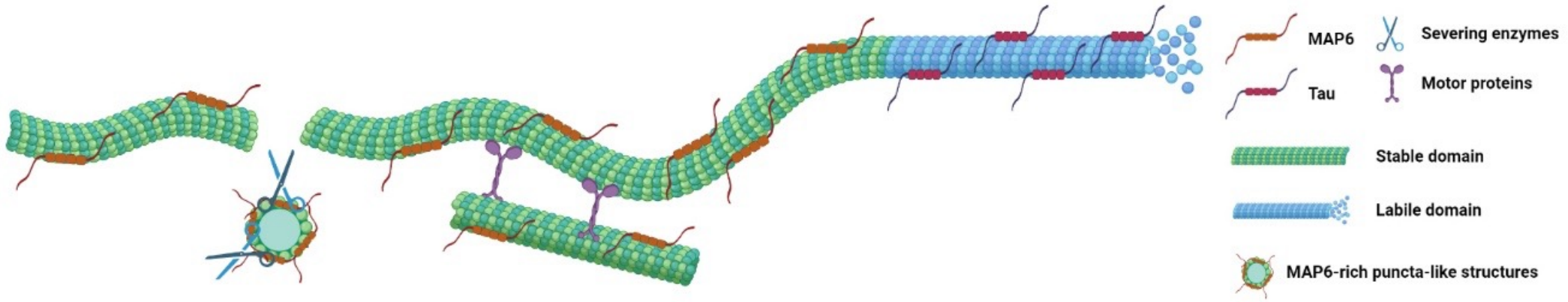
Computational model of tau and map6 organization along MT



Model features:

- MT treated as 1D array of discrete binding sites
- Tau and map6 each stochastically bind/unbind with tunable rates. Only one MAP can occupy any binding site.

Hypothetical features (can be turned on/off to test separately):

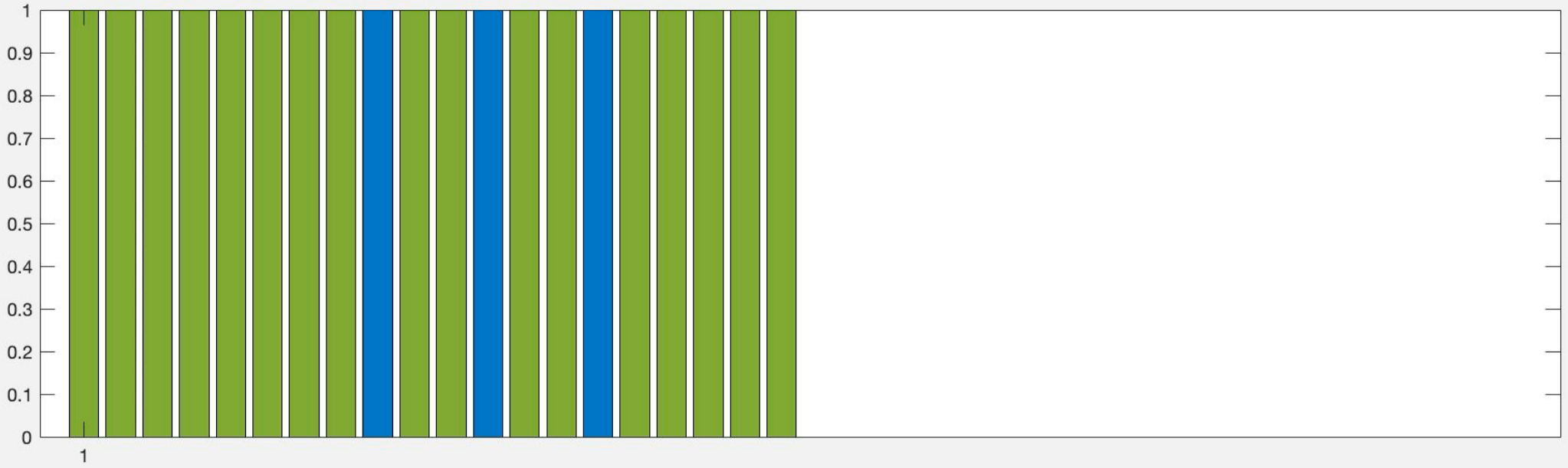
1. Stability of MT depends on presence of tau near plus-end.
    - When tau is bound near plus-end, MT is dynamic. (Grows/shrinks, following stochastic dynamic instability model). When tau is not bound near plus-end, MT is stable (static length).
2. Scaffolding effect: tau and map6 each more likely to be bound at sites adjacent to other MAPs of the same type.

Key simulation outcome:

With mechanism 1 (plus-end tau regulates stability): tau and map6 organization into labile and stable domains is an emergent pattern, arising because it is reinforced by growth of tau-decorated plus-ends. (Kind of a Brownian ratchet). Mechanism 2 by itself cannot account for emergence of organized labile/stable domains, but could help reinforce the organization.

Sample simulation:

Conditions: Tau binding rate faster than map6 binding, tau localized at plus-end promotes MT dynamics



Key: **Green** = no MAPs bound; **Blue** = map6 bound; **Purple** = tau bound

Tau and map6 organization into labile and stable domains is an emergent pattern, arising because it is reinforced by growth of tau-decorated plus-ends. (Kind of a Brownian ratchet). High variability in outcome (due to stochasticity of binding). Tau / map6 balance regulates distribution patterns and stability of MT.

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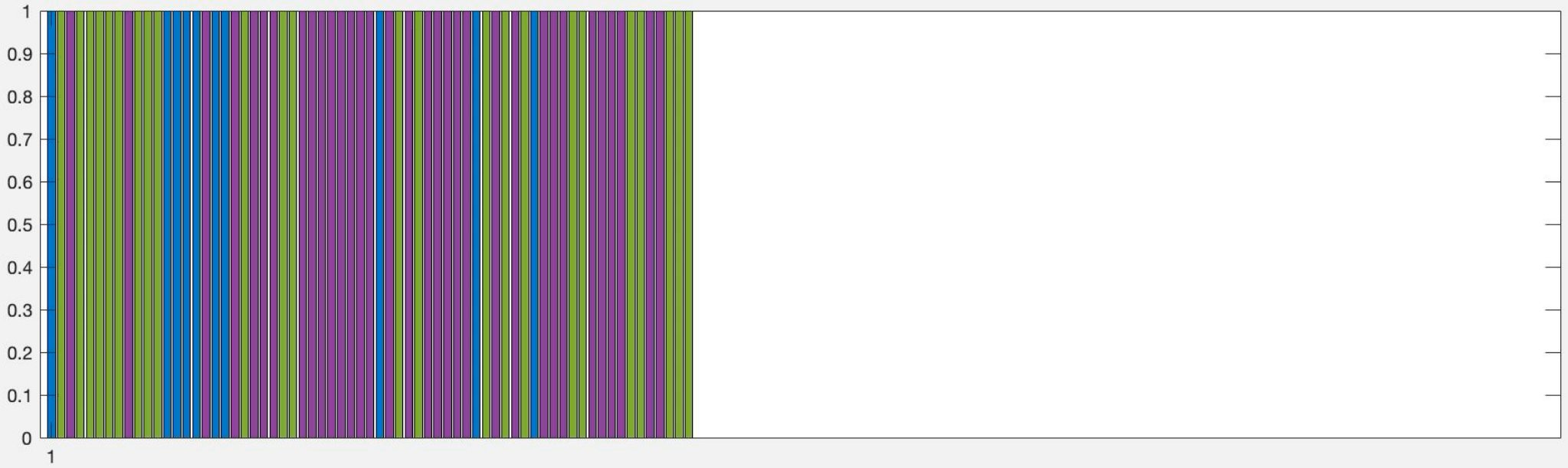

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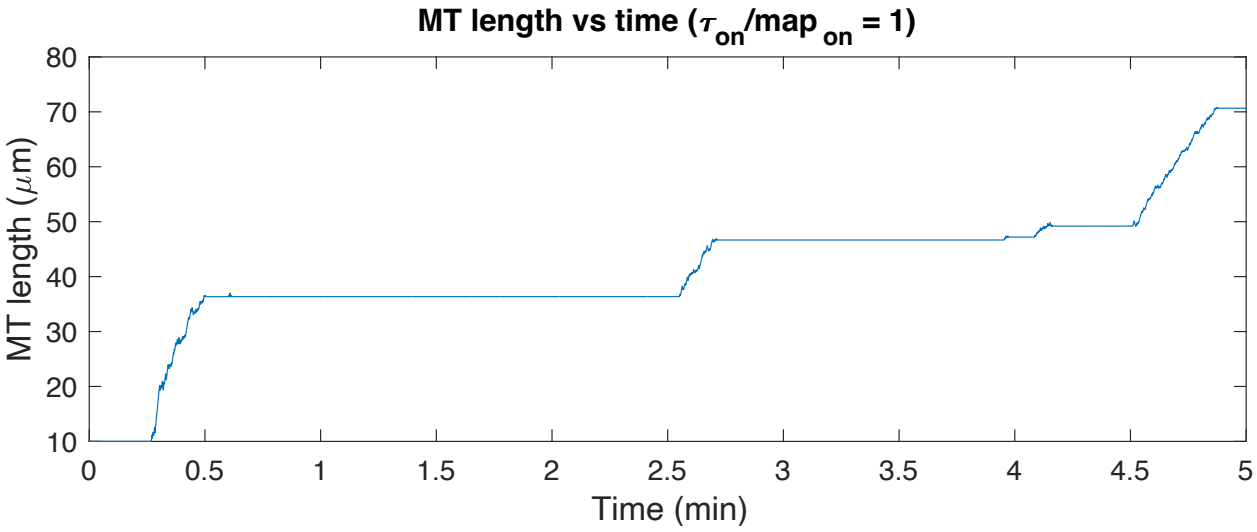
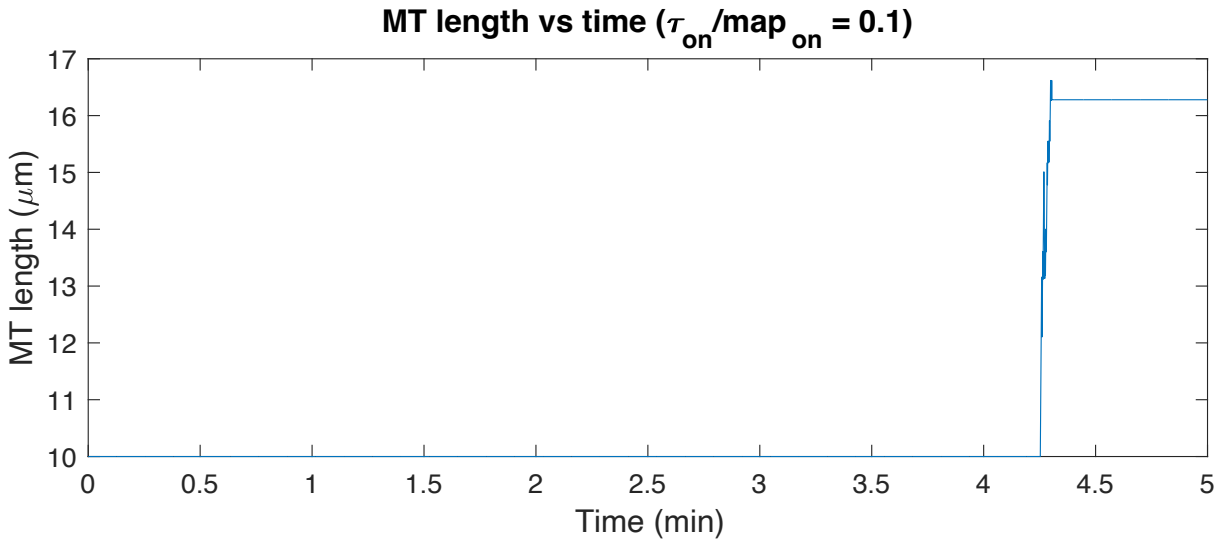
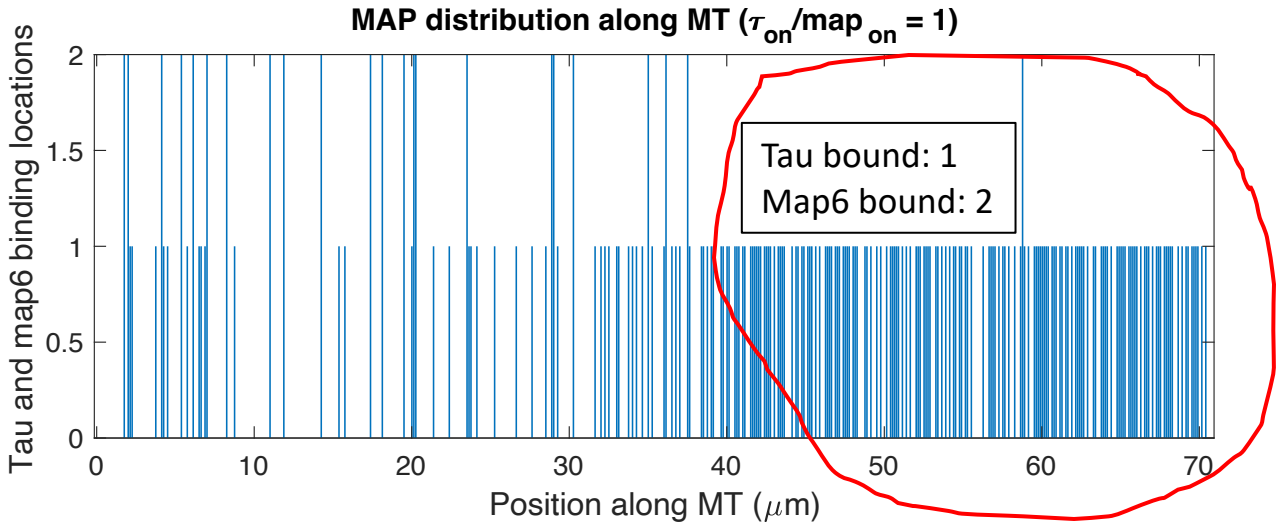
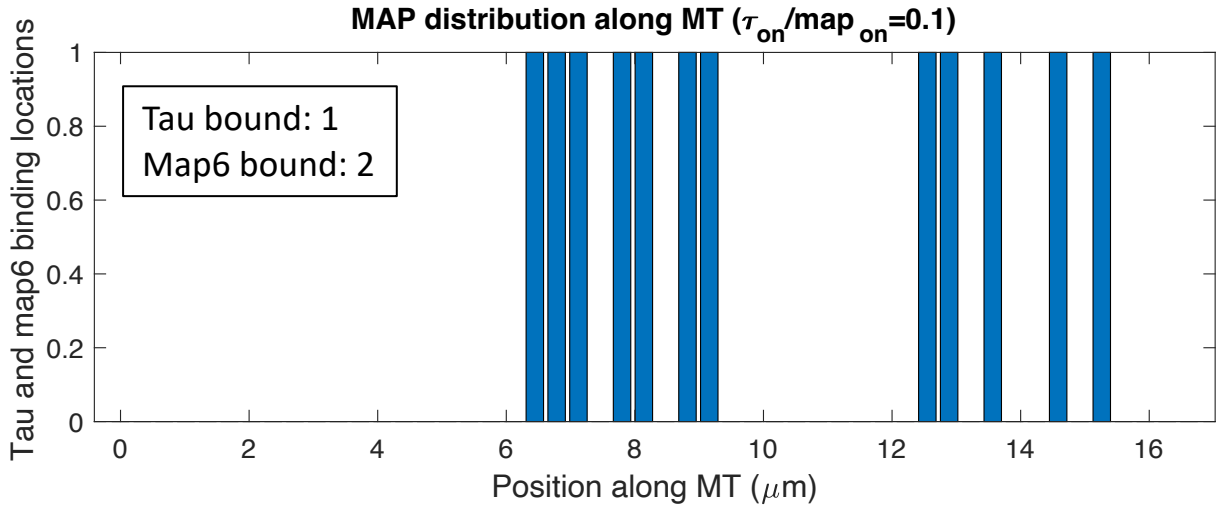
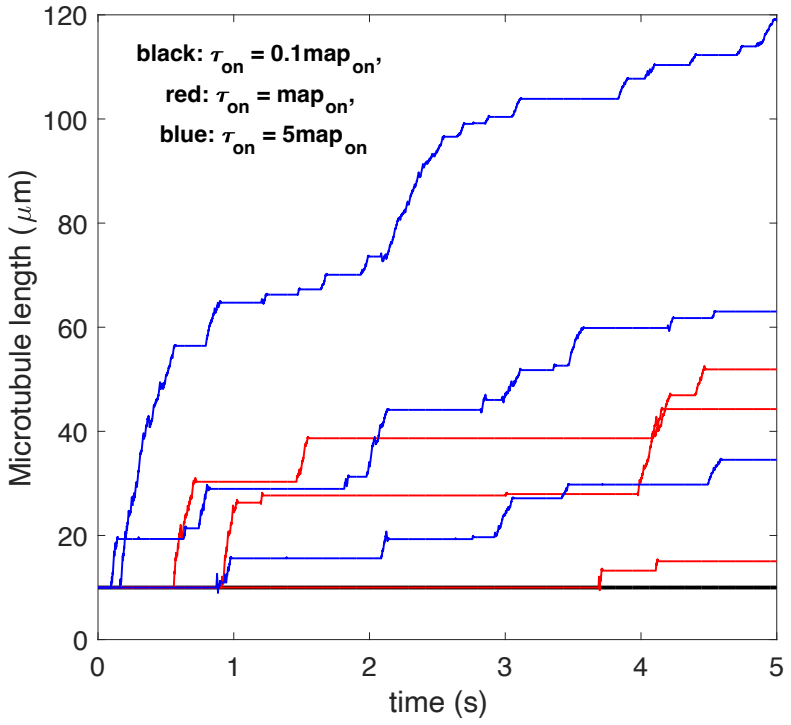


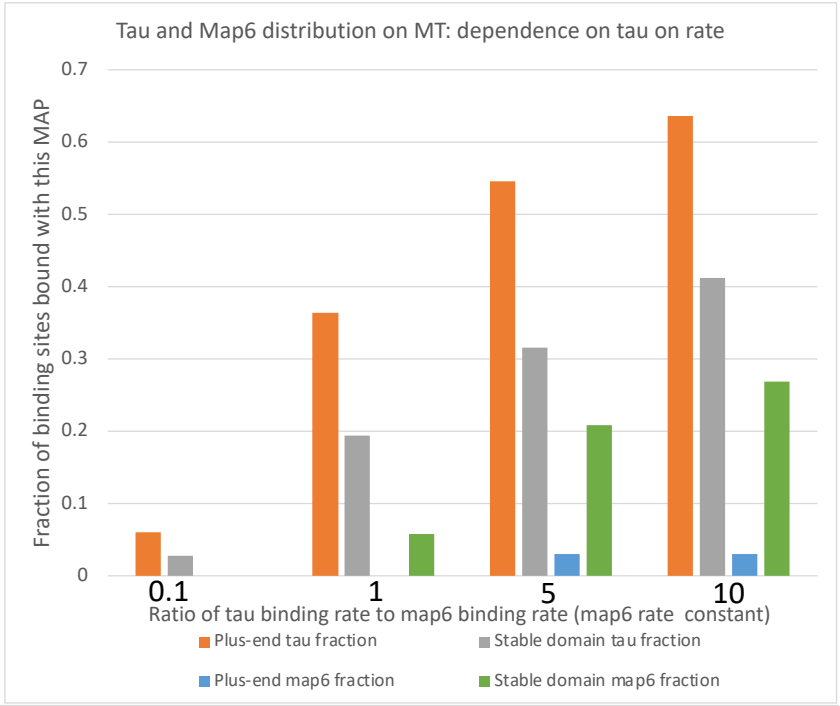


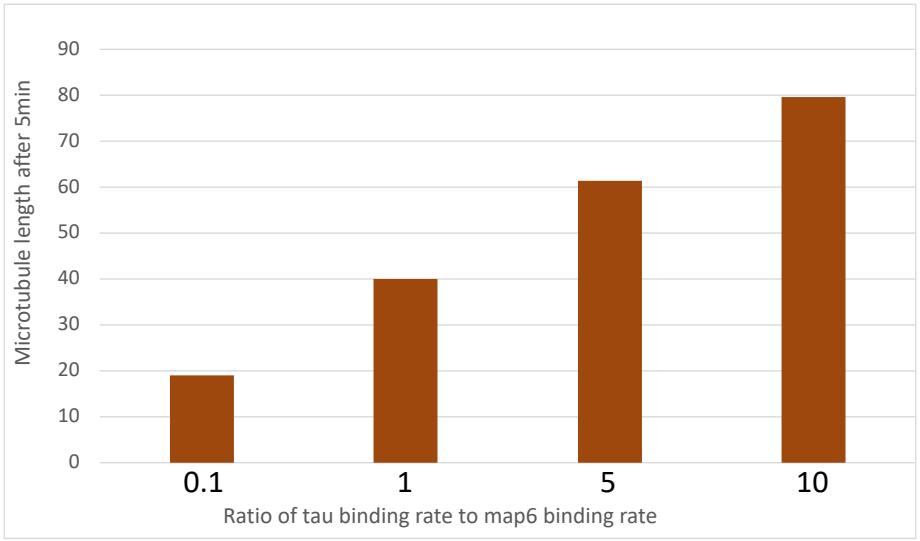


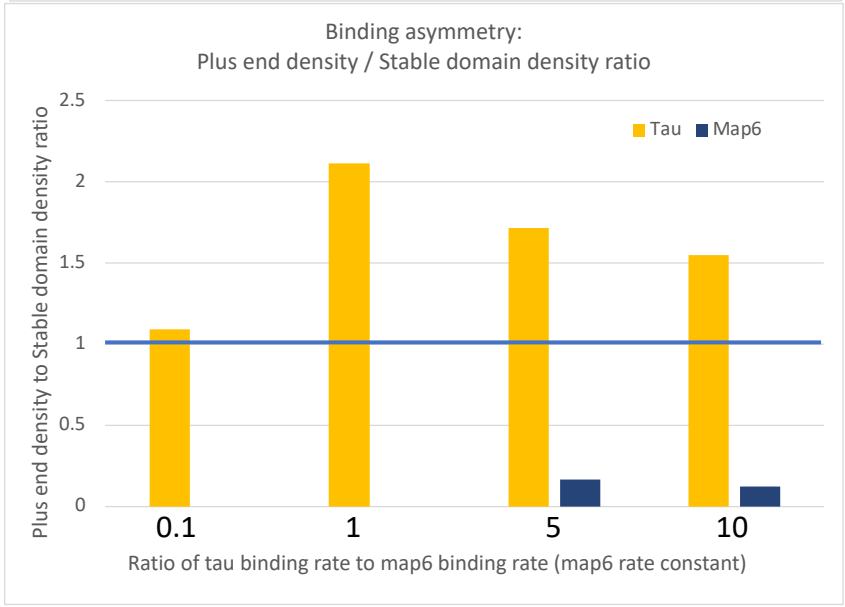


Dynamic MTs have emergent pattern of predominantly tau binding at plus end, map6 mostly binds away from plus-end.


black: τ_{on} = 0.1map$_{on}$,
red: τ_{on} = map$_{on}$,
blue: τ_{on} = 5map$_{on}$
Microtubule length (μm)
time (s)
0
20
40
60
80
100
120
0
1
2
3
4
5


Tau and Map6 distribution on MT: dependence on tau on rate
Fraction of binding sites bound with this MAP
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.1
1
5
10
Ratio of tau binding rate to map6 binding rate (map6 rate constant)
Plus-end tau fraction
Stable domain tau fraction
Plus-end map6 fraction
Stable domain map6 fraction


Microtubule length after 5min
0
10
20
30
40
50
60
70
80
90
0.1
1
5
10
Ratio of tau binding rate to map6 binding rate


Binding asymmetry:
Plus end density / Stable domain density ratio
Plus end density to Stable domain density ratio
0
0.5
1
1.5
2
2.5
Tau
Map6
0.1
1
5
10
Ratio of tau binding rate to map6 binding rate (map6 rate constant)