Cargo transport by catch bonded motors in optical trapping assays

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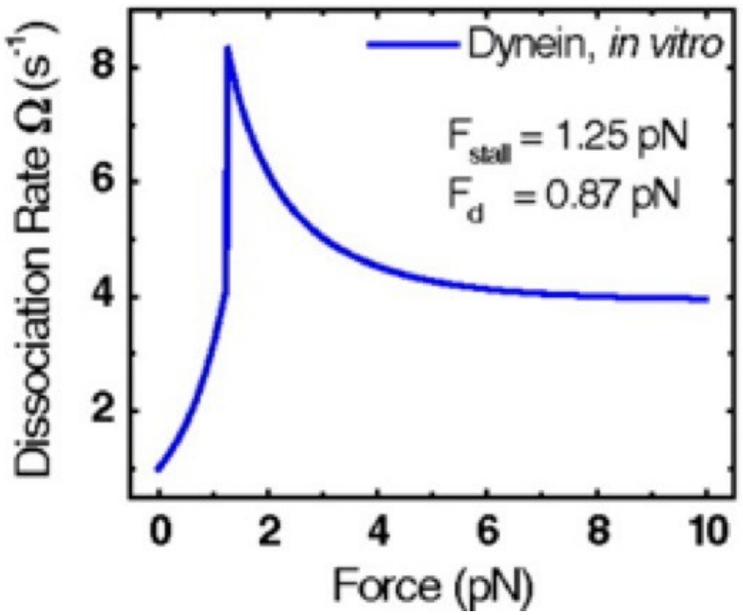
Financial Support: SERB project No. EMR/2017/001335

Catchbonding

Protein-ligand binding when subject to force:

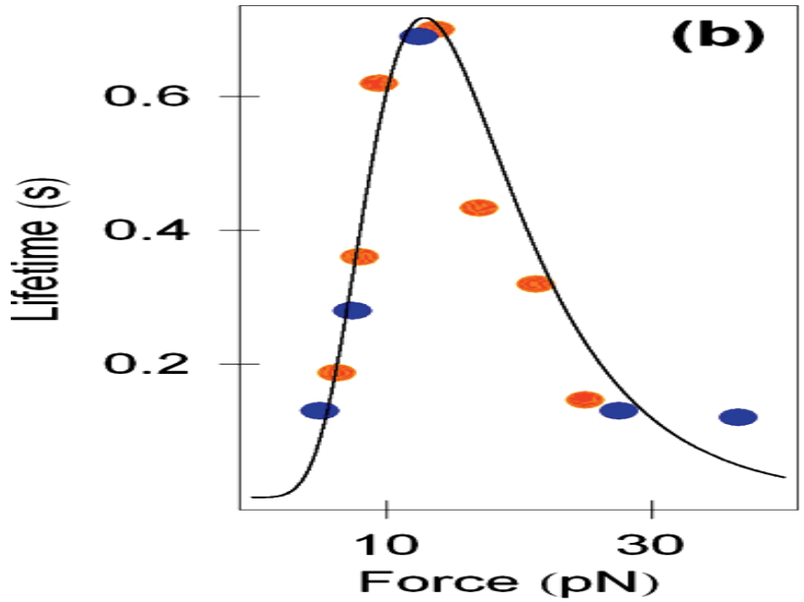
Catch Bond : Increase in Force —> Bond lifetime increases (unbinding rate decreases)

Slip Bond : Increase in Force —> Bond lifetime decreases



Binding of Dynein motor to MT filament

Kunwar et.al, PNAS (2011)



P-selectin binding to endothelial cells

Prezhdo et.al, Acc. Chem. Res (2013)

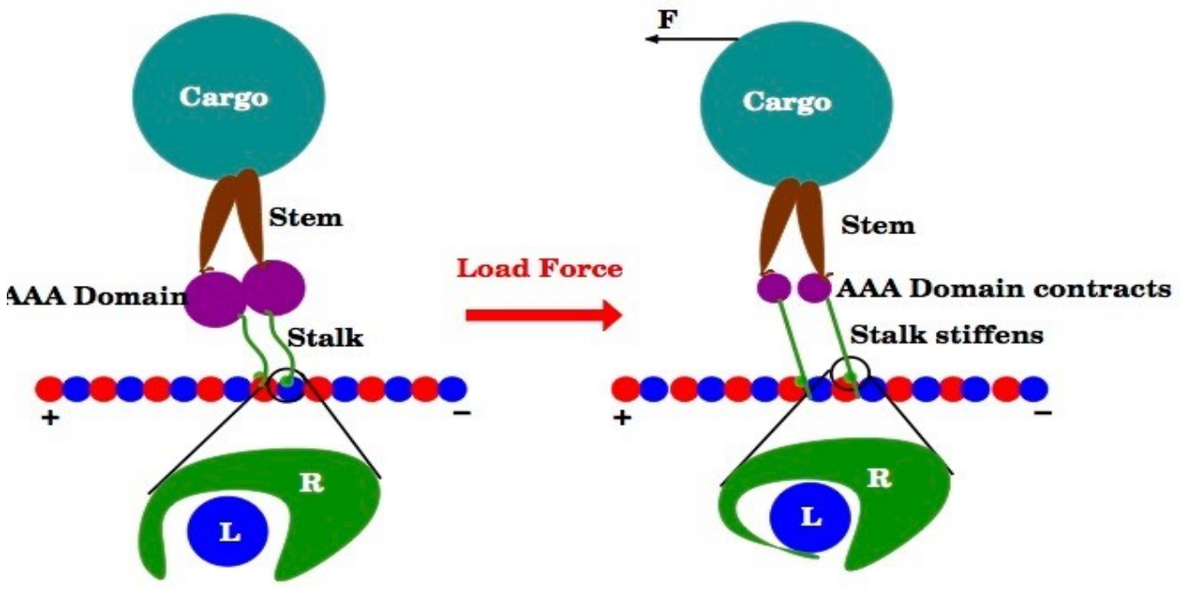
Modeling catchbond in dynein motor

Threshold Force Bond Deformation (TFBD) model

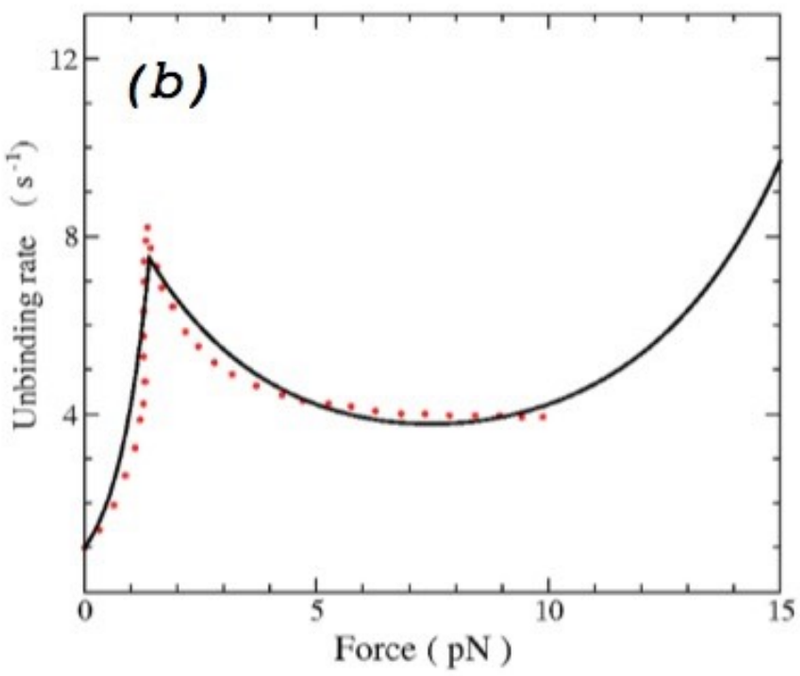
- **Allosteric deformation results in catchbonding**
- **Catch-bonding activates beyond a threshold force**

Unbinding rate: $\varepsilon(f) = \varepsilon_o \exp[-E_d(f) + f/f_d]$

$$E_d(f) = \Theta(f - f_m)\ \alpha \left[1 - \exp\left(-\frac{f - f_m}{f_o}\right)\right]$$



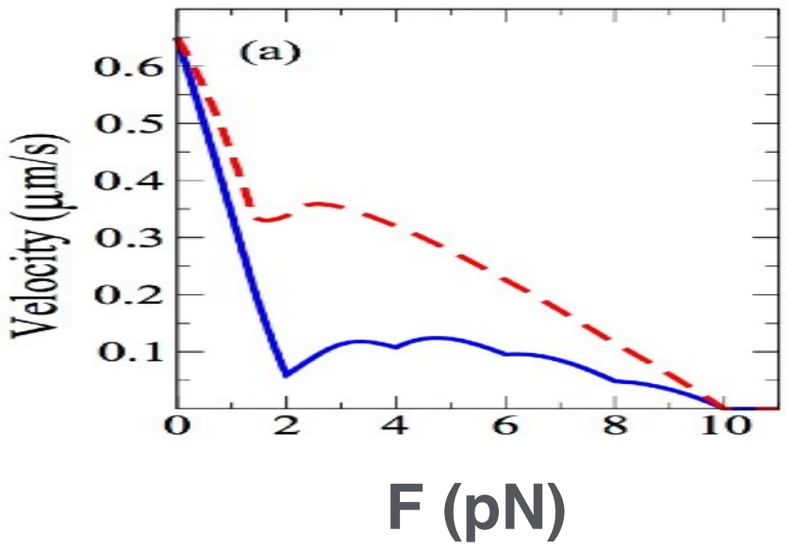
A. Nair, S. Chandel, M. Mitra, SM & A Chaudhuri PRE (2016)



Experiment: Kunwar, et.al , PNAS (2011)

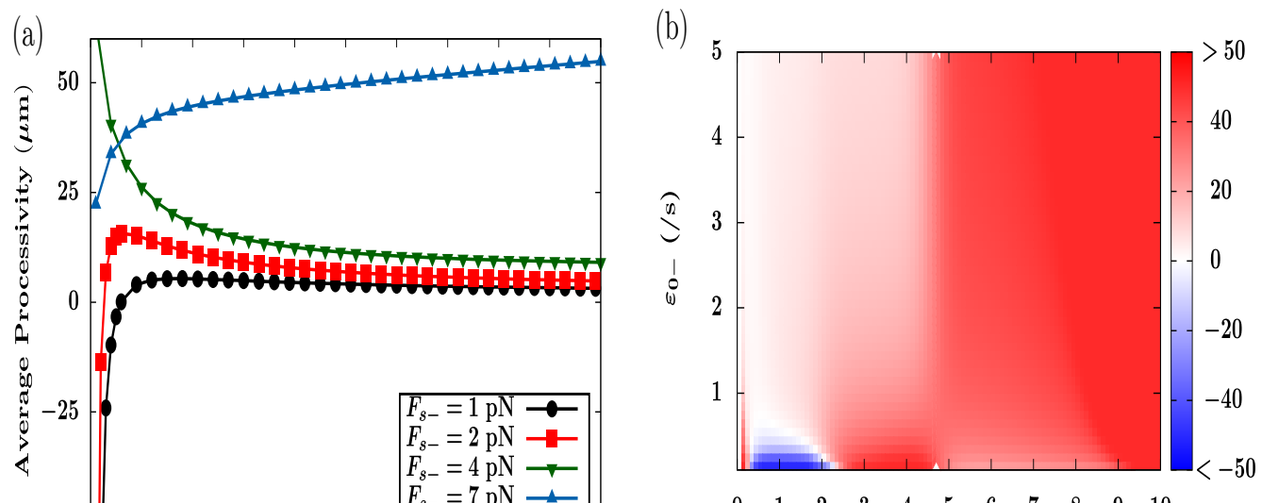
Manifestation of catchbond within cell

- **Anamolous Unidirectional transport**

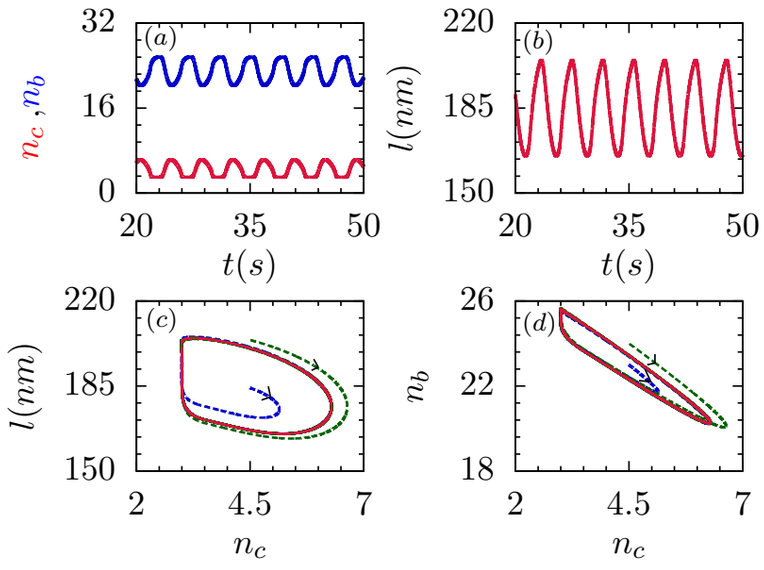


A.Nair, S. Chandel, M.K. Mitra, SM & A. Chaudhuri (PRE, 2016)

- **Regulation of bidirectional transport & resolution of Paradox of Codependence**



Puri et.al . Phys. Rev. Res (2019)

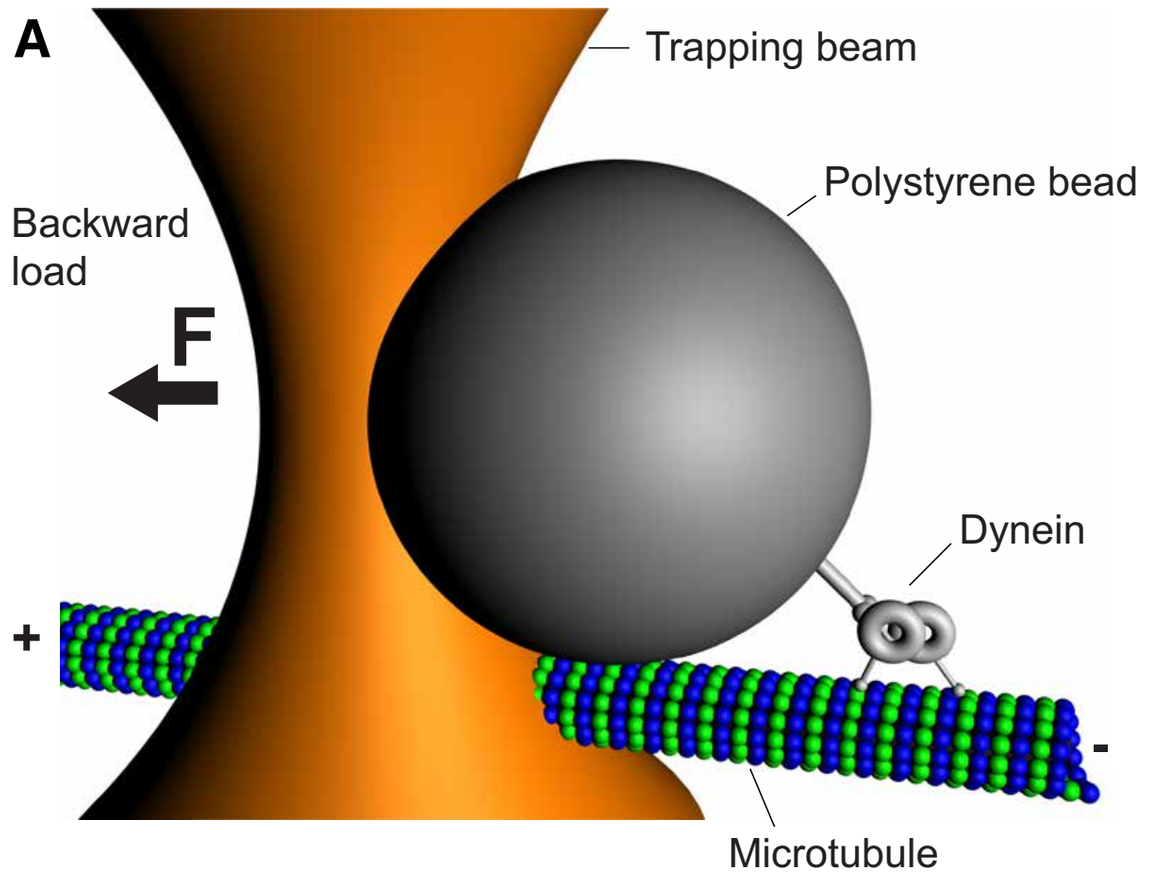


- **Generation of spontaneous oscillation in motor-filament complexes**

N. Sundararajan, S. Guha, M.K. Mitra & SM (Biophys. J, 2021)

QUESTION

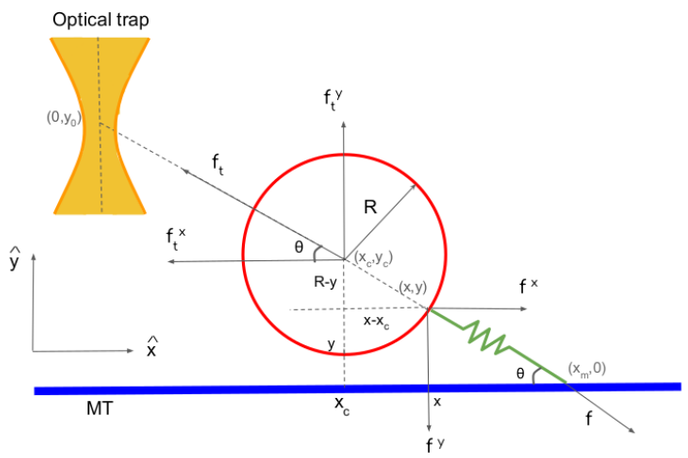
- **How does catchbonding affect transport characteristics in optical trapping assay (Variable force ensemble) ?**



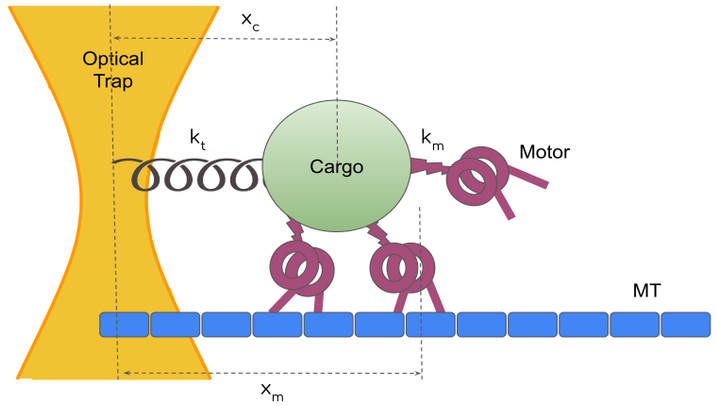
Brenner et.al , Sci. Adv. 6 (2020)

Cellular cargo transport in optical trap

2D schematic



1D schematic



Force balance :

$$k_t x_c = k_m \Theta(l_m - l_o)\left[(x_m - x) - l_o \frac{(x - x_c)}{R}\right]$$

$$k_t(y_o - y_c) = k_m \Theta(l_m - l_o)\left[y - l_o \frac{(y_c - y)}{R}\right]$$

$$(x - x_c)^2 + (y - y_c)^2 = R^2$$

$$tan\theta = \frac{y}{x_m - x} = \frac{y_c}{x_m - x_c}$$

Force balance : $k_t x_c = \Theta(x_m - x_c - l_o) k_m (x_m - x_c - l_o)$

Force on motor : $f(t) = k_t x_c(t) = \Theta(v_o t - l_o) f_s \left[1 - \exp\left(-\frac{k_t k_m (v_o t - l_o)}{(k_t + k_m) f_s}\right)\right]$

Survival probability distribution: $S(t) = \exp\left[-\int_0^t \varepsilon dt'\right]$

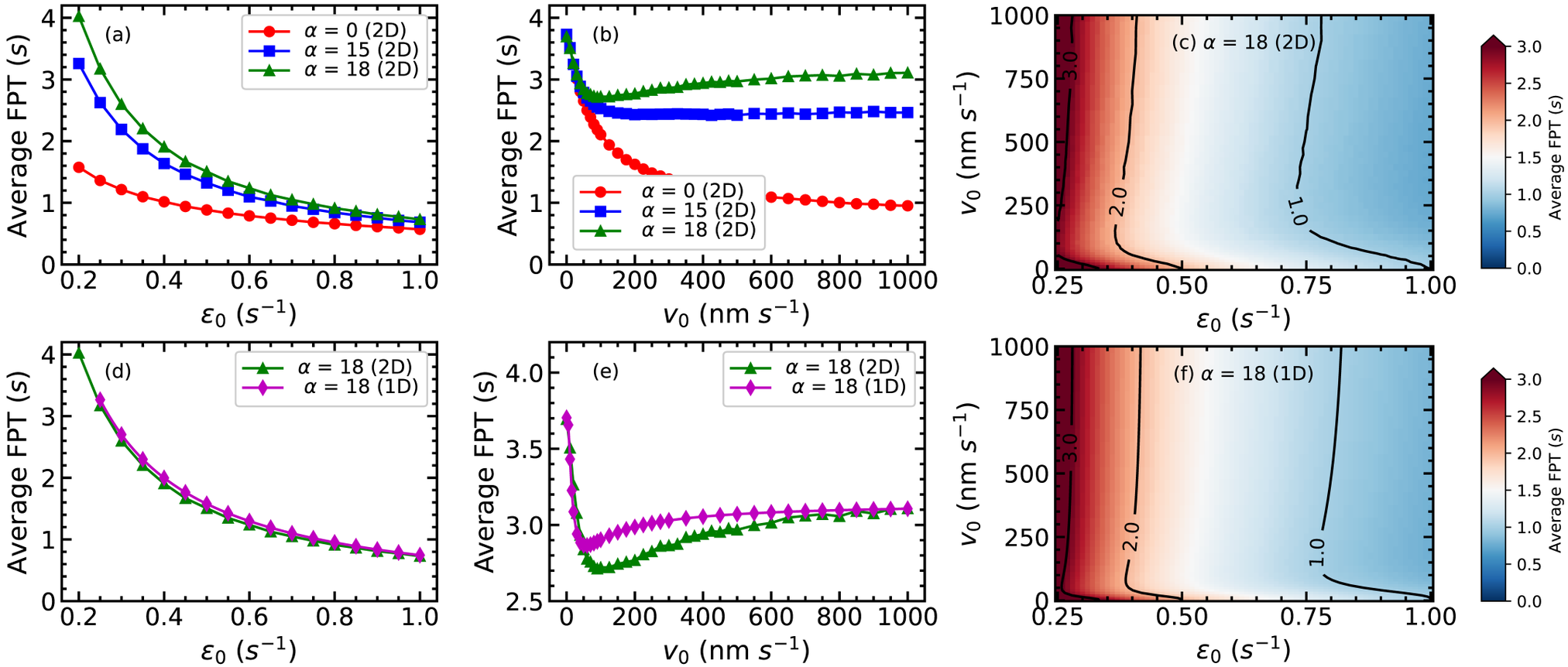
First passage time distribution : $F(t) = -\frac{dS}{dt}$

Assumptions:

- Linear Force-Velocity Relation : $v_m = v_0(1 - f/f_s)$
- Zero backward velocity in superstall condition

Transport by single motor in optical trap

Average First Passage time

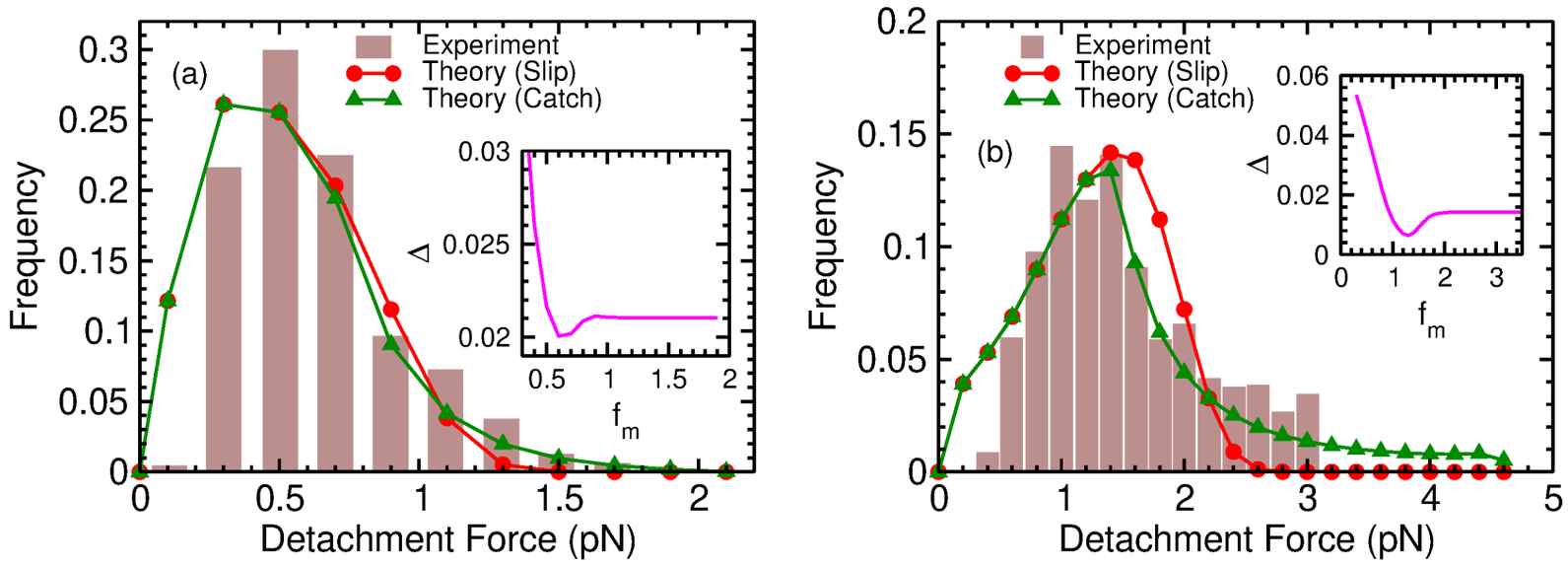


- **Non-monotonic behaviour of FPT as a function of v**

Detachment force distribution

Comparison between theory and experiments

Brenner et.al , Sci. Adv. 6 (2020)



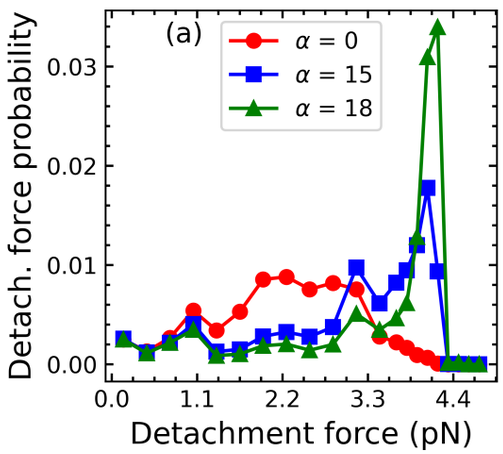
- **Theoretical distribution which incorporates catchbonding exhibits good match with the experimental curve**

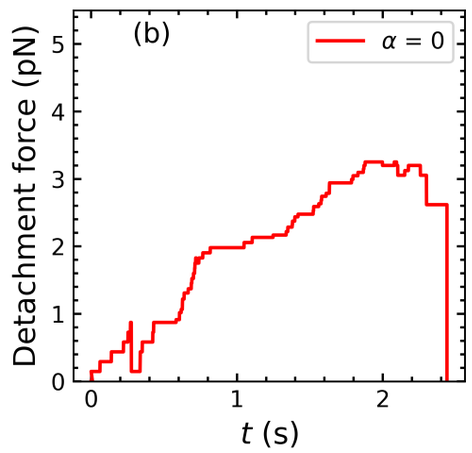
- **The catchbond force scale f_m has to be lower than maximum stall force f_s**

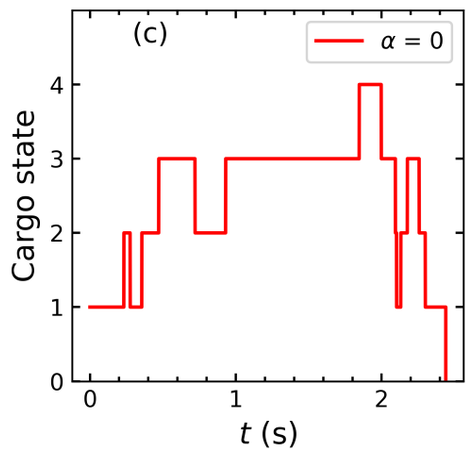
- **Provides an estimate of the catchbond force scale f_m :**

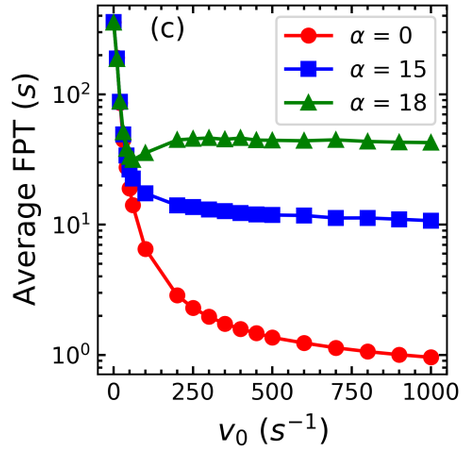
  (Obtained from least square fit of deviations from experimental curve)

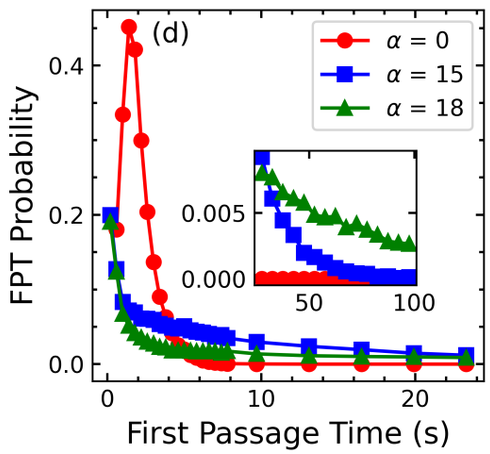
Effects of catch bond on transport by multiple motors

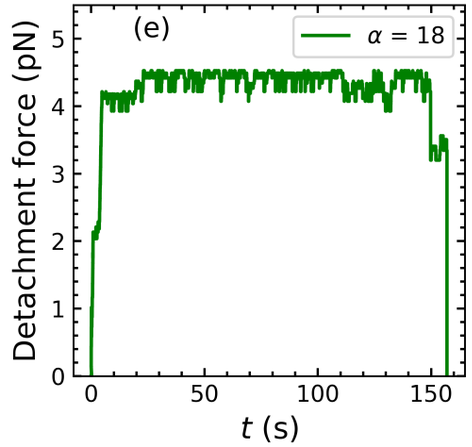


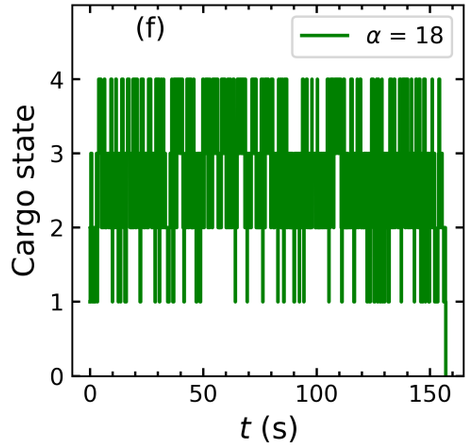


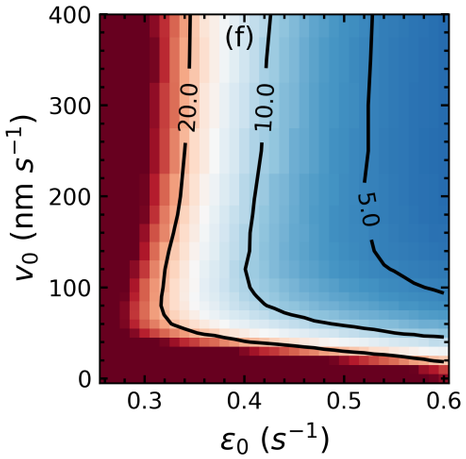






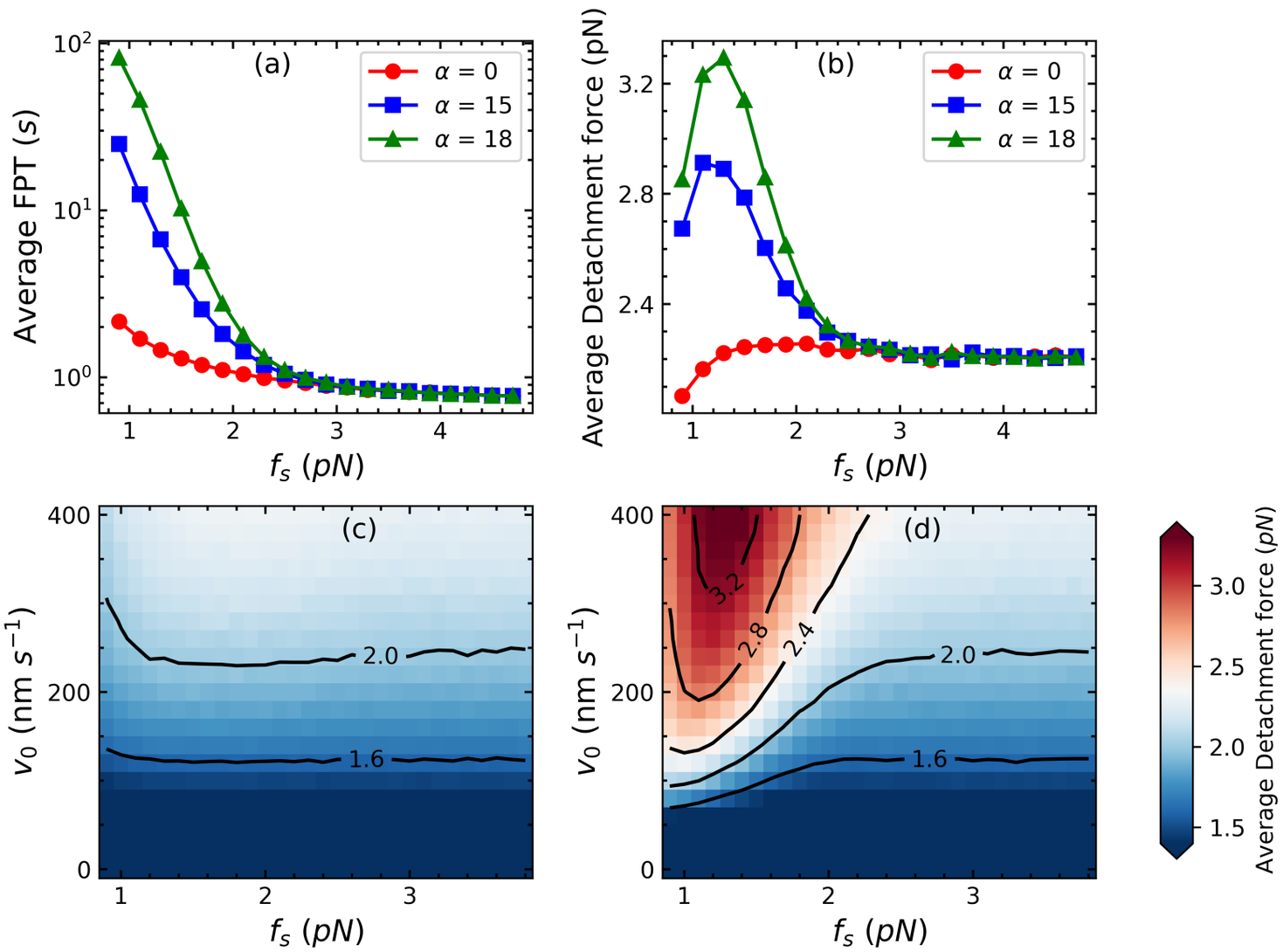






- **Catchbonding leads to higher FPT**
- **Non-monotonic behaviour of FPT as a function of motor velocity**

Effects of varying stall force on average FPT & detachment force



- **Non-monotonic behaviour of FPT as a function of stall force**

SUMMARY AND OUTLOOK

- **Catchbonding provides means for regulating transport & manifests itself in transport characteristics in optical trapping assays.**

- **Non-monotonic behaviour of FPT as a function of velocity & stall force**

- **Model with catchbond exhibits good match with experimental detachment force characteristics**

- **Provides a way of estimating the catchbond force scale f_m**

N. Sundararajan, S. Guha , SM & M. Mitra, Soft Matter, 20, 566 (2024)

How stochastic (un)binding of motors attached to bead in optical trap can be utilized to function as stochastic heat engine ?