PS#3 due today
(in class, or Rm. 68-371, before 3 PM)

Recitation topic this week
‘Stochastic simulations using MATLAB’

Last lectures: L13-14: Stochastic Chemical Kinetics

**Figure 1:** The implications of discreteness

**Figure 3:** The large number limit

**Figure 4:**
A stochastic bistable system

Fokker-Planck equation
**L15: 14 Lectures past and 11 to go**

**Part I: ‘The cell as a well-stirred bioreactor’**

*topics*

- Lambda phage lysis-lysogeny switch
- Lactose operon
- Synthetic genetic switch
- Synthetic genetic oscillators
- Chemotaxis: perfect adaptation or not?
- Stochastic chemical kinetics

*main assumption*

- well-stirred reactor
- absence of chemical gradients
  (justification: small cells, diffusion mixes)

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**Switch from**

**Systems Microbiology**

to

**Systems Cell Biology**

**The importance of diffusion and gradients for cellular regulation**

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**Part II: Systems Cell Biology**

‘Importance of gradients and diffusion in cellular regulation’

After two lectures on diffusion and reaction-diffusion equations, we will focus during the coming lectures on the following biological systems:

1. Eukaryotic chemotaxis
   
   Gradient sensing in *Dictyostelium* (aka’amoeba’)

2. Computing the middle of a cell
   
   Pole-to-pole oscillations in *Escherichia coli*

3. Self organization of the cytoskeleton

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**Prokaryotic versus eukaryotic cells**

e.g. *E. coli*, cyanobacteria

~ $10^6$ bp, ~ 5000 genes
Prokaryotic versus eukaryotic cells

e.g. yeast, amoeba, plants, flies, man & mice ...

~ 10^9 bp, ~ 40000 genes !!

Topic I: Spatial oscillation in E. coli

similar to genetic oscillators, but now we cannot ignore the spatial dimensions

biological function:
determine the center of the cell, to prepare for proper cell division

gfp-minC
GFP-minD is localized in a ring.
gfp-minE is localized in a ring.
Recent results demonstrate that the min proteins assemble in helices.

**Topic II: Gradient sensing**

Similar to chemotaxis of E. coli, but now we cannot ignore the spatial dimensions.

*Dictyostelium* (amoeba) sensing a gradient of cAMP.

**Response of Dictyostelium to cAMP**

- **Uniform step in cAMP**
- **cAMP gradient**

**Initial distribution**

- Uniform step in cAMP
- t = 3 s

**Steady-state distribution**

- Uniform and transient
- t < ∞

- Polarized and persistent
**GFP-PH** binds special lipids in membrane: PIP2 and PIP3

The molecules in the model:

- **Plasma Membrane**
  - PI
  - PIP2
  - PIP3
  - PI4P
  - PI4P5K
  - PIP
  - PIP5K
  - PIP5K
  - PI(4,5)P2
  - PI(3,4)P2

- **Cytosol**
  - Inositol
  - IP3

- **Endoplasmic Reticulum**
  - PA

**Aggregation of a population of amoeba**

**Biological function:**
- Development of a multicellular structure

**Powerful reporter**

- PH-GFP
Topic III: Self-organization of the cytoskeleton

Center finding in an eukaryotic cell: fission yeast

The importance of the cytoskeleton

Chang et al.
Positive feedback as a mechanisms for spontaneous cell polarization?

Cue-dependent polarization
- Neutrophils/Dickeyostelium
- Yeast
- Light
- Fucus zygote
- Ciliates

Random polarization
- No gradient
- Lacking BUD1
- No stimulus
- Uniform activation

Calcofluor staining

In the absence of the actin cytoskeleton symmetry breaking still occurs, but Cdc42p activity patch is immobilized

What is the dynamics of this symmetry breaking?
Experimental probe: Gic2p\(_{(1-208)}\)-GFP (CRIB-GFP)

In the absence of the actin cytoskeleton symmetry breaking still occurs, but Cdc42p activity patch is immobilized