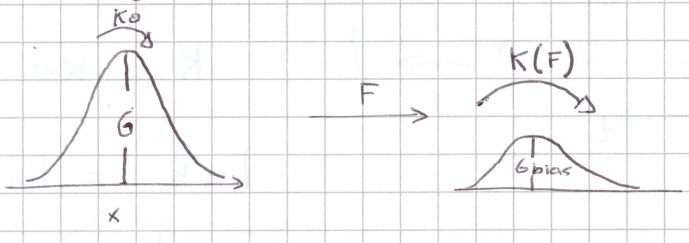
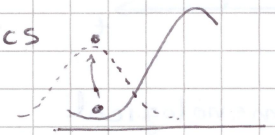
L5. # Non-equilibrium simulations

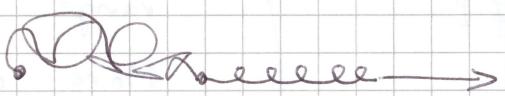
Reasons to apply external forces:

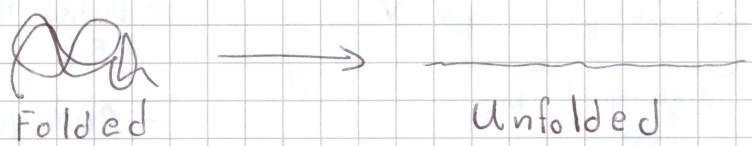
- Not to wait forever until something happens
- 

- Many biomolecules are mechanosensitive.
  - Muscle (titin) PNAS, 105 · 13385, 2008
  - Mechanosensitive channels, Ranade, Neuron, 87: 1162-2015
  - von Willebrand factor, Springer, Blood. 124: 1412 (2014)
- Compare directly with AFM && optical tweezer experiments

Some Types of non-eq. sims.

1. Umbrella sampling 
2. Flooding / metadynamics  Grubmüller, 52, 1995 PRE
3. Pulling simulations:

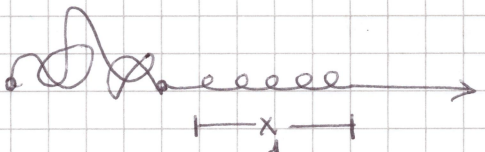




Advantage:
Compare to AFM or optical tweezers

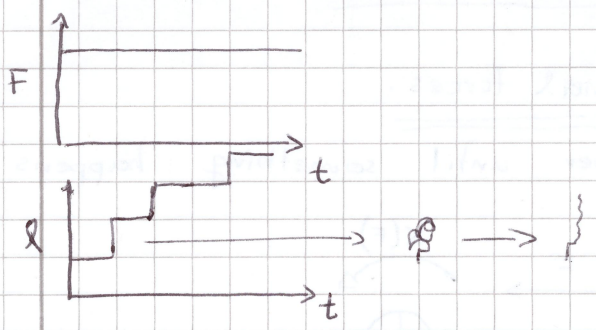
Types:

3.1 Constant force



variable to maintain F constant.

Observable:

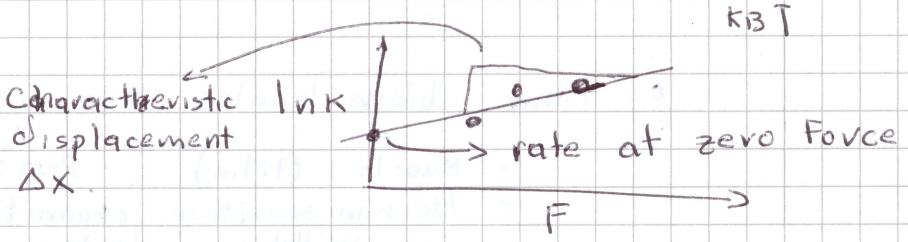


$K \rightarrow$ rate : # of transitions per time

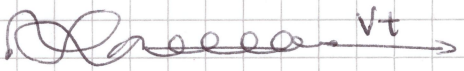
Bell Kinetics:

$$k = k_0 e^{F \Delta x / k_B T}$$

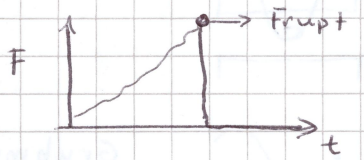
$$\ln k = \ln k_0 + F \frac{\Delta x}{k_B T}$$



3.2 Constant pulling velocity

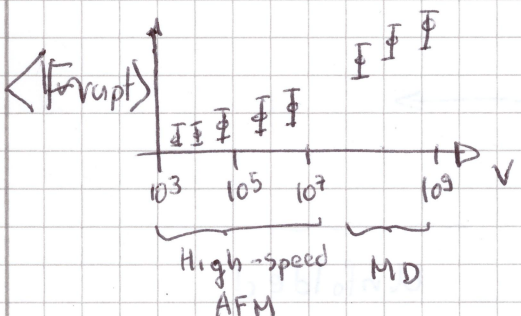


Observable rupture force



Phenomenological Approach

$$\langle F_{rupt} \rangle \sim \ln V$$



However it does not hold for an entire "V" range.

More general approaches

- Dudko Hummer Szabo PRL, 96, 108101, 2006
- Bullerjahn Sturm Kroy Nat Comms 5: 4463, 2014