Mathematical Cell Biology Graduate Summer Course

University of British Columbia, May 1-31, 2012

Leah Edelstein-Keshet

Microtubules, polymer size distribution and other balance eqn models

mprime

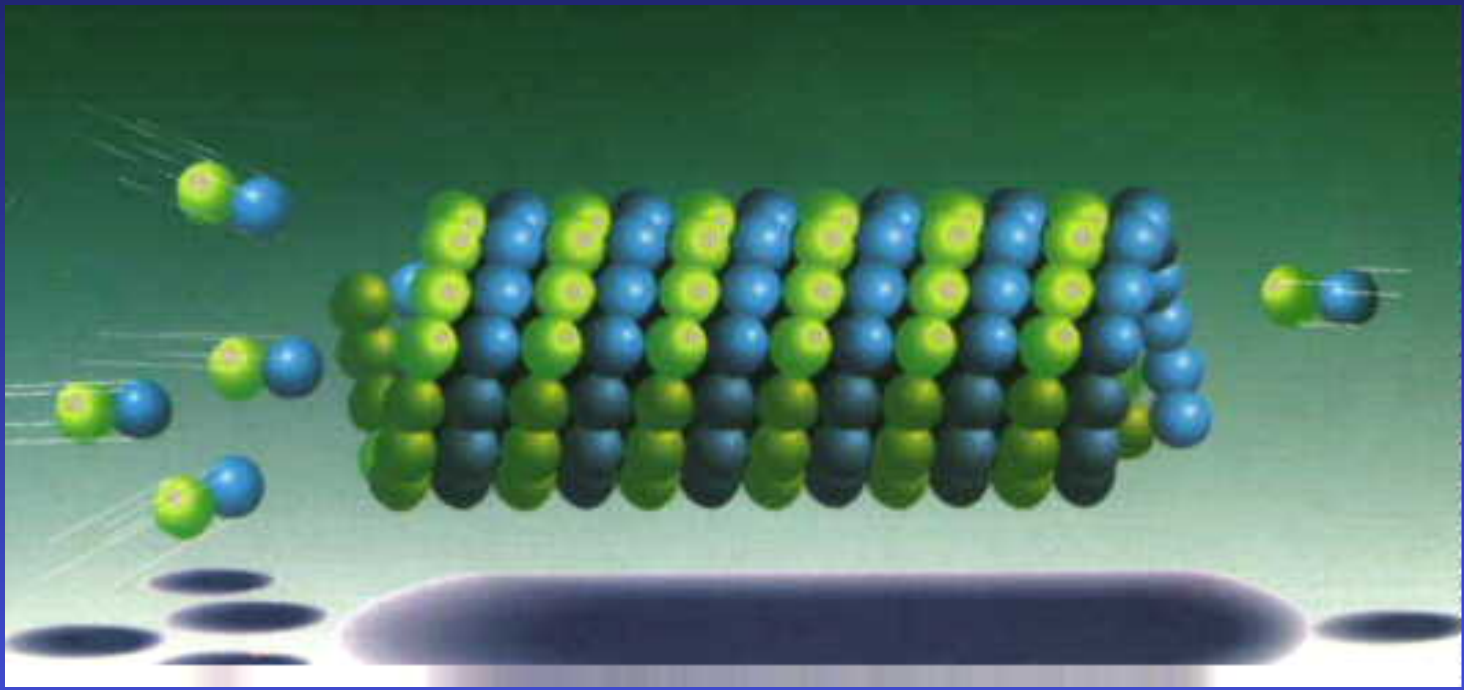
PIMS

www.math.ubc.ca/~keshet/MCB2012/

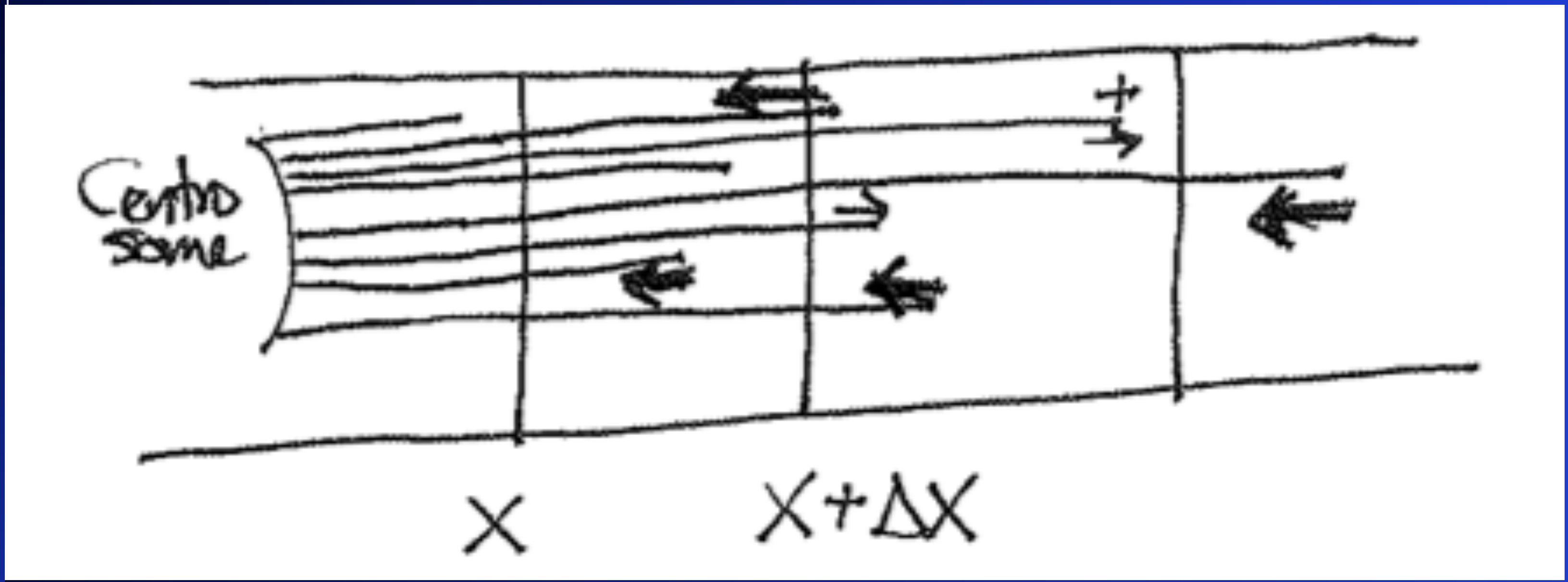
Microtubule (MT) dynamics

Actin filament:

Microtubule:



Growing and shrinking MT



Some Movies…..

http://www.youtube.com/watch?v=9iXoXzgmEXw

http://www.youtube.com/watch?v=PCI_GUHJJaY

MT dynamics

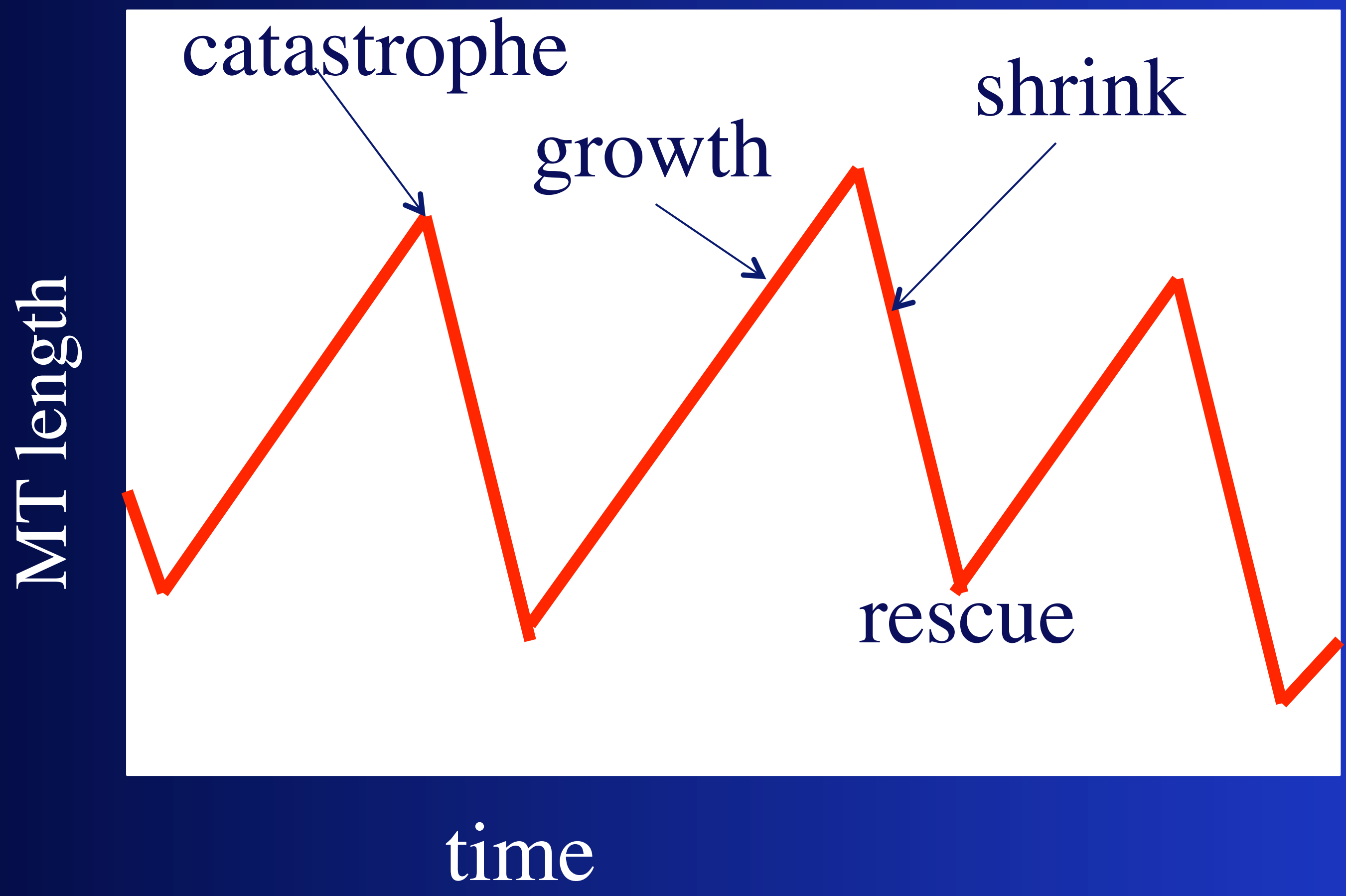
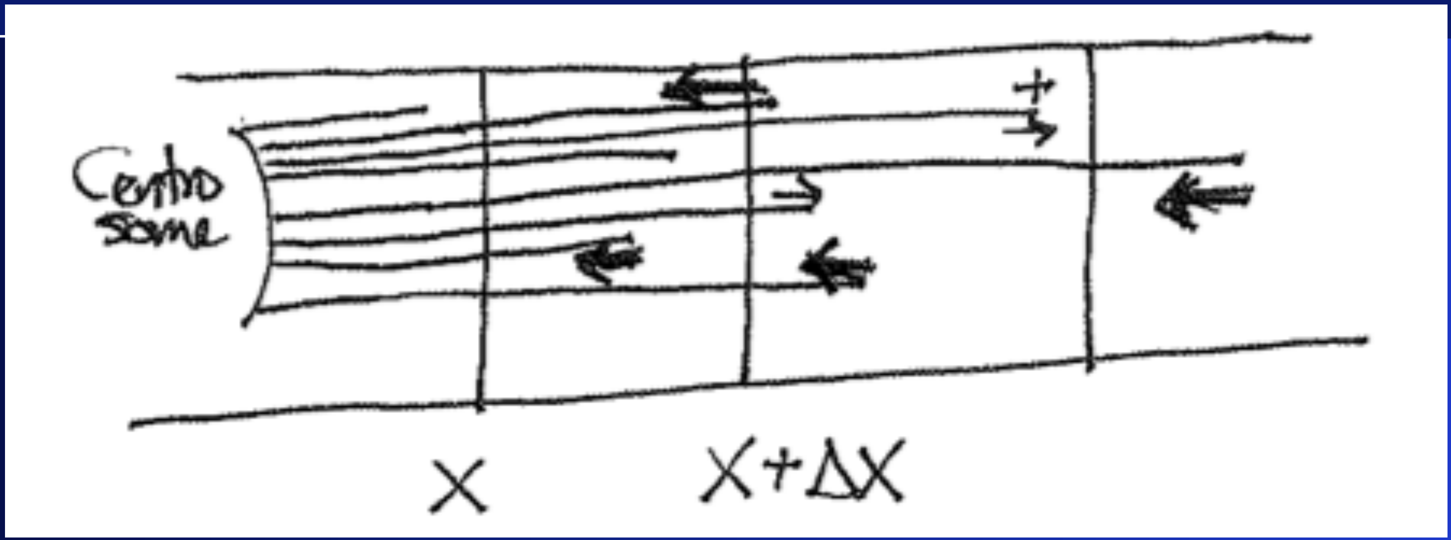
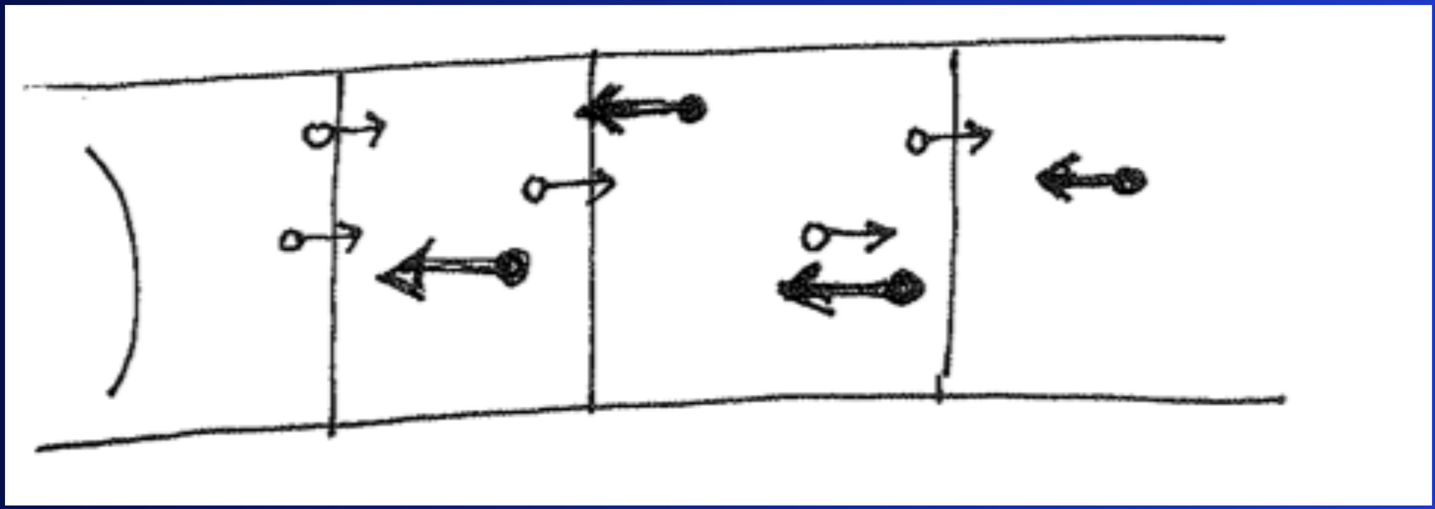


Figure adapted from

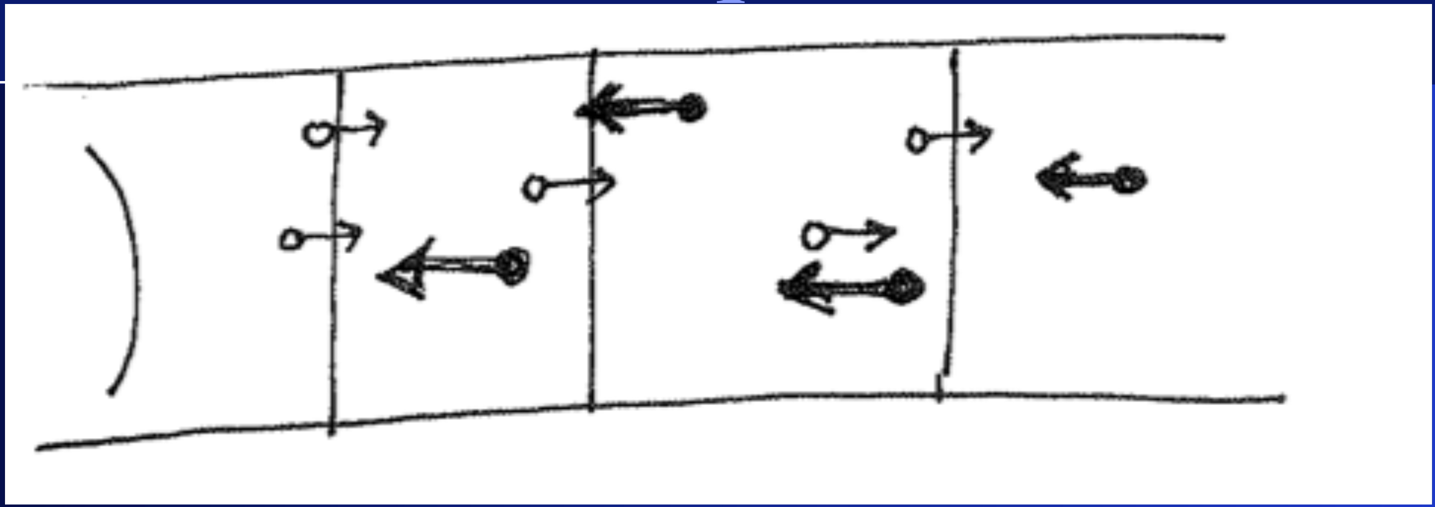
Janulevicius Biophysical Journal Volume 90 February 2006 788–798

Growing and shrinking tips





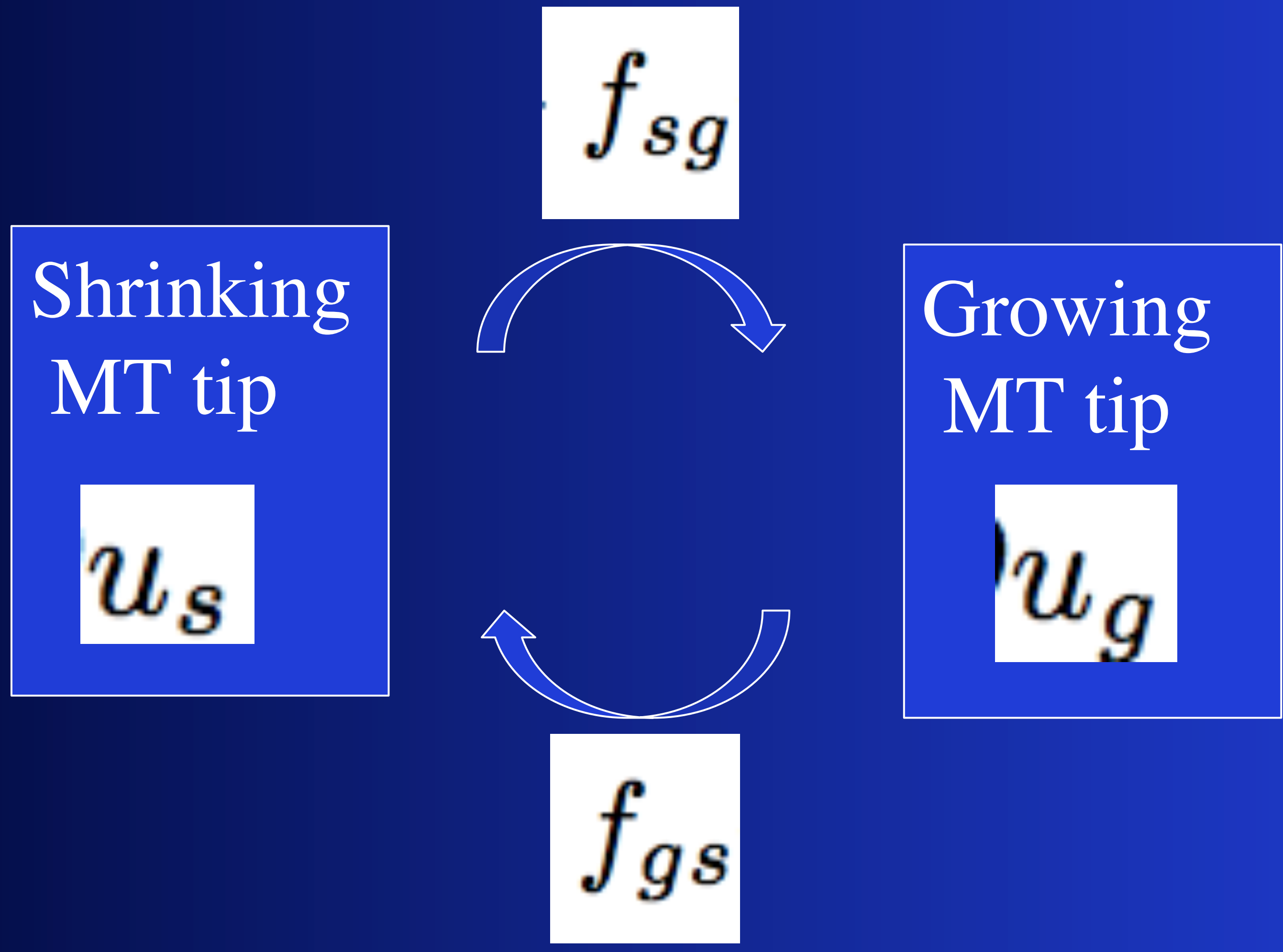
Balance equations



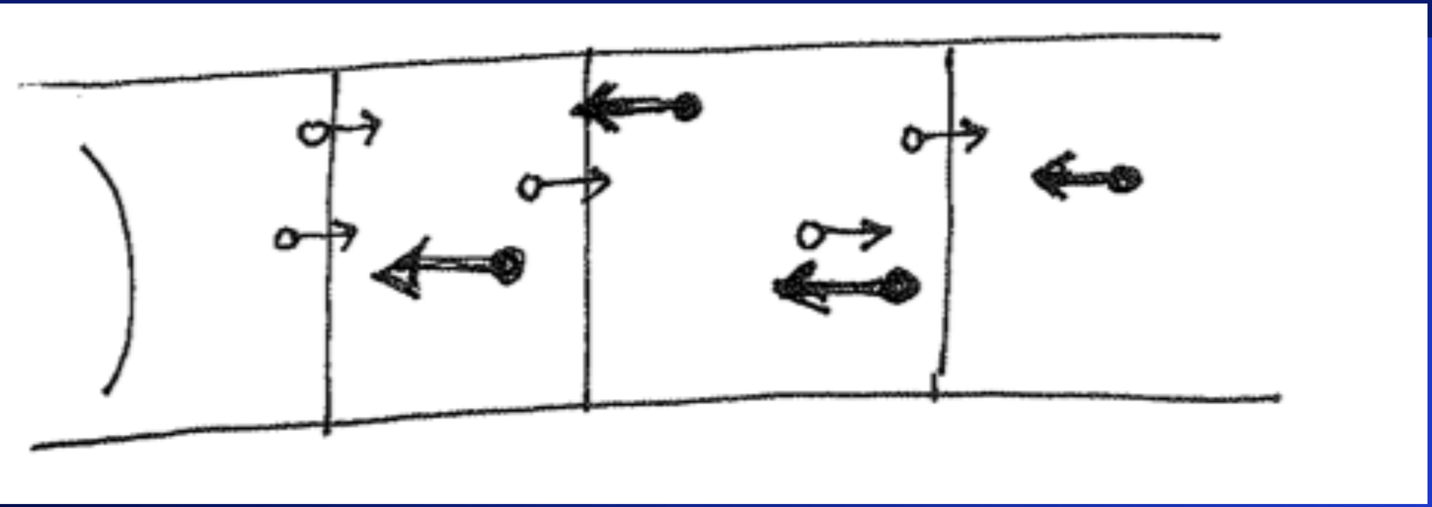
M. Dogterom and S. Leibler. Physical aspects of the growth and regulation of microtubule structures. *Phys. Rev Lett.*, 70:1347–1350, 1993.

M Dogterom, AC Maggs, and S Leibler. Diffusion and Formation of Microtubule Asters: Physical Processes Versus Biochemical Regulation. *PNAS*, 92(15):6683–6688, 1995.

Catastrophe and rescue



Tip fluxes:



$$J_g = u_g v_g, \quad J_s = -u_s v_s$$

Balance equations

$$\frac{\partial u_g}{\partial t} = -v_g \frac{\partial u_g}{\partial x} - f_{gs} u_g + f_{sg} u_s,$$

$$\frac{\partial u_s}{\partial t} = v_s \frac{\partial u_s}{\partial x} + f_{gs} u_g - f_{sg} u_s,$$

Spatial terms

Exchange kinetics

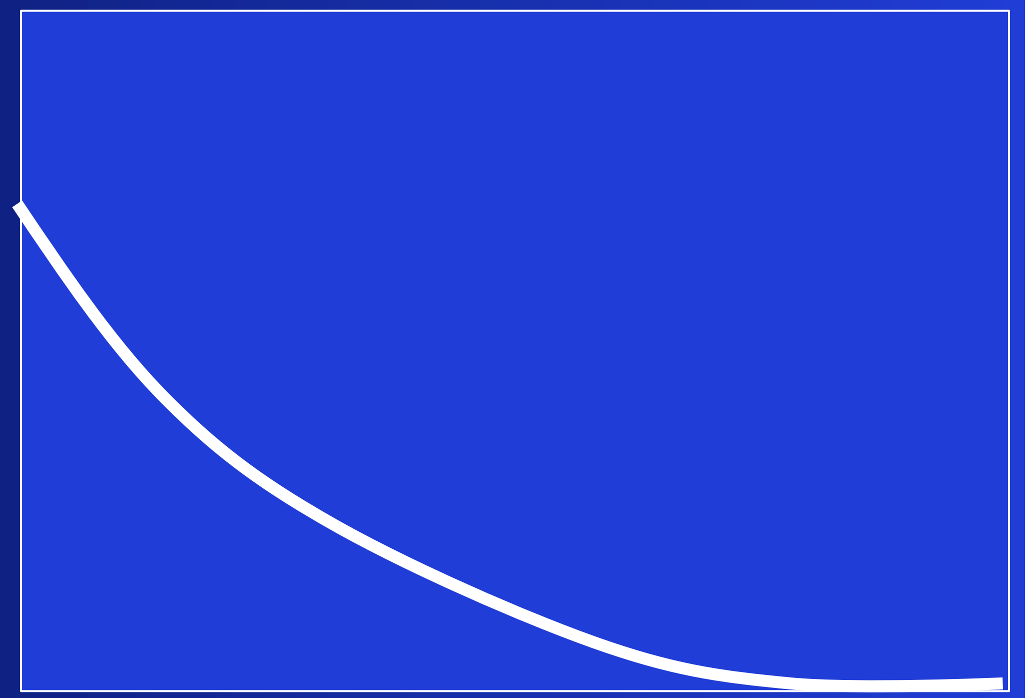
Steady state equations:

$$\frac{du_g}{dx} = \frac{1}{v_g}\left(-f_{gs}u_g + f_{sg}u_s\right),$$

$$\frac{du_s}{dx} = \frac{1}{v_s}\left(-f_{gs}u_g + f_{sg}u_s\right),$$

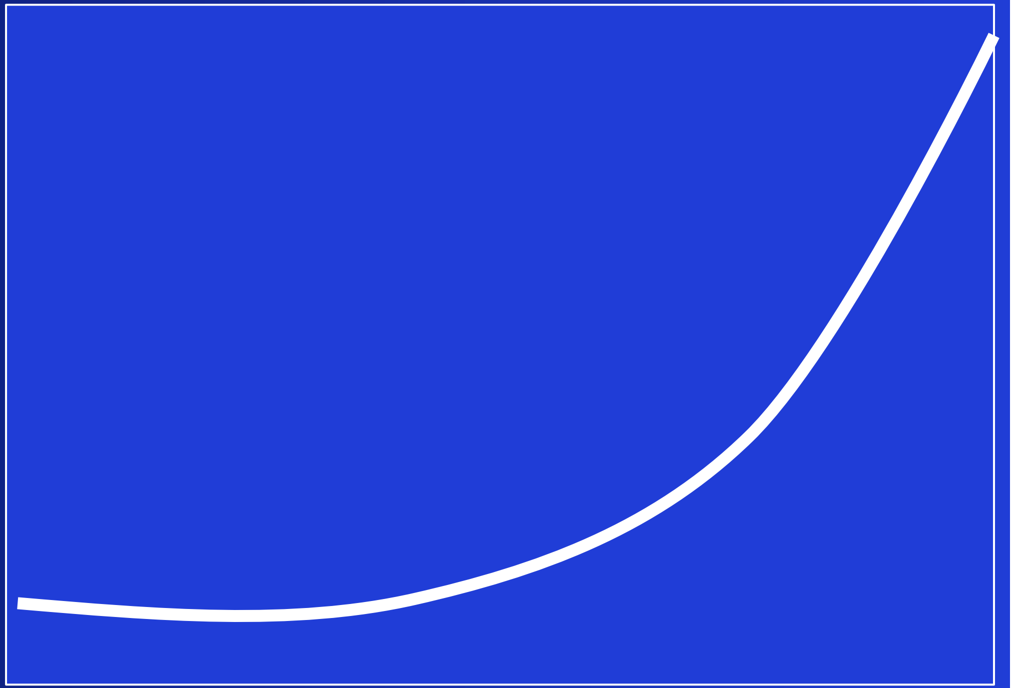
Behaviour

$$\frac{f_{sg}}{v_s} < \frac{f_{gs}}{v_g}$$



Behaviour

$$\frac{f_{sg}}{v_s} > \frac{f_{gs}}{v_g}$$



Distance from centrosome, *x*

Experimental work (Komarova)

Life cycle of MTs: persistent growth in the cell interior, asymmetric transition frequencies and effects of the cell boundary

Yulia A. Komarova[1,2,*], Ivan A. Vorobjev[2] and Gary G. Borisy[1]

Journal of Cell Science 115, 3527-3539

Now back to the begining

Polymer size distribution

Filament size distribution

It is very common in math-biology to consider size classes and formulate equations for the dynamics of size distributions (or age distributions, or distribution of some similar property).

Number of filaments of length j :

$$\frac{dx_j(t)}{dt} = \underbrace{k^+ a x_{j-1}}_{\text{Growth of shorter filament}} - \underbrace{(k^- + a k^+) x_j}_{\text{Monomer loss or gain}} + \underbrace{k^- x_{j+1}}_{\text{Shrinking of longer filament}}$$

Growth of shorter filament

Monomer loss or gain

Shrinking of longer filament

Steady state size distribution for constant pool of monomer

$$\frac{dx_j(t)}{dt} = k^+ a x_{j-1} - (k^- + a k^+) x_j + k^- x_{j+1}$$

Find the steady state size distribution (assume that a, k+, k- are constant.)

Express this in terms of $r = a\, k+/k-$

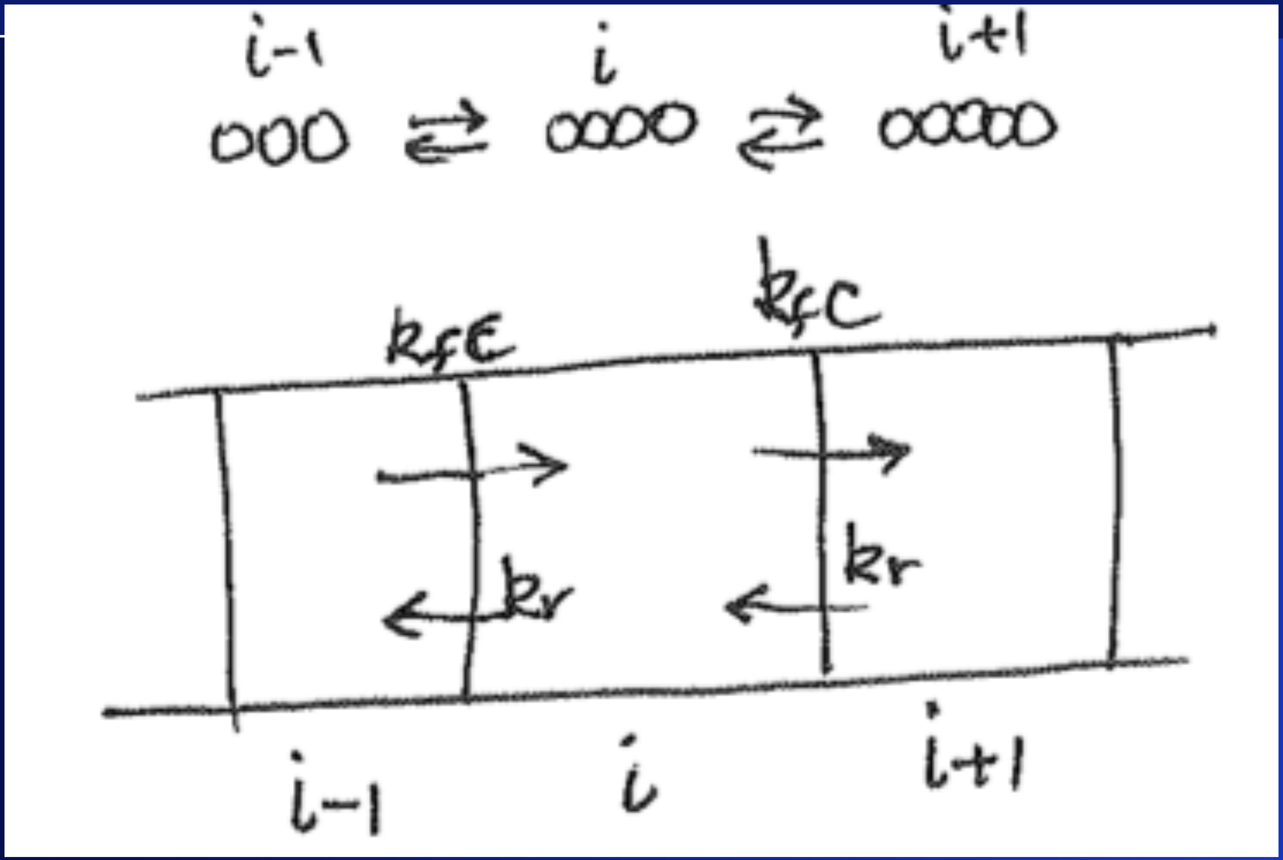
To consider

- The solution will havesome arbitrary constant(s). This means we need some additional constraint(s)..

- What do we use?

- (Consider the case that polymerization has to be started by cluster of n monomers)

Broader context

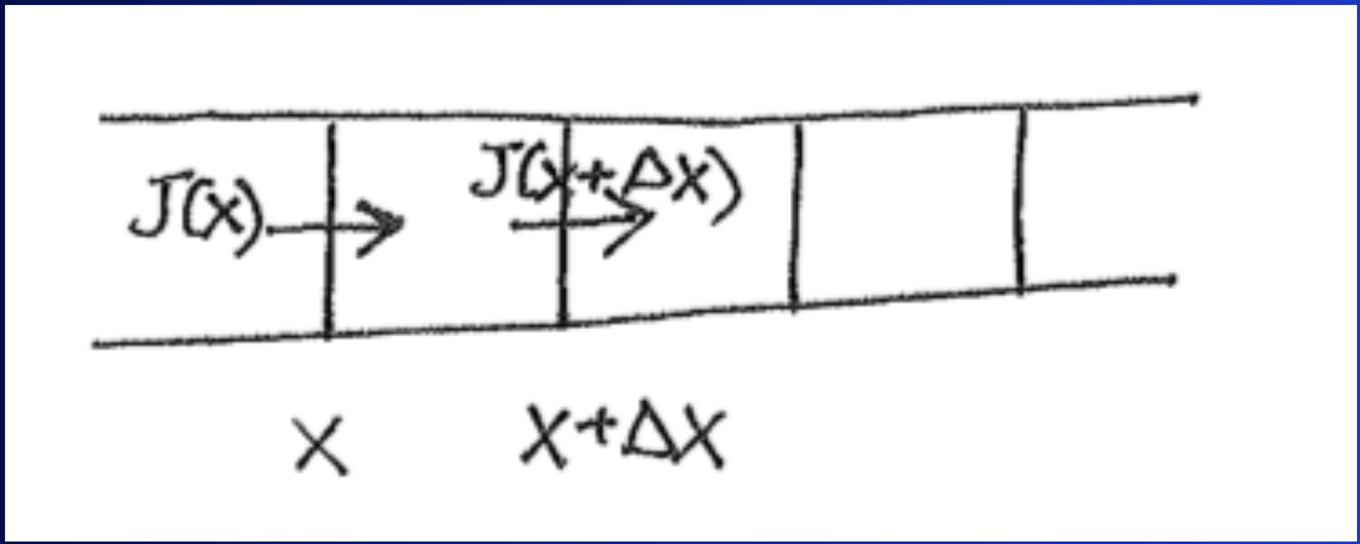


"Motion between size classes"

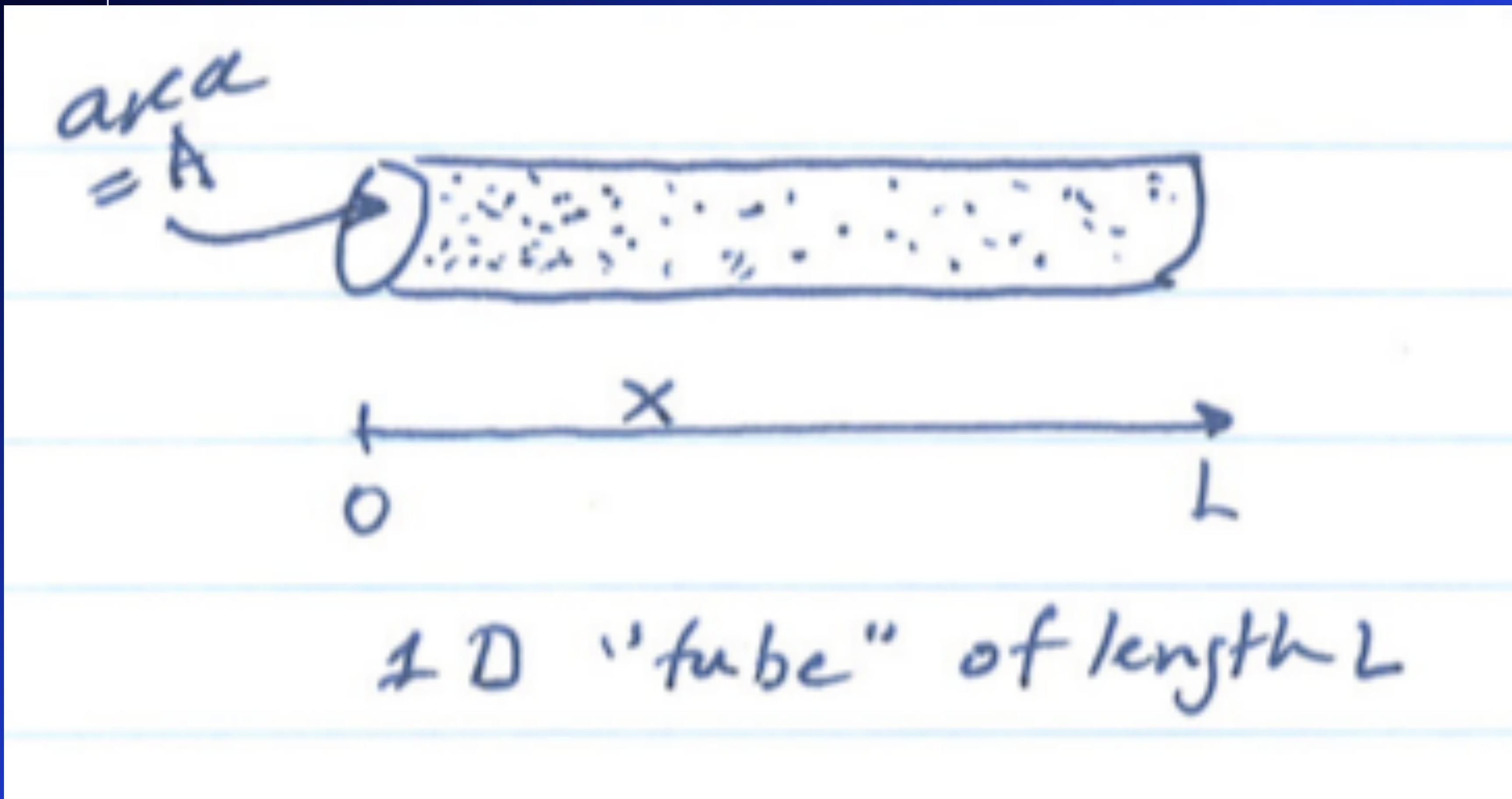
Keeping track of how many in class i

Rate of change in class *i*	=	Rate entry from class *i-1*	+	Rate entry from class *i+1*	+	Rate loss from class *i* to *i-1* and *i+1*

Other balance equations



Continuous version



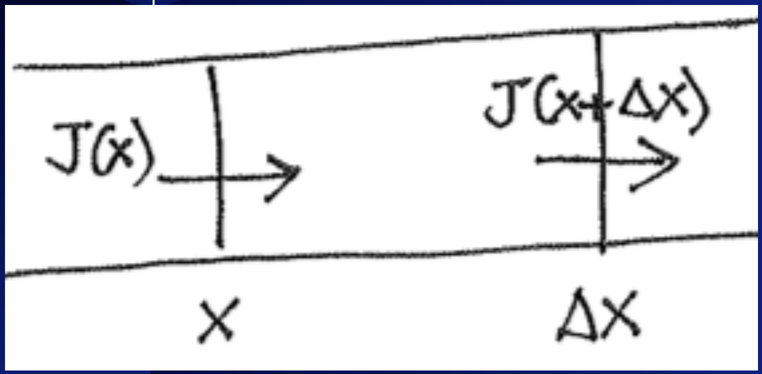
Flux

$\vec{J}(x,t) =$ (net number of particles crossing a unit area at x and time t in +ve x direction

unit area

Note: $\vec{J}$ is a vector whose magnitude has units $(\text{area})^{-1}(\text{time})^{-1}$

Consider a small segment between x and Δx



$$\text{Concentration} = c(x,t),$$

$$\text{Number} = c(x,t)A\Delta x,$$

$$\frac{d(\text{Number})}{dt} = [\text{Rate in} - \text{rate out}] + \text{rate produced}$$

Balance equation

$$\frac{d(\text{Number})}{dt} = [\text{Rate in} - \text{rate out}] + \text{rate produced}$$

$$\frac{d(A\Delta x c)}{dt} = A\,[J(x) - J(x + \Delta x)] + (A\Delta x)\sigma$$

$$\frac{dc}{dt} = \frac{1}{\Delta x}\,[J(x) - J(x + \Delta x)] + \sigma$$

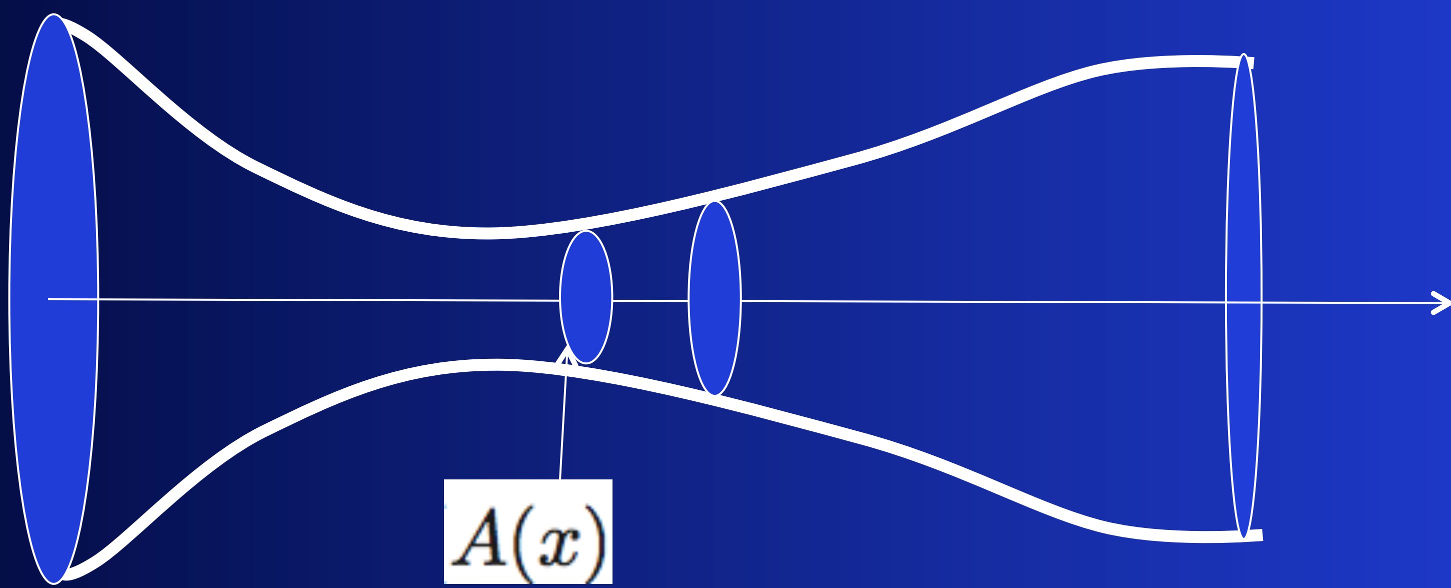
In the limit as $\Delta x \rightarrow 0$..

$$\frac{dc}{dt} = \frac{1}{\Delta x}\left[J(x) - J(x + \Delta x)\right] + \sigma$$

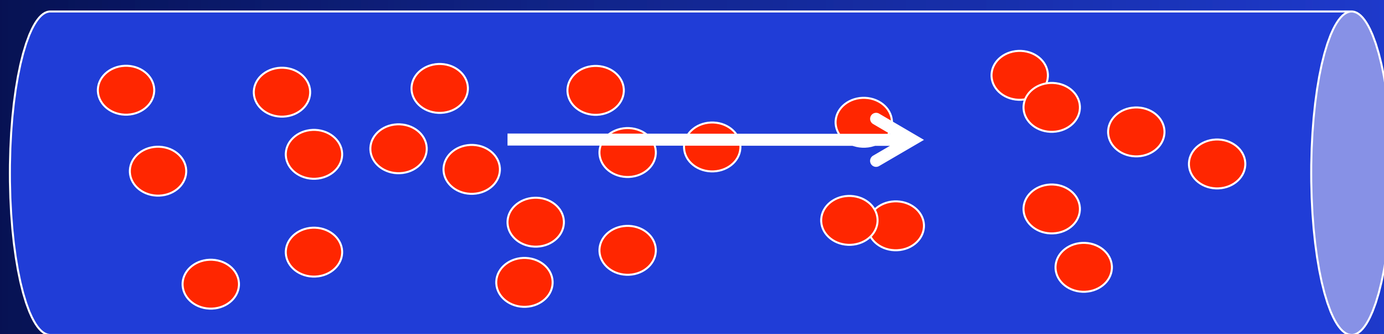
$$\frac{\partial c}{\partial t} = -\frac{\partial J}{\partial x} + \sigma$$

Nonconstant "tube" diameter

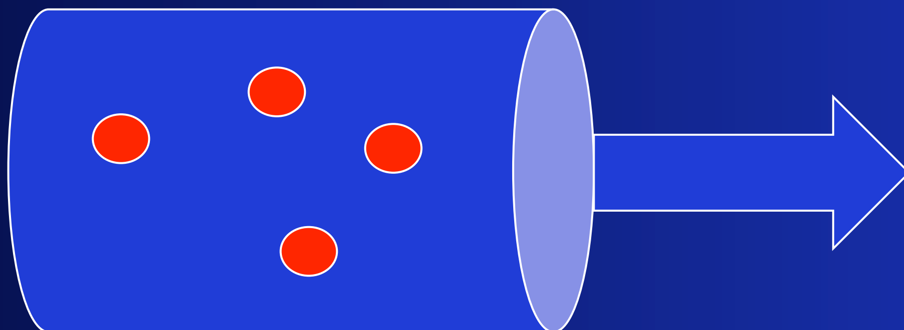
$$\frac{d(A(x)\Delta x c)}{dt} = [A(x)J(x) - A(x+\Delta x)J(x+\Delta x)] + (A(x)\Delta x)\sigma$$



Transport at velocity *v*

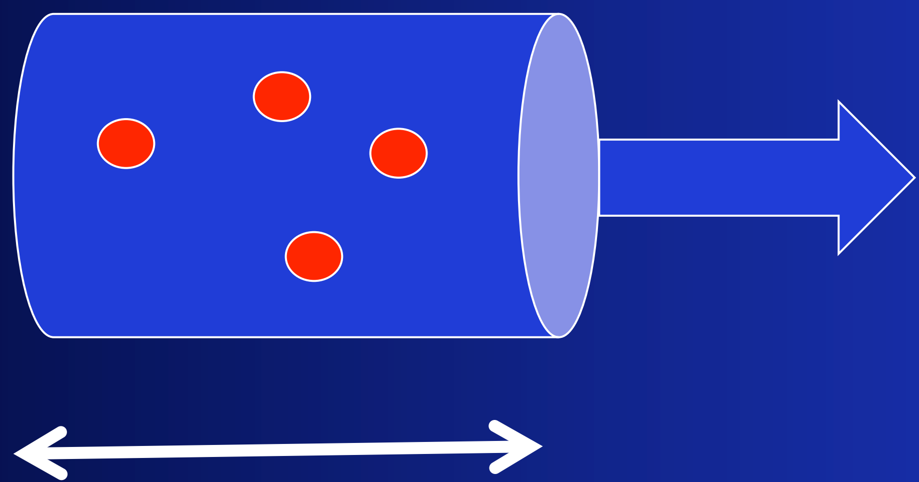


Transport at velocity v



What is the flux?

Transport at velocity v

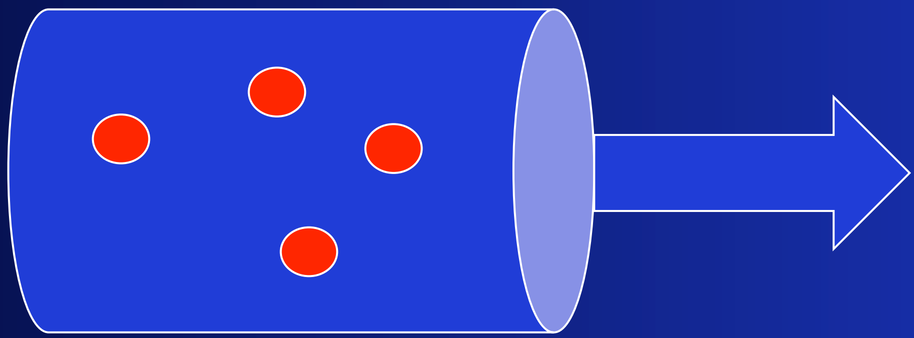


Volume $Av\,\Delta t$

Concentration c so $(cAv\,\Delta t)$ molecules cross during time Δt

Flux $J = vc$

Convective flux (transport)



$$\text{Convective flux} = J_c = vc.$$

Transport equation

Convective flux $= J_c = vc.$

$$\frac{\partial c}{\partial t} = -\frac{\partial vc}{\partial x} + \sigma$$

Diffusion: Fick's Law

Flux proportional to concentration gradient

$$J = -D\frac{\partial c}{\partial x}$$

D = diffusion coefficient

Diffusion

$$\frac{\partial c}{\partial t} = -\frac{\partial}{\partial x}\left(-D\frac{\partial c}{\partial x}\right) + \sigma$$

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} + \sigma$$

Boundaries

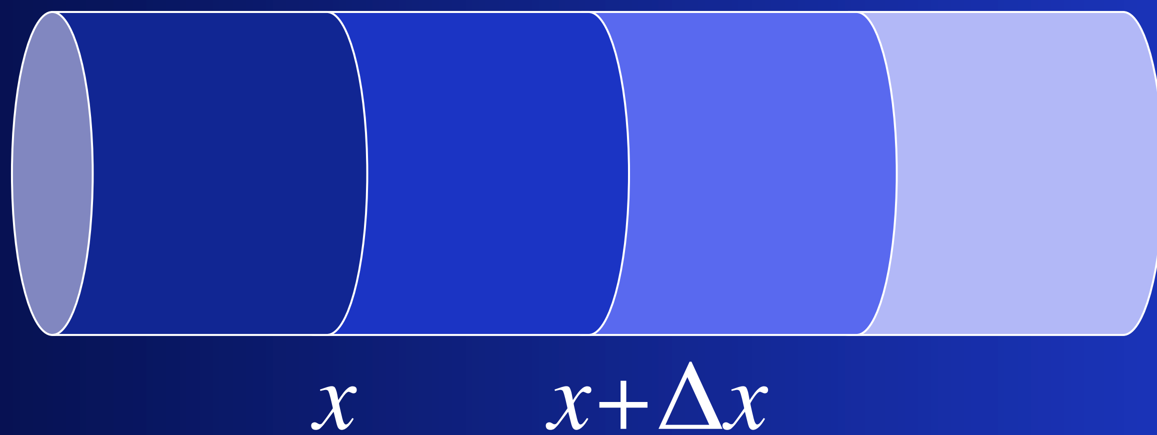
Typical Boundary Conditions

Q: How many are needed? A: This depends on the order of the highest spatial derivative.

- Presence of diffusion term $\Leftrightarrow$ 2nd derivative $\frac{\partial^2 c}{\partial x^2}$

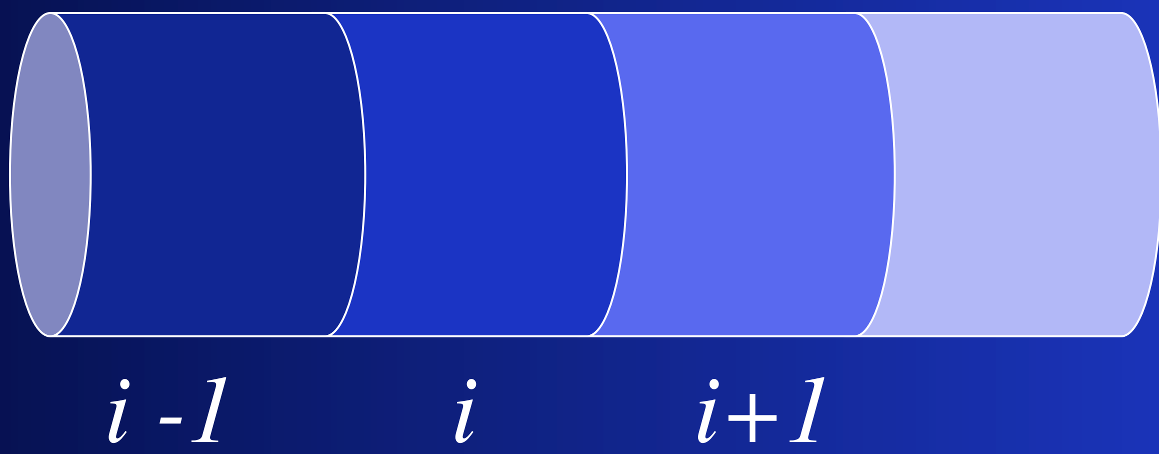
  $\Leftrightarrow$ two BC's needed, one for each domain end.

Discrete Diffusion Equation



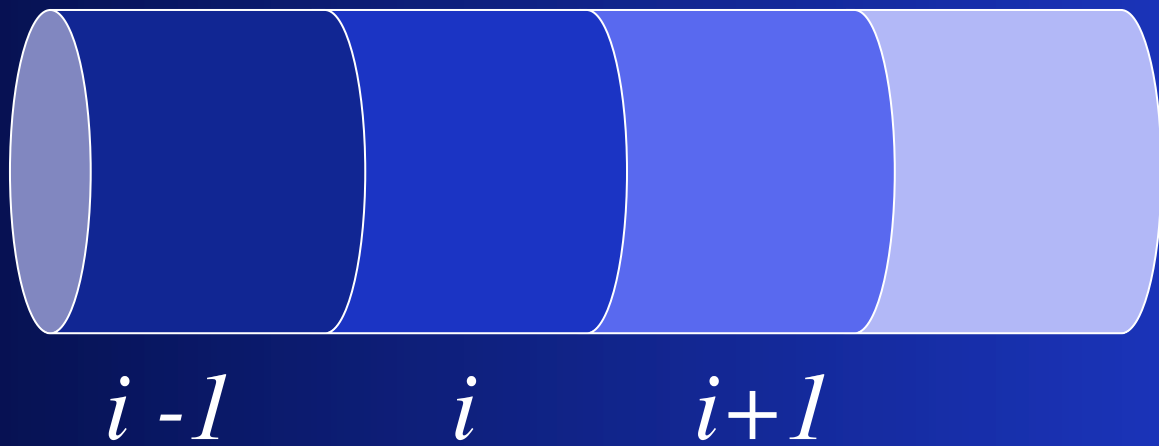
$$\frac{\partial c(x,t)}{\partial t} = \frac{D}{\Delta x^2}\left[c(x-\Delta x,t) - 2c(x,t) + c(x+\Delta x,t)\right]$$

Discrete Diffusion Equation



$$\frac{\partial c(x,t)}{\partial t} = \frac{D}{\Delta x^2}\left[c_{i-1} - 2c_i + c_{i+1}\right] + \sigma$$

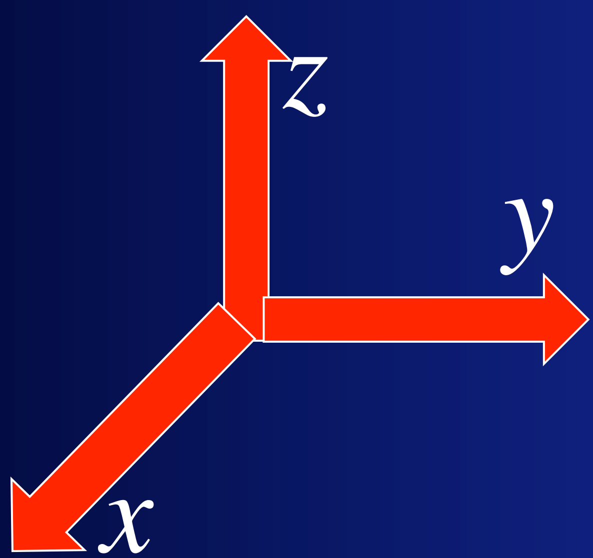
Discrete Diffusion Equation

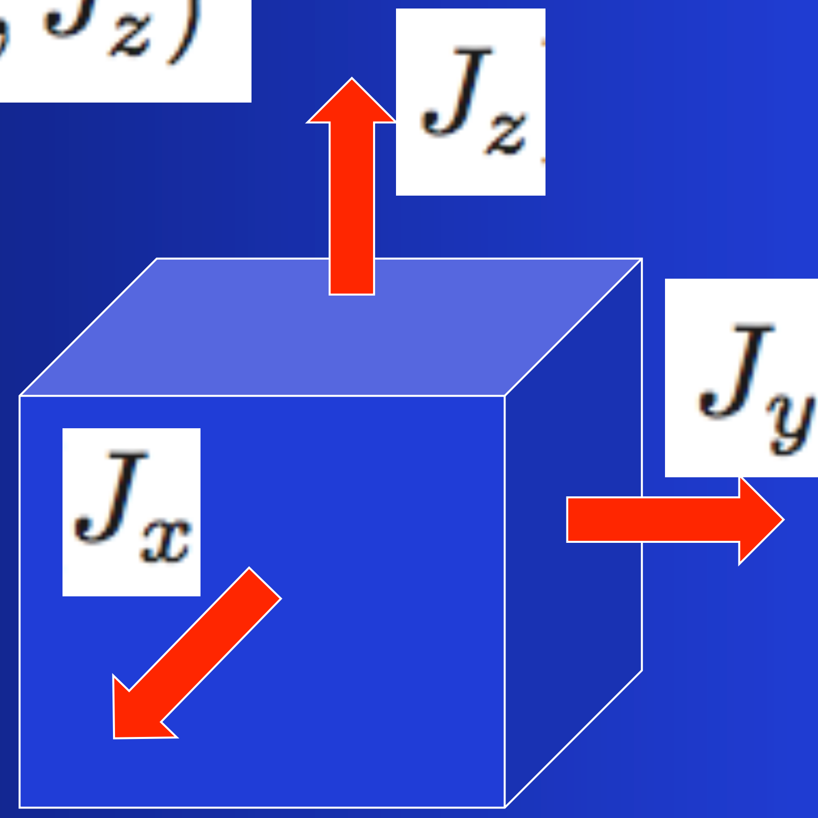


$$\frac{\partial c(x,t)}{\partial t} = \frac{D}{\Delta x}\left(\left[\frac{c_{i+1} - c_i}{\Delta x}\right] - \left[\frac{c_i - c_{i-1}}{\Delta x}\right]\right)$$

Higher dimensions

$$\vec{J} = (J_x, J_y, J_z)$$





Higher dimensions

$$\vec{J} = (J_x, J_y, J_z)$$

$$\nabla = \left(\frac{\partial}{\partial x}, \frac{\partial}{\partial y}, \frac{\partial}{\partial z}\right)$$

$$\frac{\partial c}{\partial t} = -\nabla \cdot \vec{J}$$

Higher dimension: Diffusion

$$\vec{J} = -D\nabla c$$

$$\frac{\partial c}{\partial t} = -\nabla \cdot (-D\nabla c)$$

$$\frac{\partial c}{\partial t} = D\nabla^2 c$$

$$\frac{\partial c}{\partial t} = D\Delta c + \sigma$$

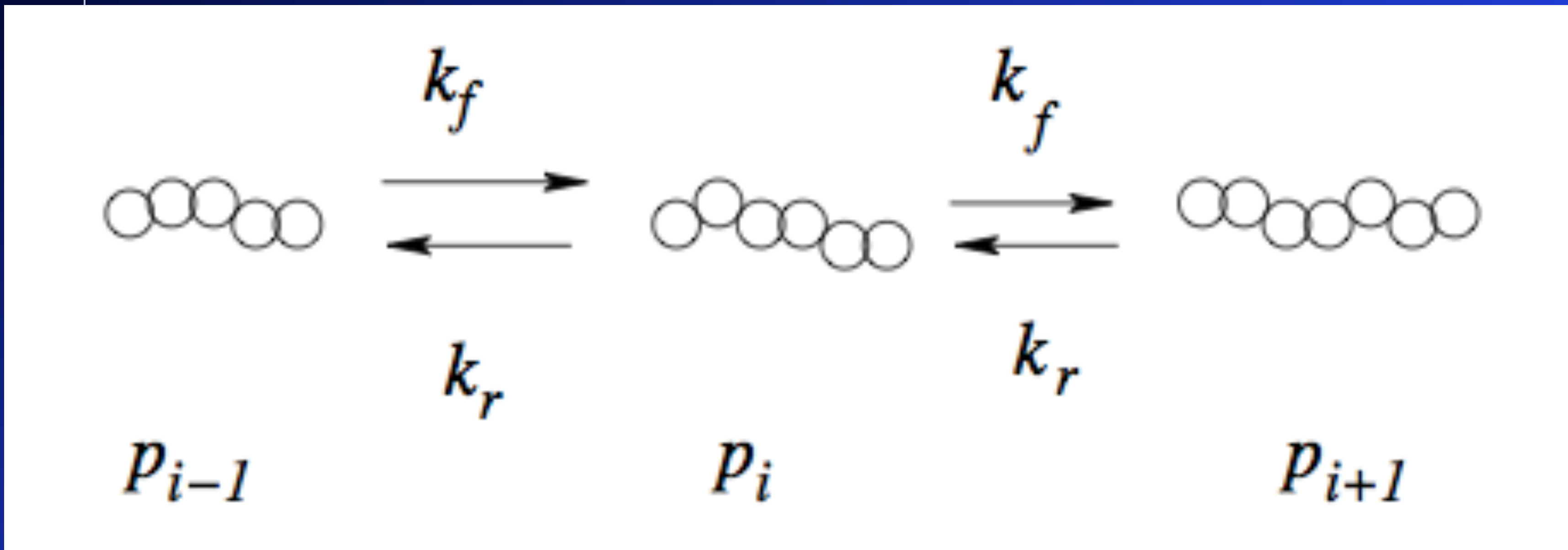
Higher dimension: transport

$$\vec{J} = \vec{v}c$$

$$\frac{\partial c}{\partial t} = -\nabla \cdot (\vec{v}c) + \sigma$$

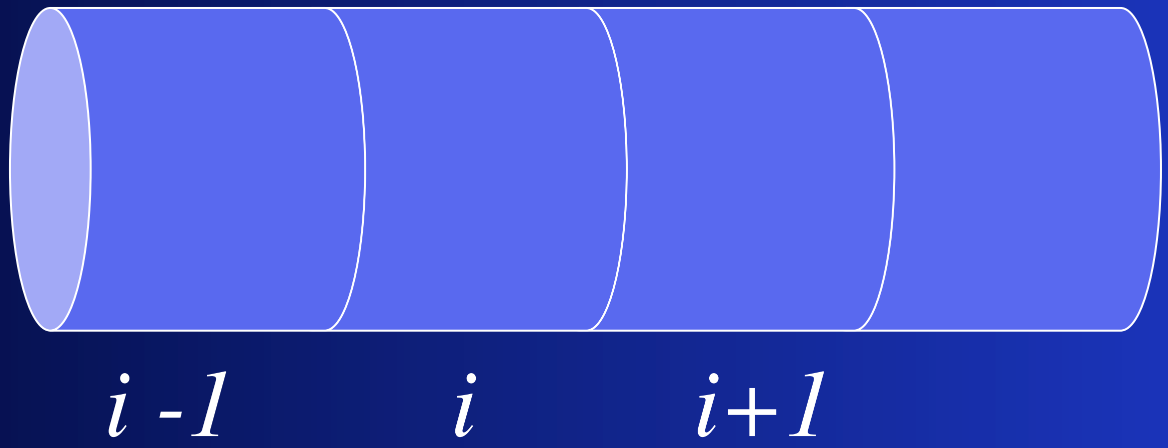
Polymer size distribution

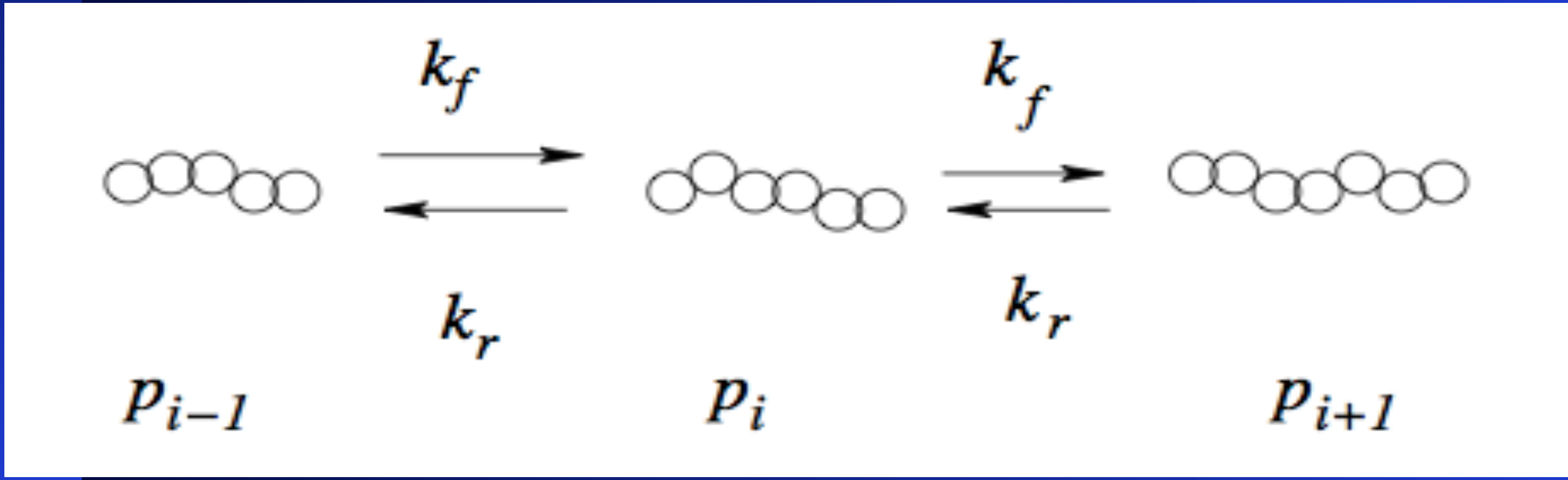
Size classes



$$k_f = k^+ a, \quad k_r = k^-$$

Discrete size classes





Balance equation

$$\frac{dp_i}{dt} = ck_f p_{i-1} - (ck_f + k_r)p_i + k_r p_{i+1}$$