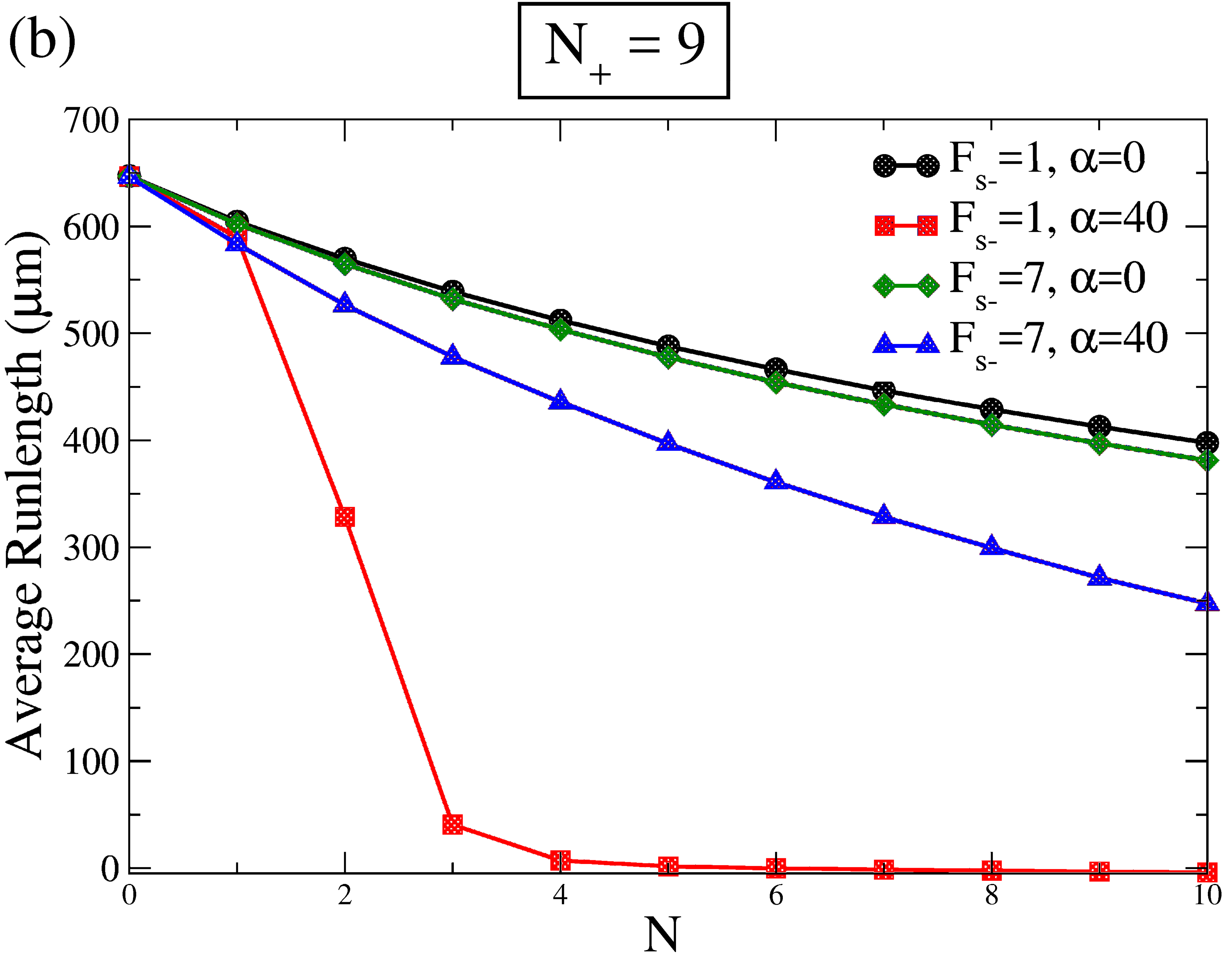
Binding rate $\pi_n = (N - n)\pi_{ad}$

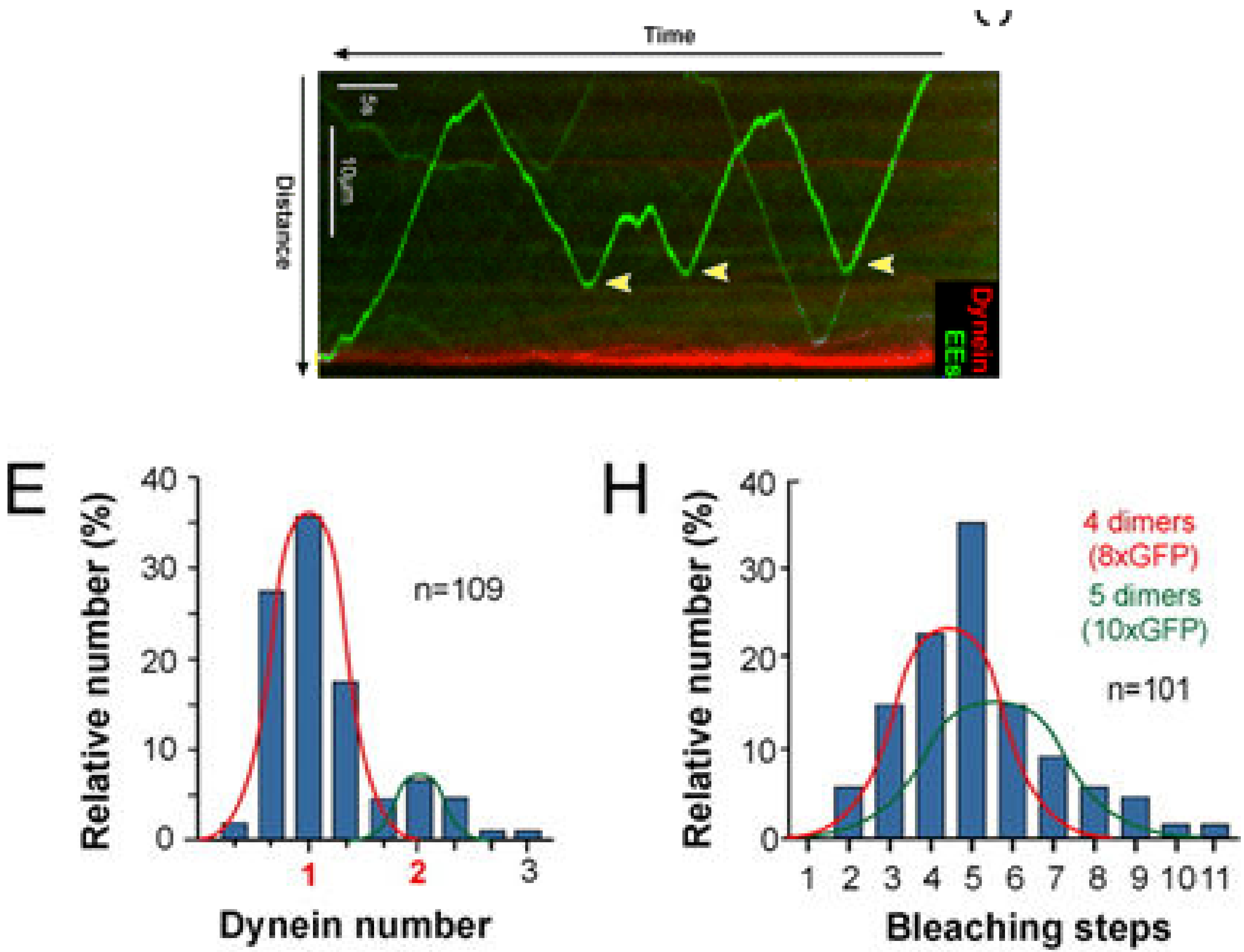
Velocity Model $v_n(F) = v_0(1 - F/n f_s)$

Muller et. al. PNAS 2005

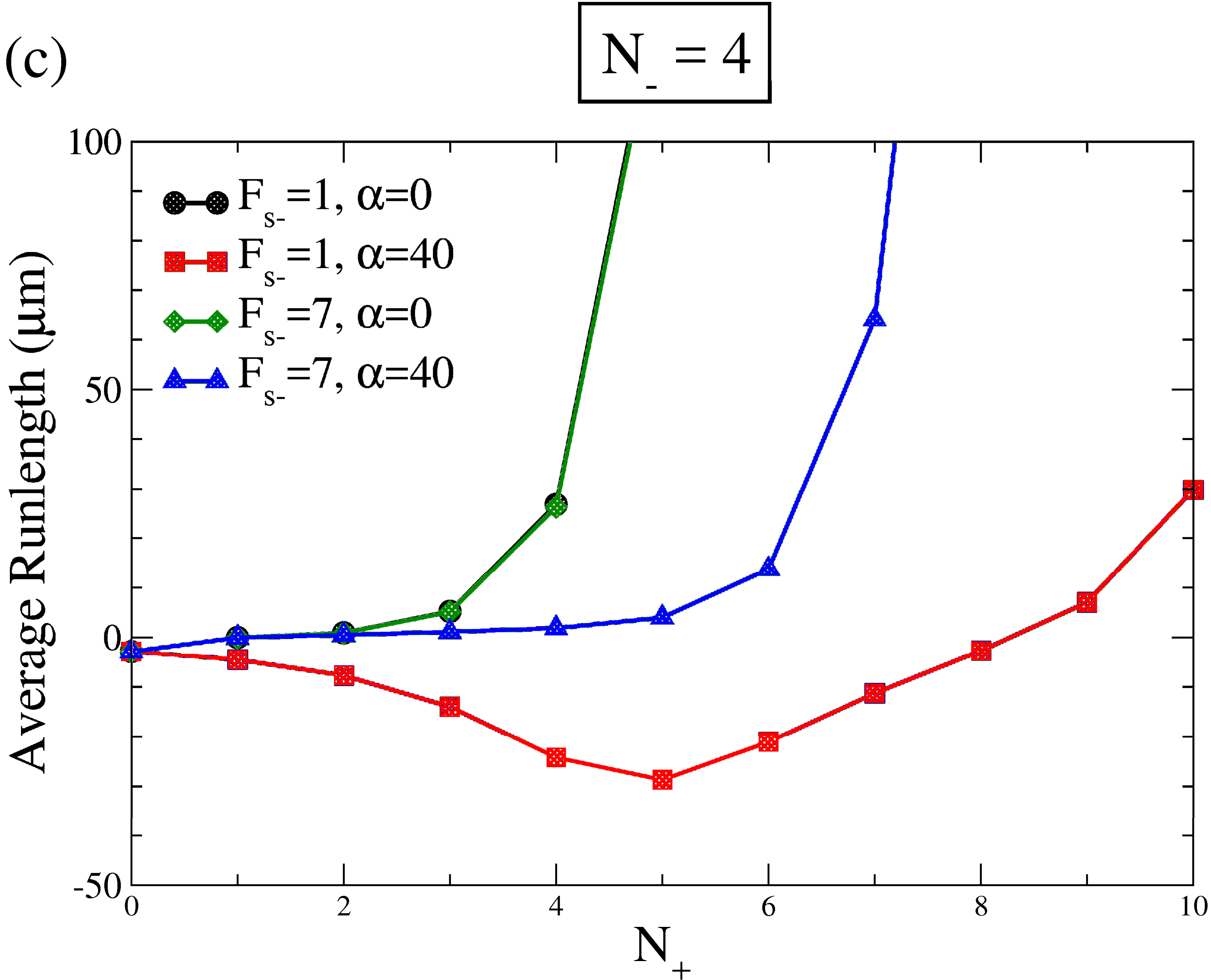


(a)
N+ = 4
Average Runlength (μm)
50
25
0
-25
-50
-75
0
2
4
6
8
10
N-
Fs-=1, α=0
Fs-=1, α =40
Fs-=7, α=0
Fs-=7, α=40

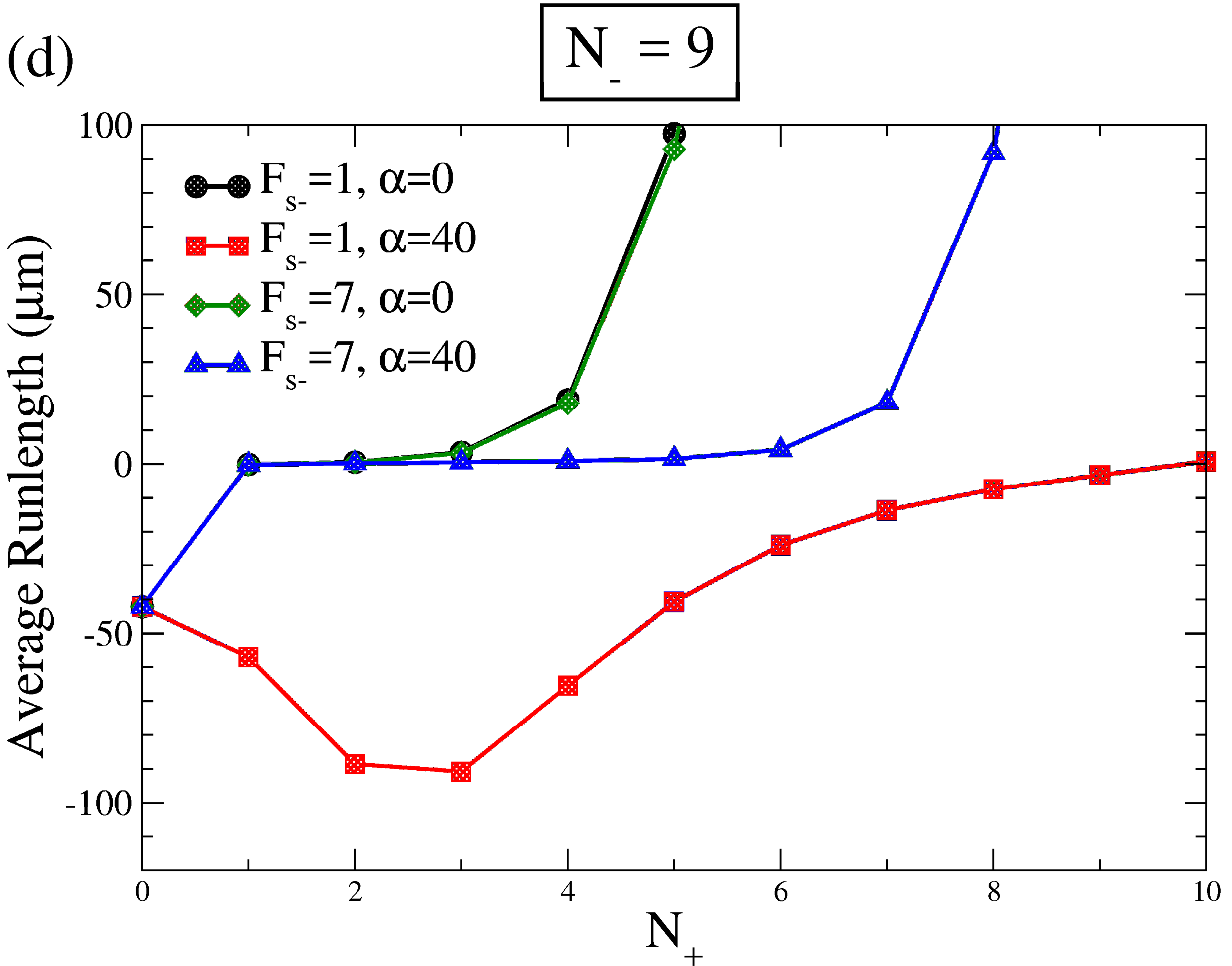

(b)
N+ = 9
Average Runlength (μm)
N
700
600
500
400
300
200
100
0
0
2
4
6
8
10
F_s- =1, α=0
F_s- =1, α=40
F_s- =7, α=0
F_s- =7, α=40

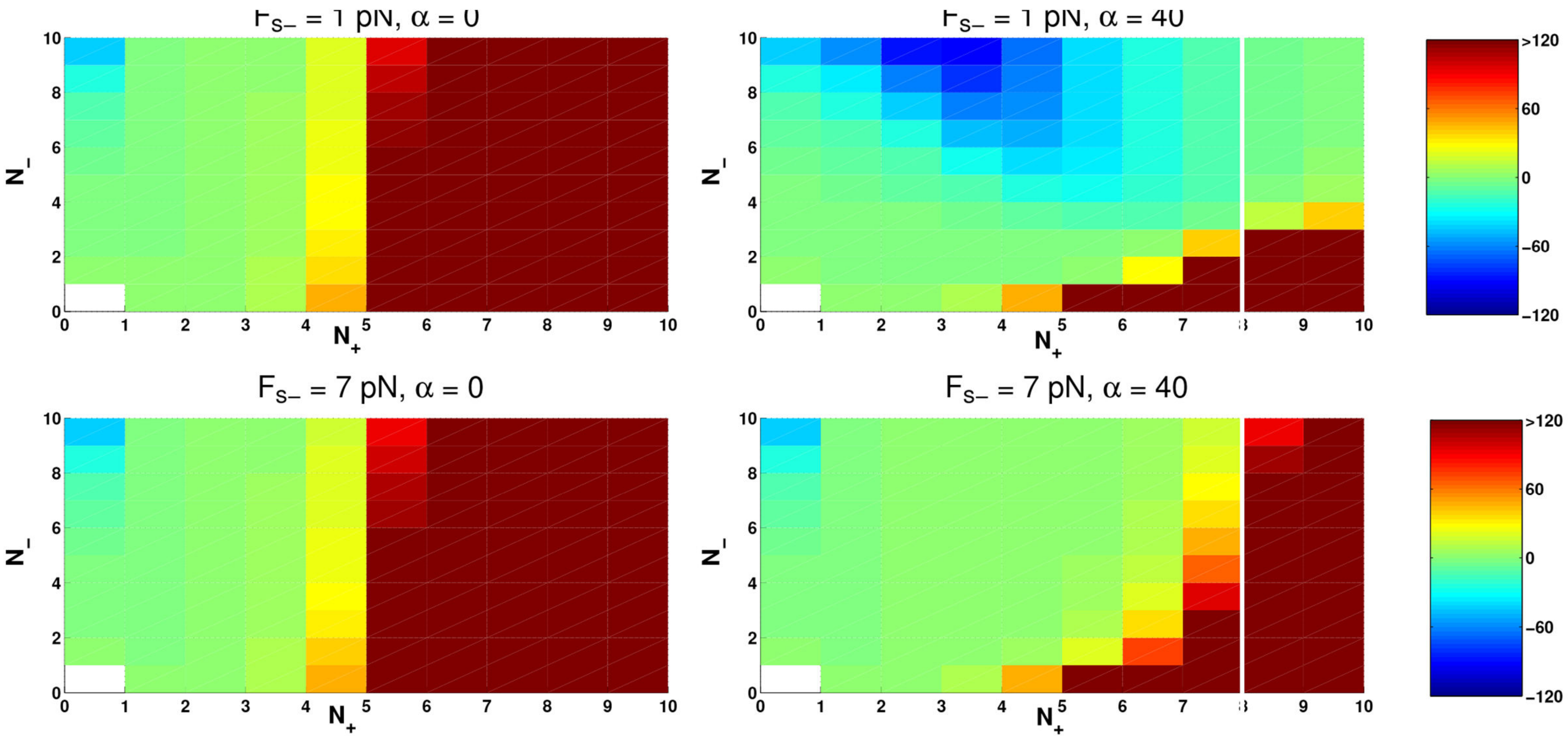



Schuster et. al. PNAS 2011

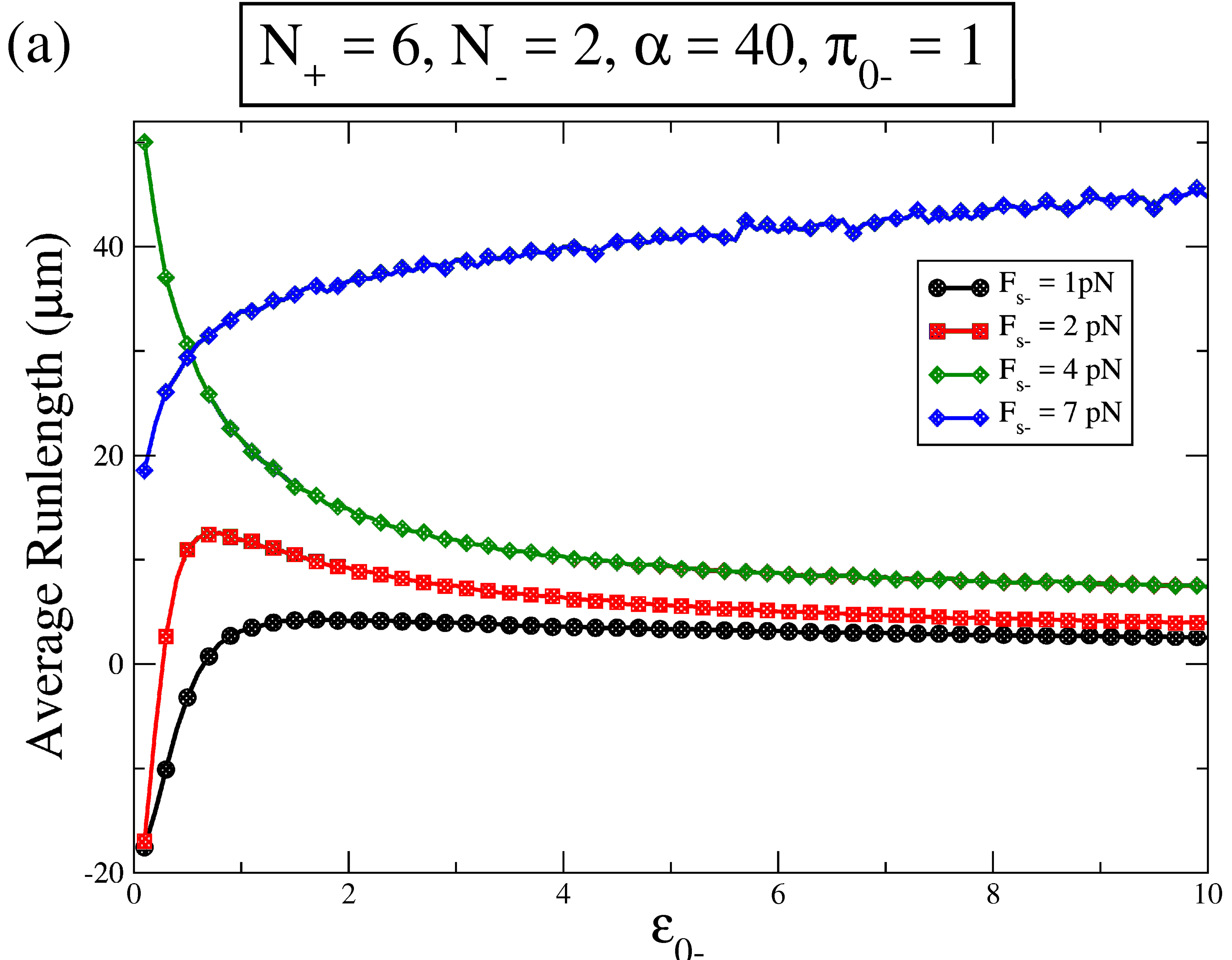


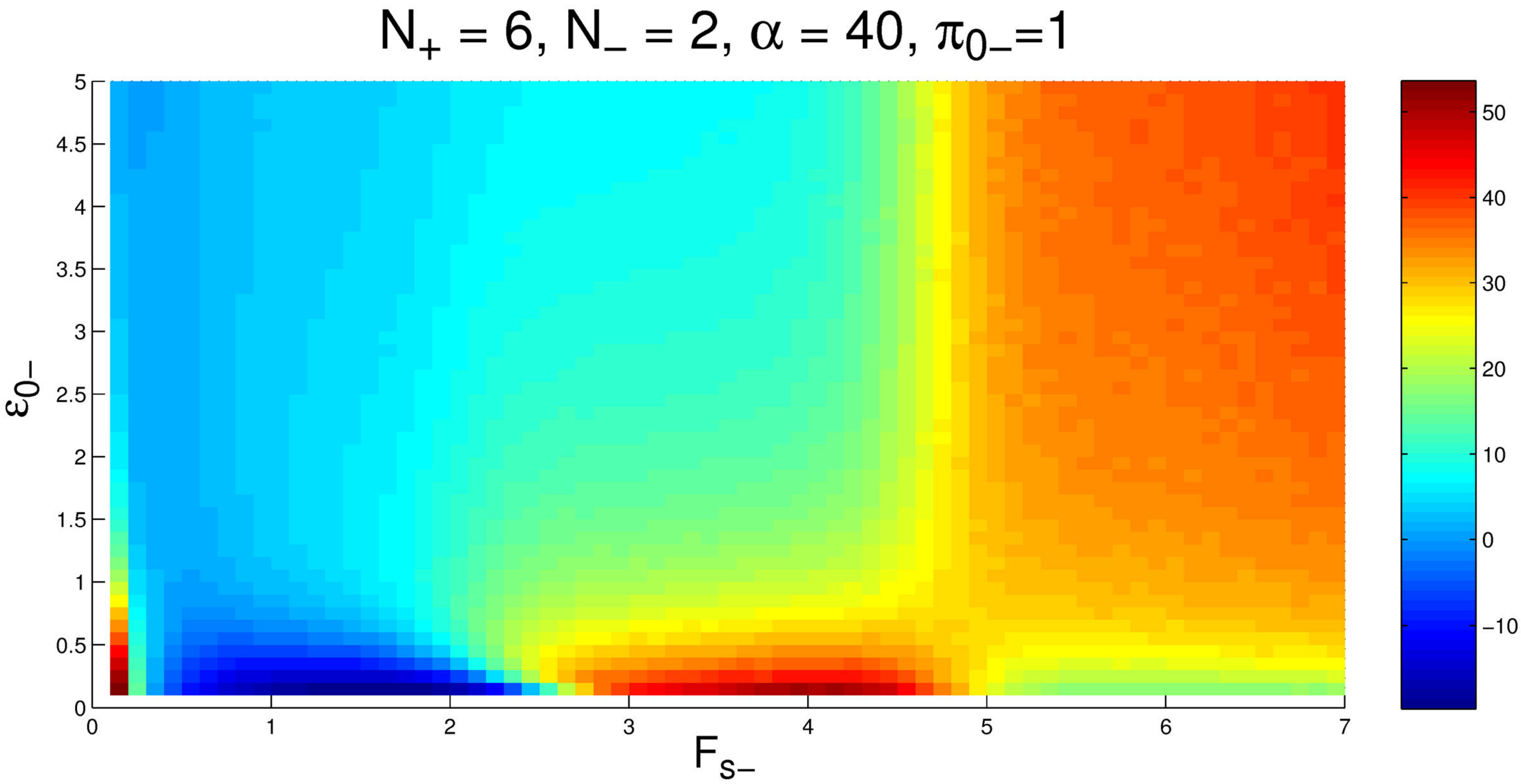
(c)
N_ = 4
Average Runlength (μm)
N+
100
50
0
-50
0
2
4
6
8
10
F s- =1, α=0
F s- =1, α=40
F s- =7, α=0
F s- =7, α=40


(d)
N_ = 9
Average Runlength (μm)
N+
Fs- =1, α=0
Fs- =1, α=40
Fs- =7, α=0
Fs- =7, α=40
100
50
0
-50
-100
0
2
4
6
8
10

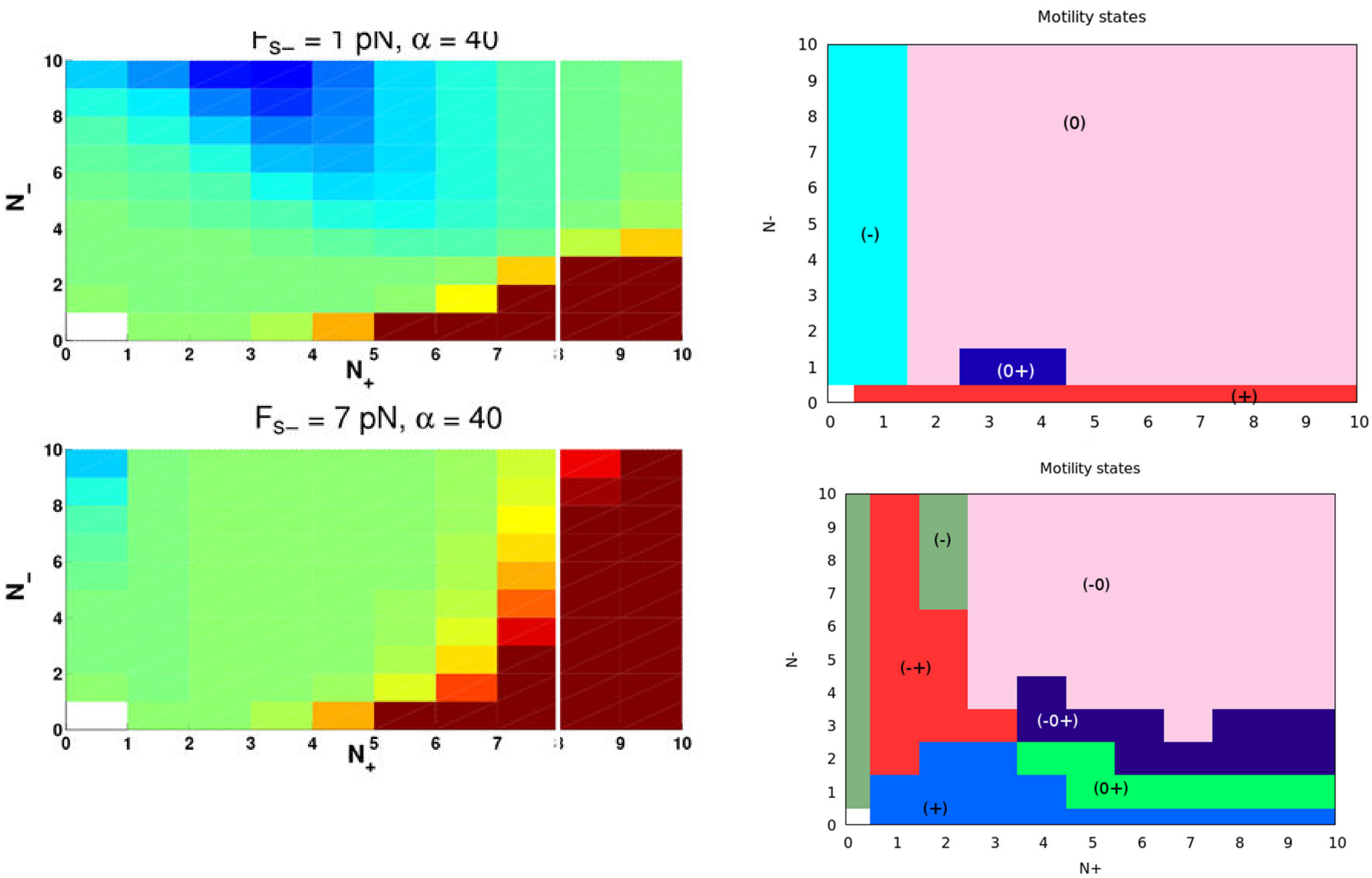


F_{S−} = 1 pN, α = 0
F_{S−} = 1 pN, α = 40
F_{S−} = 7 pN, α = 0
F_{S−} = 7 pN, α = 40
N_−
N_+
>120
60
0
−60
−120


(a)
N+ = 6, N- = 2, α = 40, π0- = 1
Average Runlength (μm)
ε0-
Fs- = 1pN
Fs- = 2 pN
Fs- = 4 pN
Fs- = 7 pN
-20
0
20
40
0
2
4
6
8
10



N+ = 6, N− = 2, α = 40, π0−=1
ε0−
Fs−
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
0
1
2
3
4
5
6
7
50
40
30
20
10
0
−10



$F_{S-}$ = 1 pN, α = 40
$F_{S-}$ = 7 pN, α = 40
$N_-$
$N_+$
Motility states
(0)
(-)
(0+)
(+)
N-
Motility states
(-)
(-0)
(-+)
(-0+)
(0+)
(+)
N+

## Tug-of-war model which incorporates dynein catch bond characteristics can reproduce both conventional tug-of-war *and* co-dependent motion characteristics.

- ❑ Unequal load sharing between attached motors
- ❑ Coupling of kinesin and dynein mechano-chemistry
- ❑ Variable step sizes for dynein
- ❑ Regulation due to various cofactors

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