Microtubule reorientation driven by severing: a competition model

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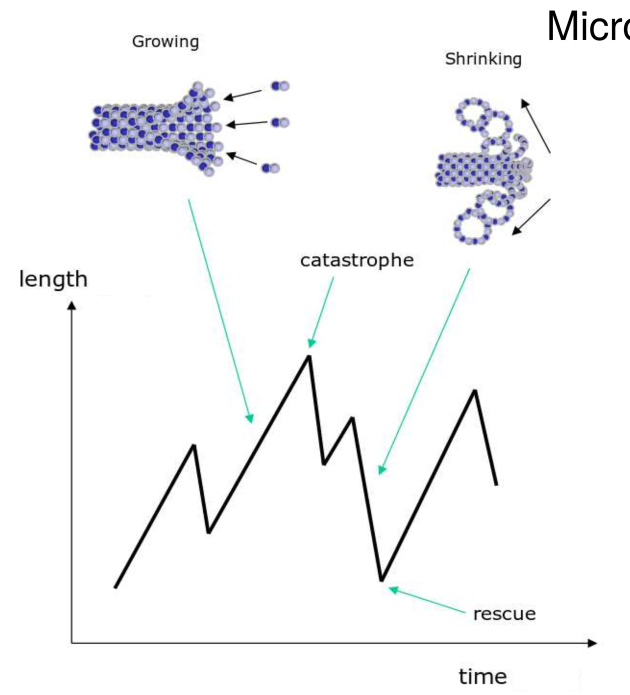
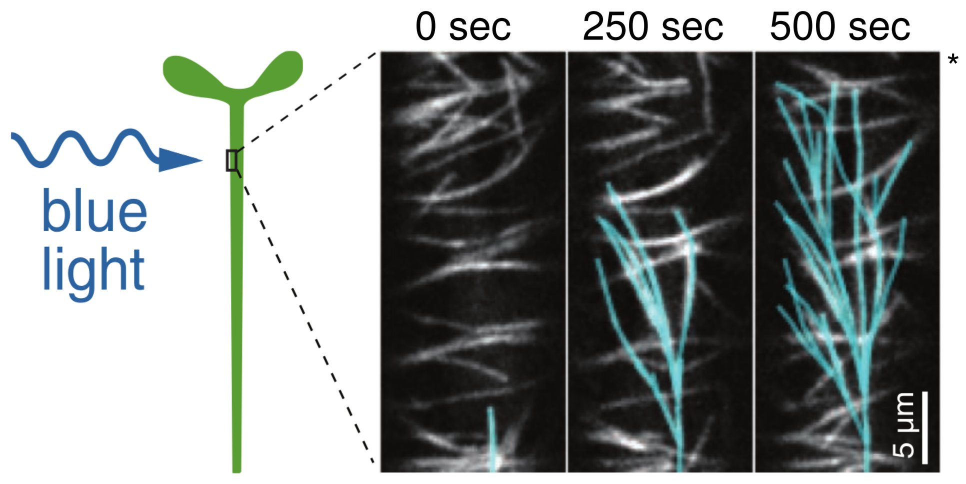
AMOLF physics of functional complex matter

INTRODUCTION

Microtubules are very dynamic polymers, and they play a very important role in the organization of cellular cytoskeleton.



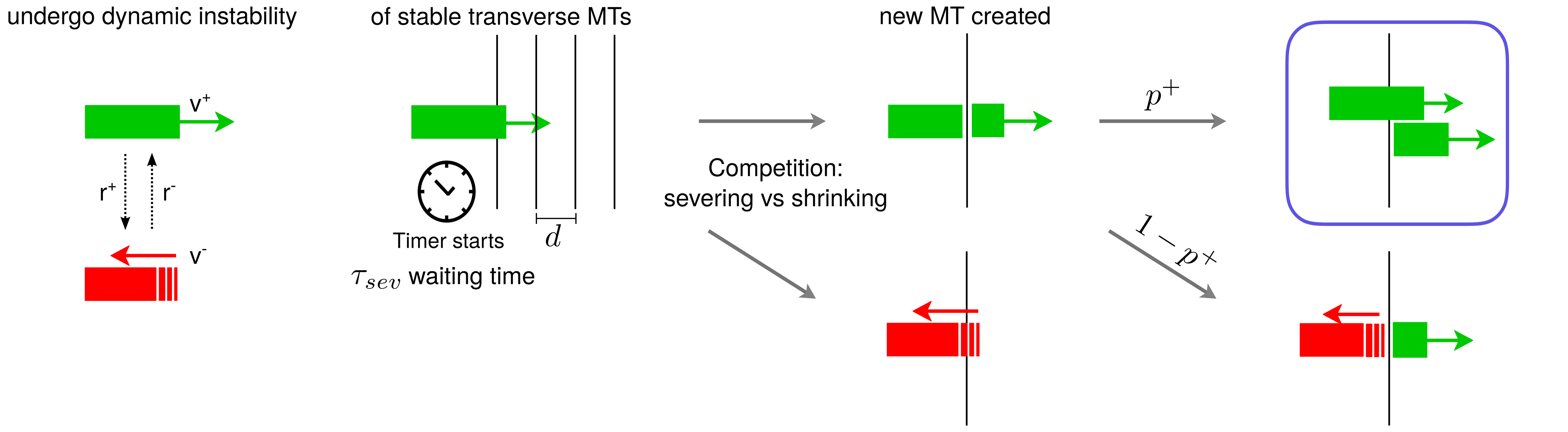
- In growing cells of plant axis, blue light causes a 90° reorientation of cortical microtubule arrays.
- Katatin is recruited at MT crossovers, and severs MTs. A fraction of newly created plus-end is stabilized and immediately grows. The repetition of the process creates, in some mutants, an amplification in the number of longitudinal MTs.

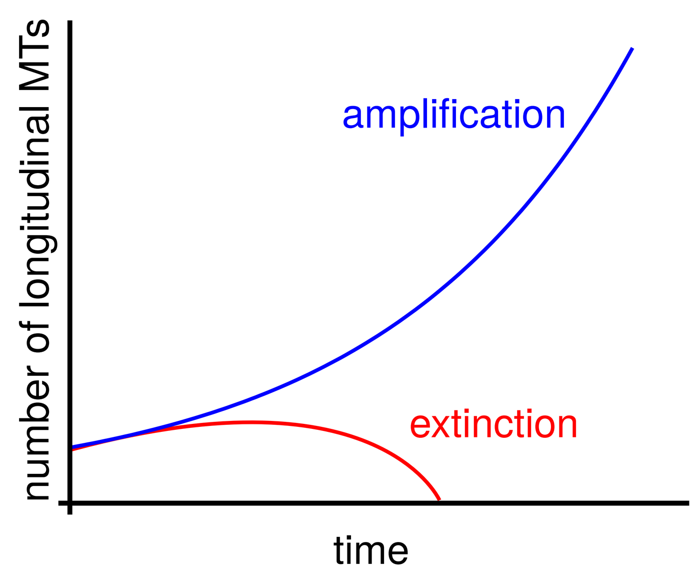


Goals:

- theoretically and computationally describe the amplification of the number of longitudinal MTs,
- identify the quantities that make such an amplification happen, through the search for critical relations between model's parameters.

THE MODEL





RESULTS

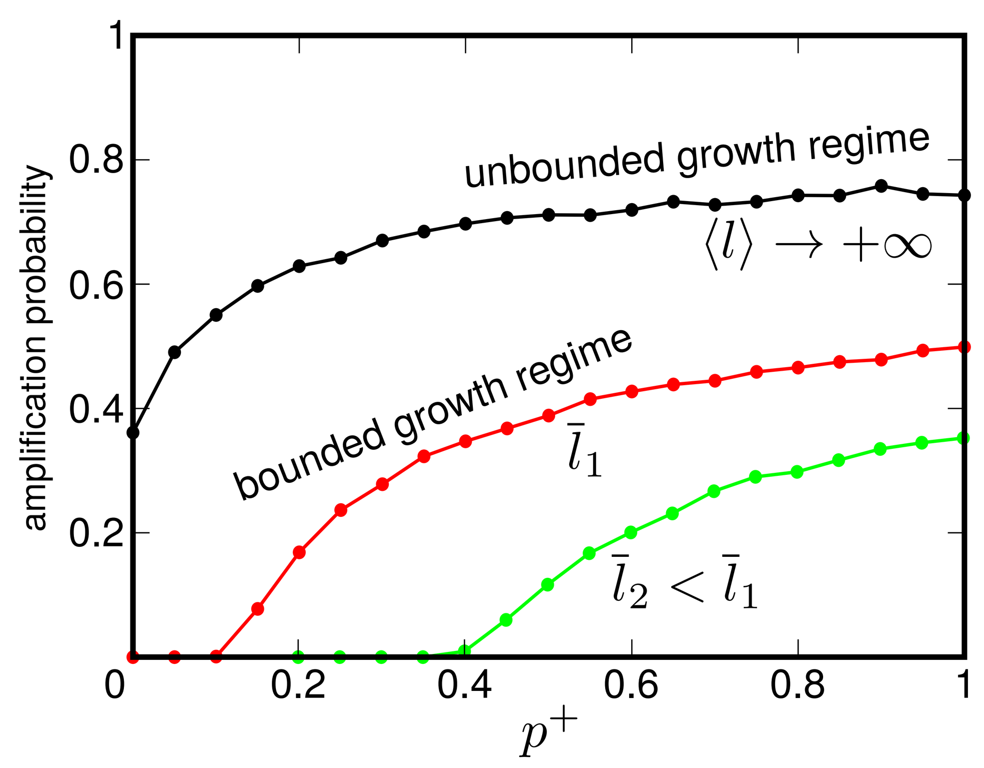
If: $v^+r^- - v^-r^+ > 0$, MTs are in the unbounded growth regime and their mean length grows in time as

$$\langle l(t) \rangle = \frac{v^+r^- - v^-r^+}{r^+ + r^-} t.$$

If: $v^+r^- - v^-r^+ < 0$, MTs are in the bounded growth regime and their mean length is limited in time

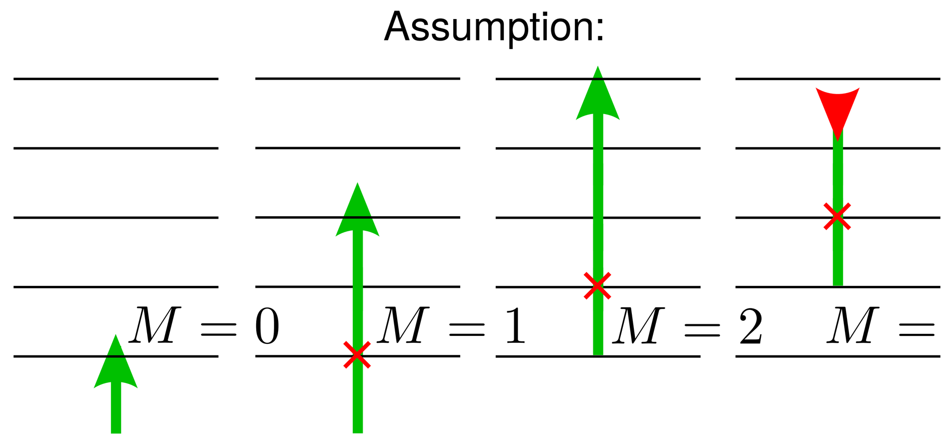
$$\bar{l} = \left(\frac{r^+}{v^+} - \frac{r^-}{v^-} \right)^{-1}.$$

In the unbounded growth regime the amplification always happens, but in the bounded growth regime it happens only if the probability of rescue after severing p^+ is great enough.



FINDING THE CRITICAL POINT

Amplification in the bounded growth regime
Assumption:



$M \equiv$ number of MTs generated by a newly-created MT during its lifetime. Must be greater than 1 in order to have amplification.

$$M = p^+M^+ + (1-p^+)\,qM^+$$

$M^+ \equiv$ number of MTs generated by a newly-created MT during its lifetime that was born in the growing state.

$q \equiv$ probability that a MT with initial length l=d and in the shrinking state recovers length l=d **before** shrinking back to length l=0.

$$q = \frac{\left(e^{d/\bar{l}}-1\right)\frac{r^-v^+}{r^+v^-}}{e^{d/\bar{l}} - \frac{r^-v^+}{r^+v^-}}$$

The critical probability of rescue after severing, can be written as a function of q and M^+.

$$p_c^+ = p^+(M=1) = \frac{1-qM^+}{(1-q)M^+}$$

Amplification never happens if: $M^+ < 1$

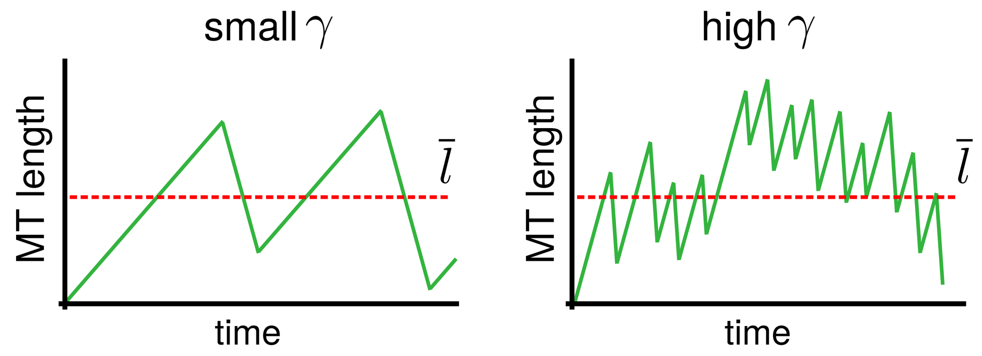
Amplification always happens if: $M^+ > \frac{1}{q}$

How to control M^+?

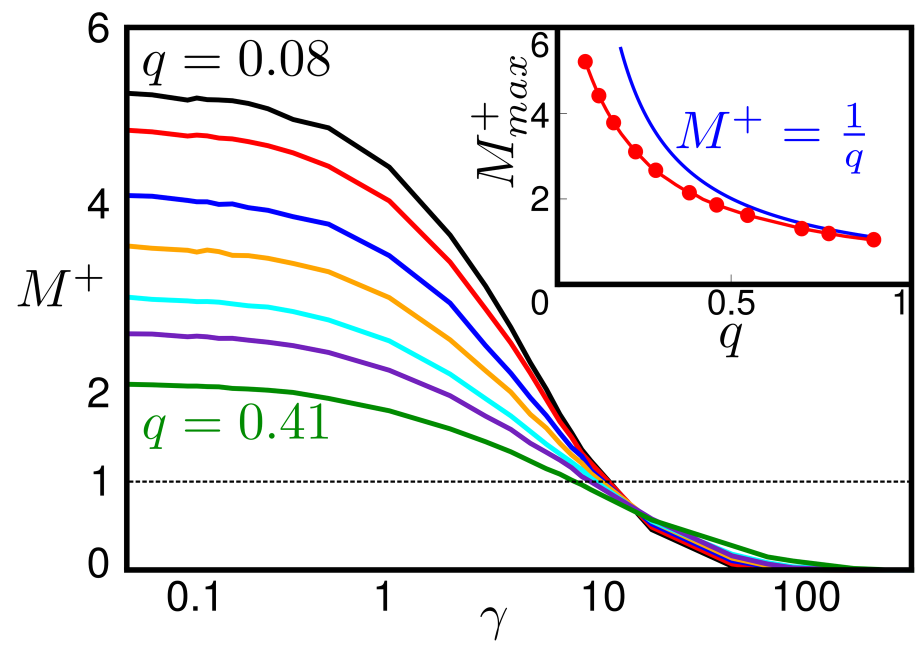
$$M^+ = M^+\left(v^+, v^-, r^+, r^-, d, \tau_{sev}\right)$$

Rescale dynamic parameters with the factor $\gamma \in (0, +\infty)$

$$\begin{pmatrix} v^\pm \\ r^\pm \end{pmatrix} \to \begin{pmatrix} \gamma v^\pm \\ \gamma r^\pm \end{pmatrix}$$



Low dynamic instability (small γ) at fixed q, corresponds to higher propensity to generate new MTs. As $\gamma \to 0$ M^+ tends to an asymptote which is smaller than $\frac{1}{q}$.



CONCLUSIONS

- MTs in the unbounded growth regime always have a finite amplification probability, while in the bounded growth regime the amplification can happen only if the probability of rescue after severing p^+ is greater than a critical value.
- M^+ plays a crucial role in the definition of the critical value for p^+. For fixed mean MT length, M^+ can be tuned by changing q and the dynamic instability of the MT.

OUTLOOK

- Find an analytical expression for M^+.
- Try to experimentally prove the existence of criticality for the amplification of the number of longitudinal MTs.

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