

From stochastic models to macroscopic PDEs

Radek Erban

Mathematical Institute

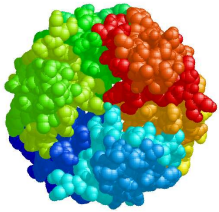
University of Oxford



Overview of my talk

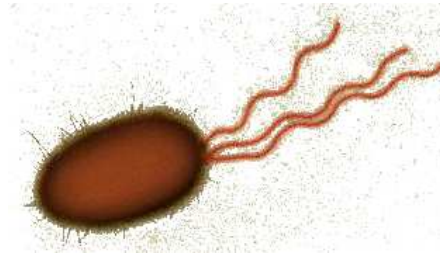
- individual-level (microscopic) behaviour is often stochastic (fluctuations, noise)
- there are many application areas in which the stochastic effects significantly contribute to the system-level behaviour:

macromolecules



genes and proteins

unicellular organisms



bacteria

animals

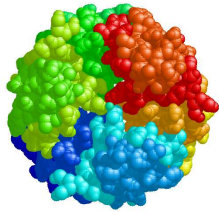


locusts

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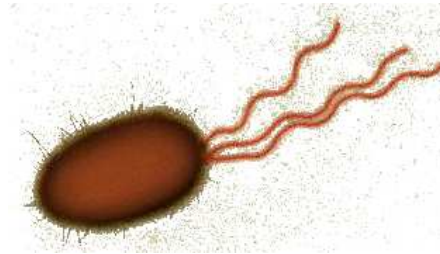
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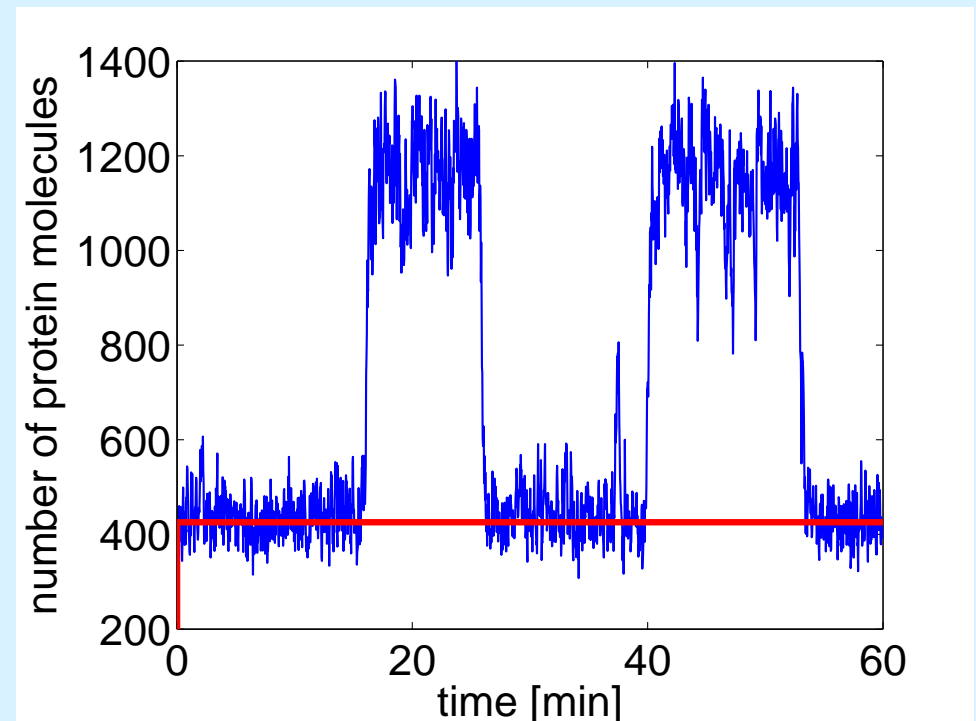
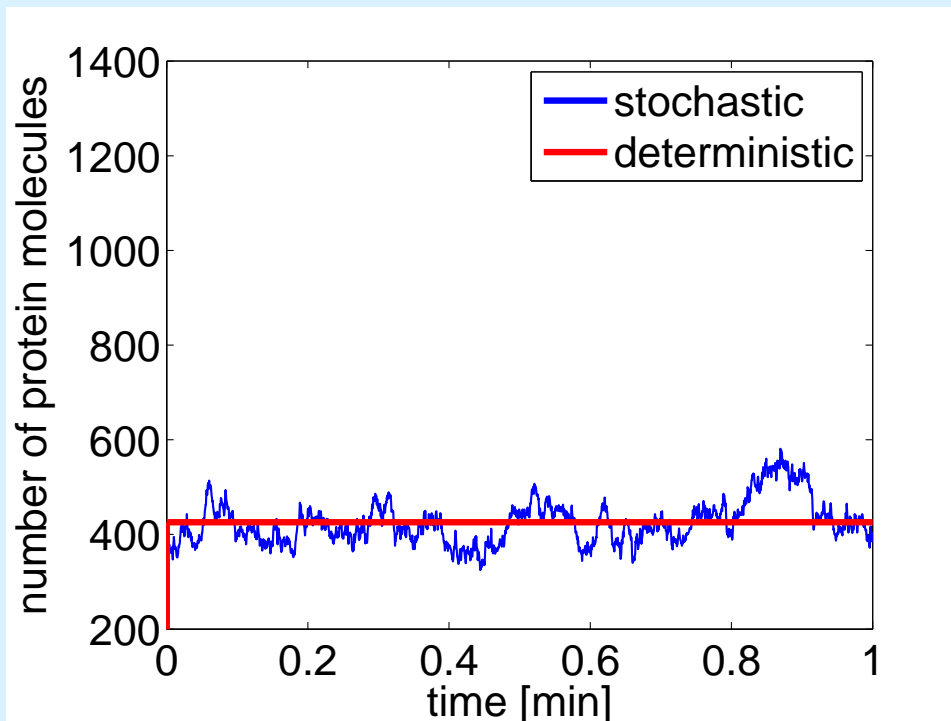
animals



locusts

- I will focus on stochastic models of chemical reactions and molecular diffusion
- macroscopic models are described in terms of nonlinear PDEs

Motivation – deterministic vs. stochastic modelling



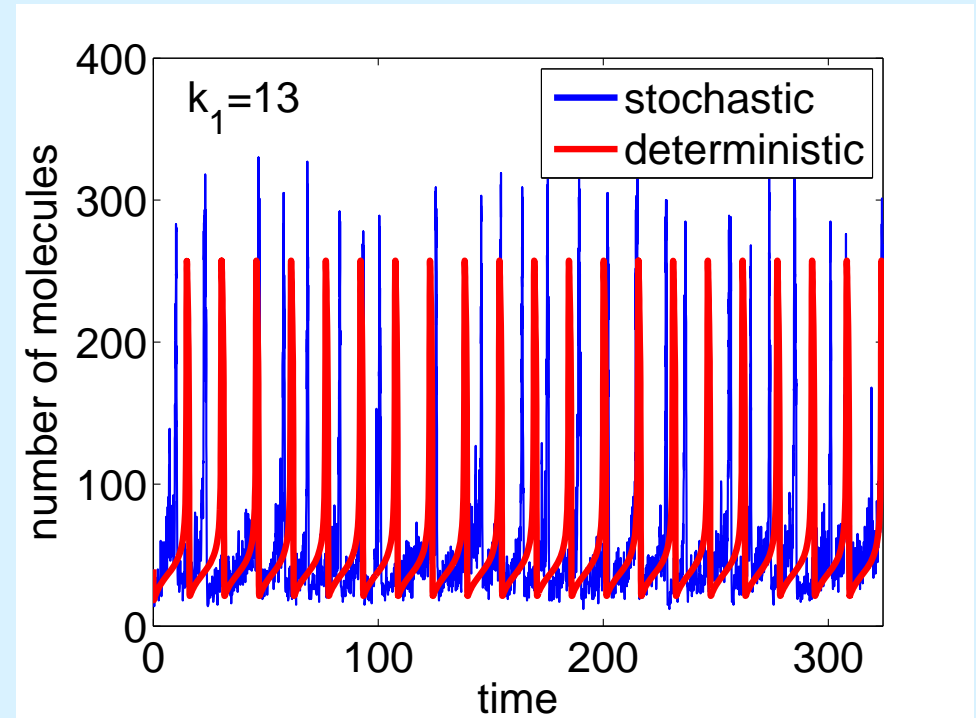
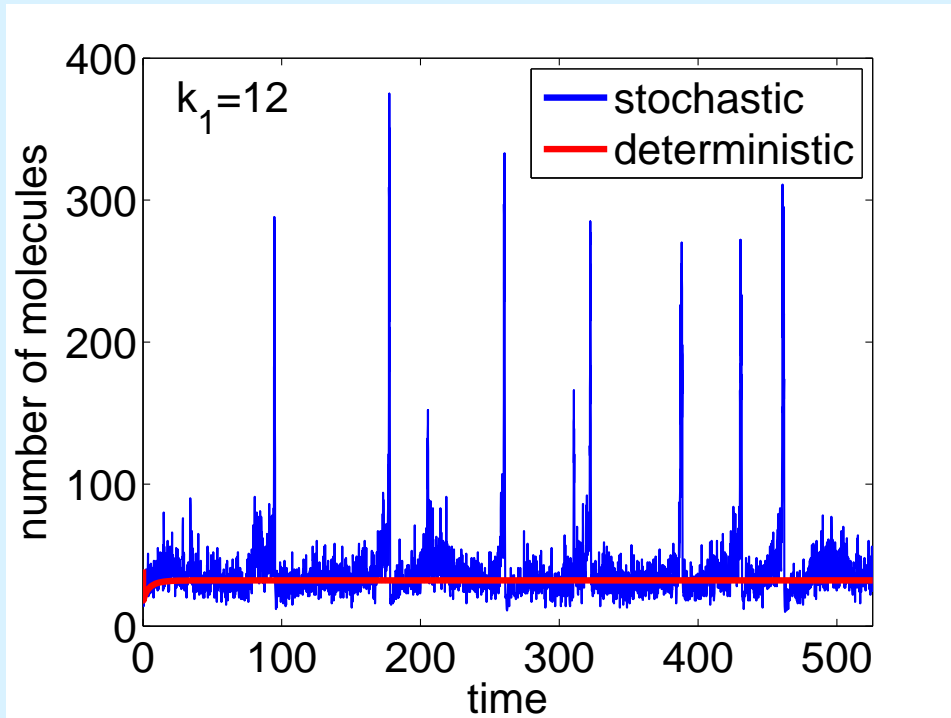
Model: gene regulatory network (mutually repressing genes and proteins)

Deterministic description: system of ODEs, two stable steady states

Stochastic description: Gillespie stochastic simulation algorithm (SSA), we can study stochastic switching between favourable states

RE, I. Kevrekidis, D. Adalsteinsson and T. Elston, Journal of Chemical Physics, 2006

Motivation – deterministic vs. stochastic modelling



Deterministic description: system of ODEs which undergoes SNIC (SNIPER) bifurcation ("saddle-node bifurcation on invariant cycle")

Stochastic description: Gillespie algorithm, stochastic model oscillates even for the parameter values for which the deterministic model does not

RE, J. Chapman, I. Kevrekidis, T. Vejchodsky, SIAM Journal on Applied Mathematics, 2009

Deterministic vs. stochastic modelling

Considering homogeneous (well-stirred) chemical systems, stochastic modelling is useful for:

- computation of rare events
- systems close to the bifurcation points of mean-field ODEs
- systems with low molecular numbers (of at least one chemical species)

What about **spatially distributed systems**?

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Deterministic modelling: PDEs for concentrations $\frac{\partial c_i}{\partial t} = D_i \Delta c_i + R(c_1, c_2, \dots, c_n)$

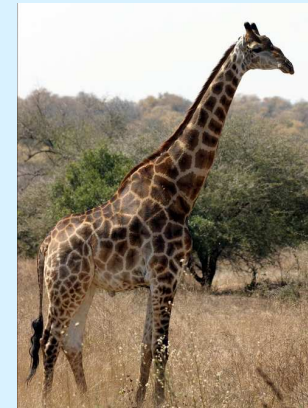
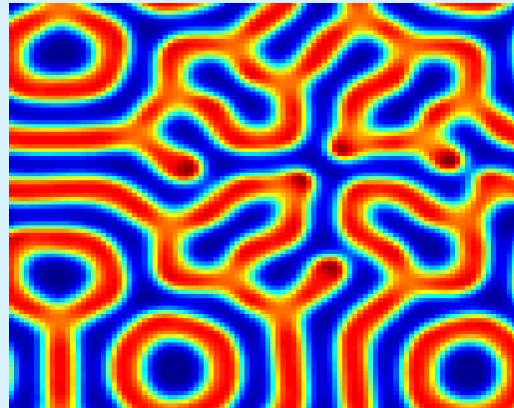
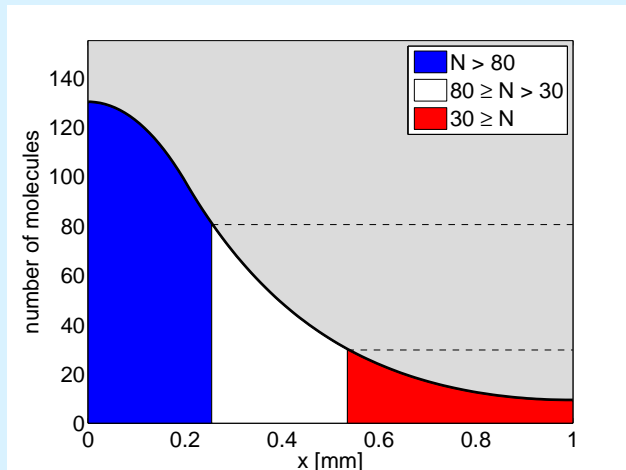
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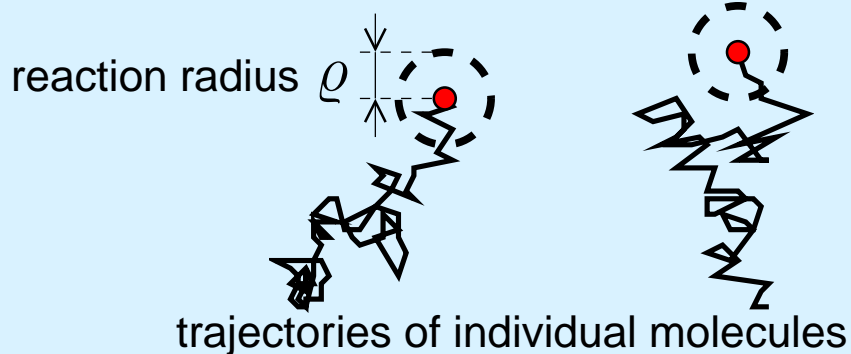
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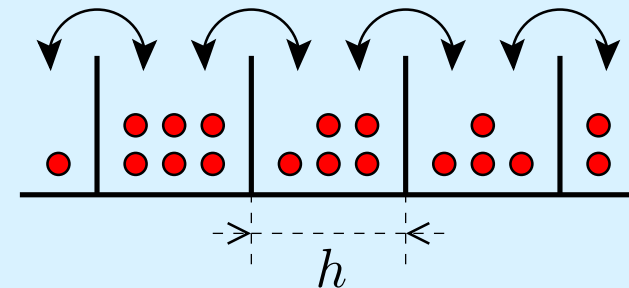
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Stochastic simulation algorithms:

Molecular-based modelling



Compartment-based modelling



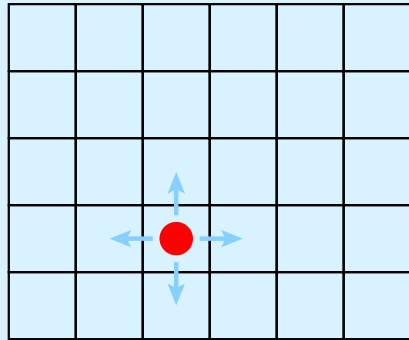
(master) equation for numbers of molecules in each compartment



Stochastic simulation algorithms of diffusion

Compartment-based model:
lattice points a distance h apart

$$[X(t + \Delta t), Y(t + \Delta t), Z(t + \Delta t)] =$$



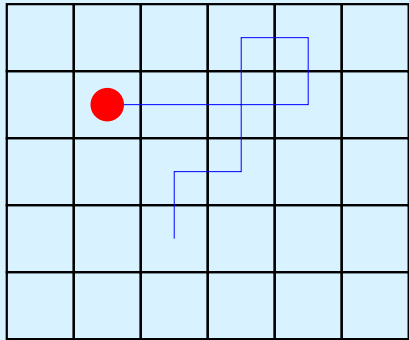
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D ... diffusion constant, Δt ... time step

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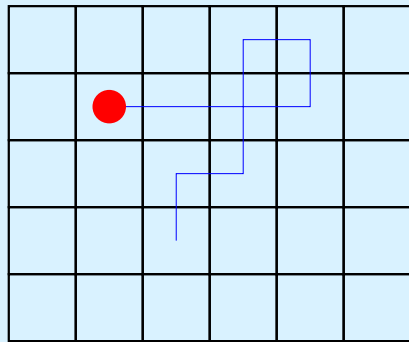
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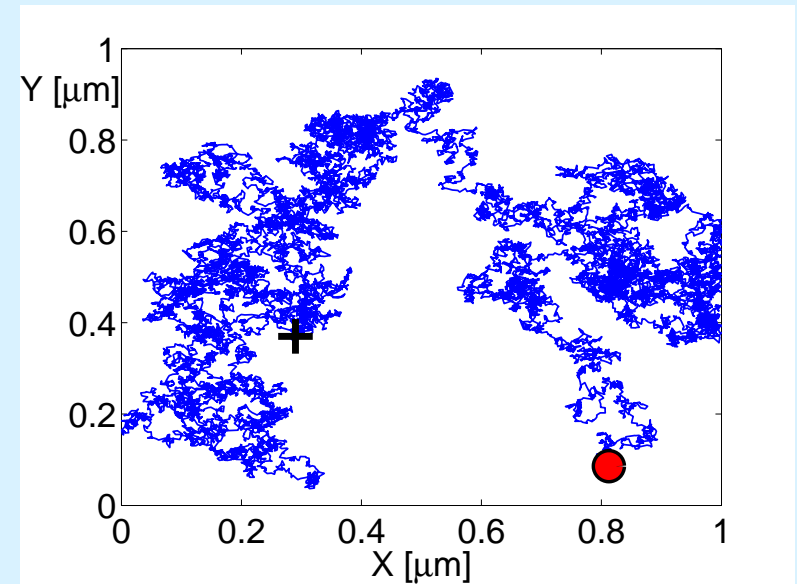
Discretized Brownian motion: off-lattice model

$$X(t + \Delta t) = X(t) + \sqrt{2D \Delta t} \zeta_x$$

$$Y(t + \Delta t) = Y(t) + \sqrt{2D \Delta t} \zeta_y$$

$$Z(t + \Delta t) = Z(t) + \sqrt{2D \Delta t} \zeta_z$$

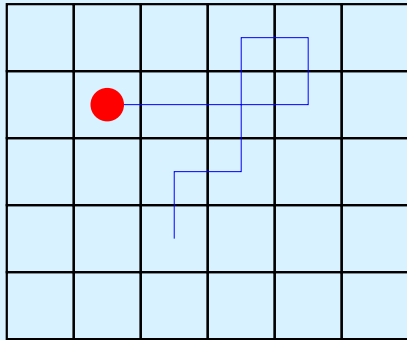
$\zeta_x, \zeta_y, \zeta_z$... normally distributed random variables with zero mean and unit variance



Diffusion models in reaction-diffusion algorithms

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software MesoRD: <http://mesord.sourceforge.net>

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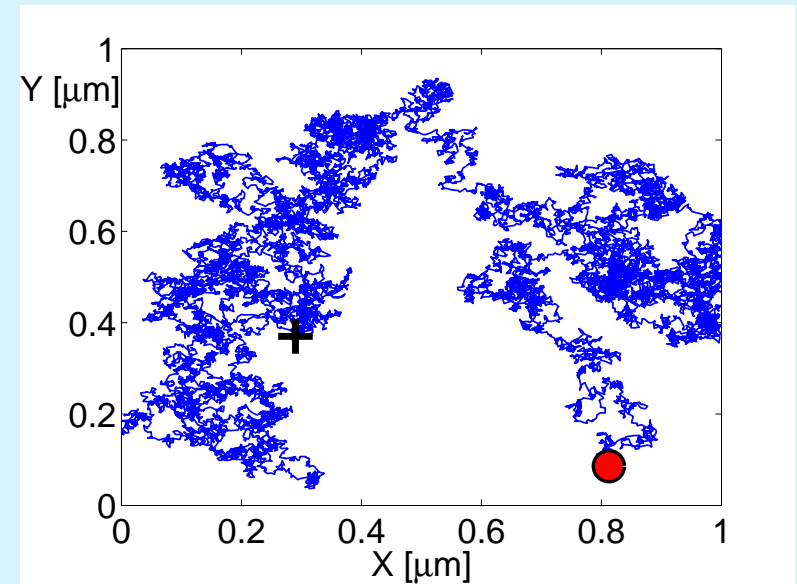
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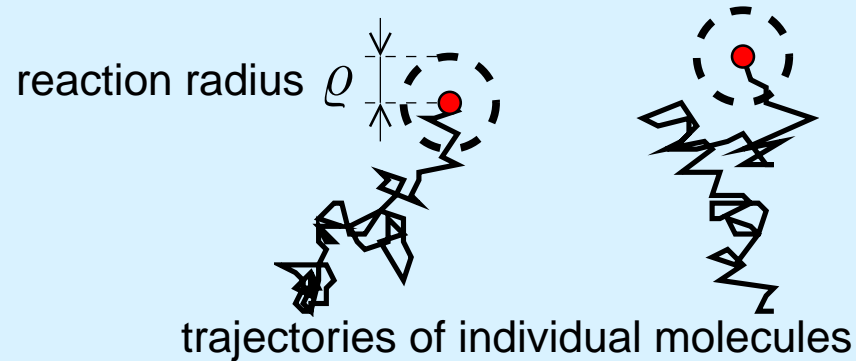
software Smoldyn: <http://www.smoldyn.org>



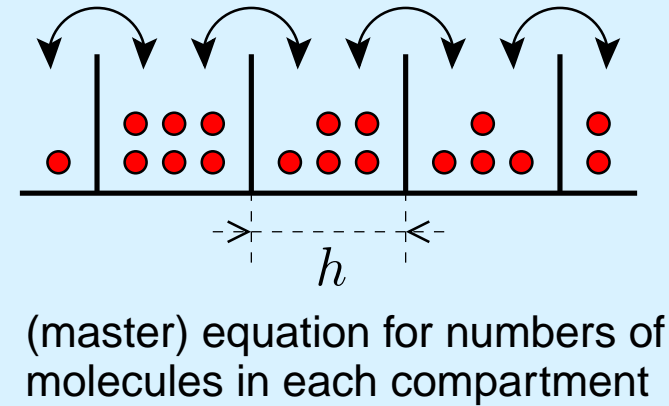
Overview of my talk

I introduced two classes of stochastic reaction-diffusion models:

Molecular-based modelling



Compartment-based modelling



In this talk, I will discuss analysis of both stochastic reaction-diffusion approaches.

There are three situations which have to be handled with care:

- (i) modelling reactive boundaries
- (ii) modelling bimolecular reactions
- (iii) modelling reversible reactions

Boundary conditions

Deterministic Modelling: 1D diffusion equation in $[0, L]$: $\frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2}$

$(c \equiv c(x, t))$... concentration of molecules; D ... diffusion constant)

Reactive (Robin) boundary condition at $x = 0$: $D \frac{\partial c}{\partial x}(0, t) = K c(0, t)$

K ... reactivity of the boundary (e.g. rate constant of boundary chemical reaction)

$K = 0$ perfect reflection of molecules (zero-flux boundary condition)

$K = \infty$... perfect adsorption of molecules (Dirichlet boundary condition)

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Stochastic Modelling: boundary condition: **whenever a molecule hits the boundary, it is adsorbed with some probability, and otherwise reflected**

$P \dots$ probability that a molecule is adsorbed, rather than reflected

What is the relation between P and K ?

Boundary conditions

Deterministic Modelling: 1D diffusion equation in $[0, L]$: $\frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2}$

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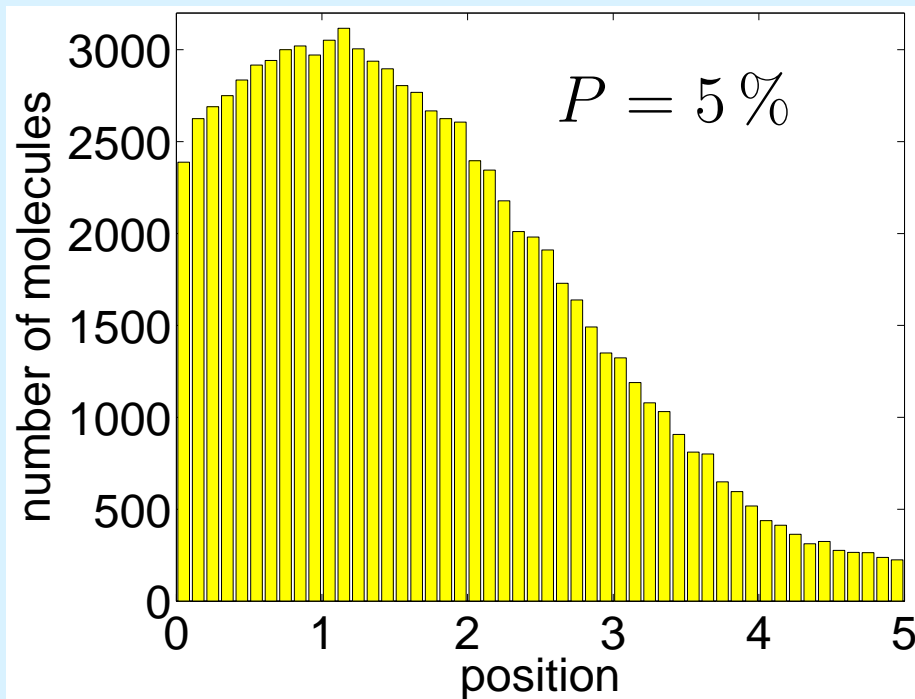
P ... probability that a molecule is adsorbed, rather than reflected

- (zero-flux boundary) $K = 0 \Leftrightarrow P = 0$ (molecules always reflected)
- value of P **depends on K and on the stochastic model for $K > 0$**

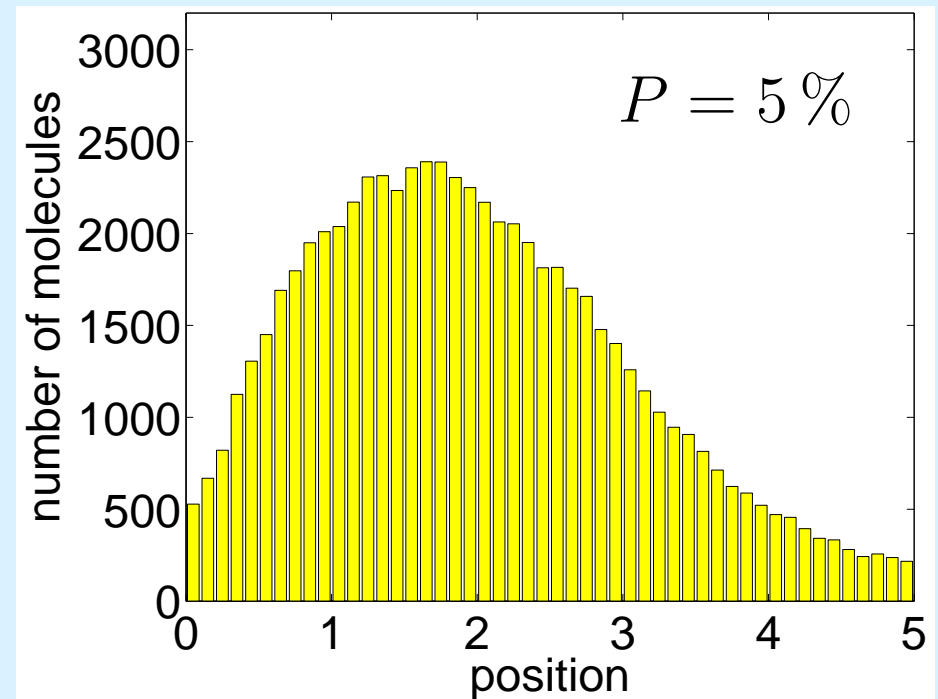
Same value $P = 5\%$ for different stochastic models

whenever a molecule hits the boundary, it is adsorbed with probability P , and otherwise reflected

Compartment-based model



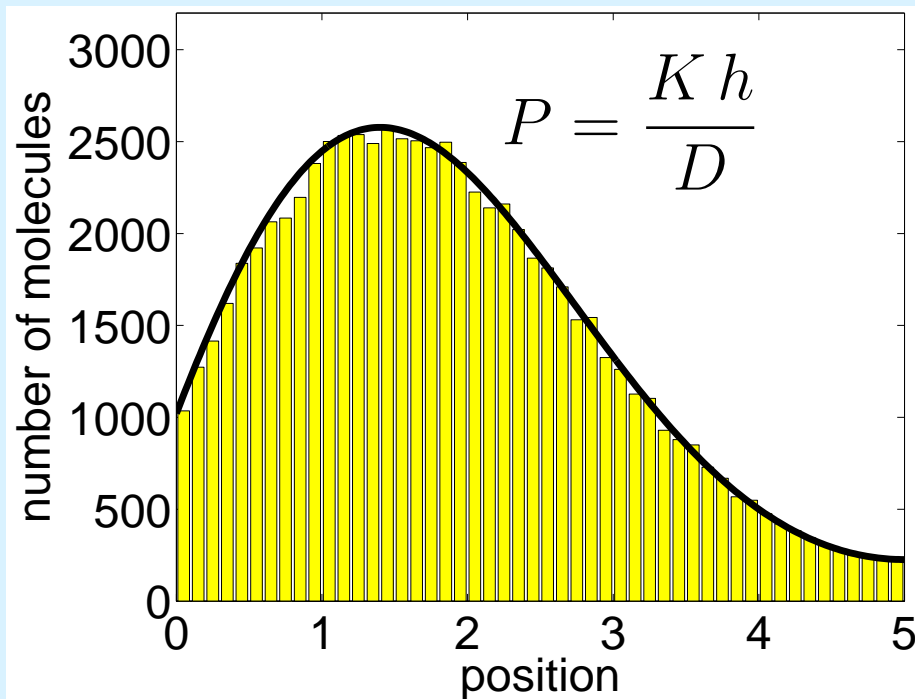
Discretized Brownian motion



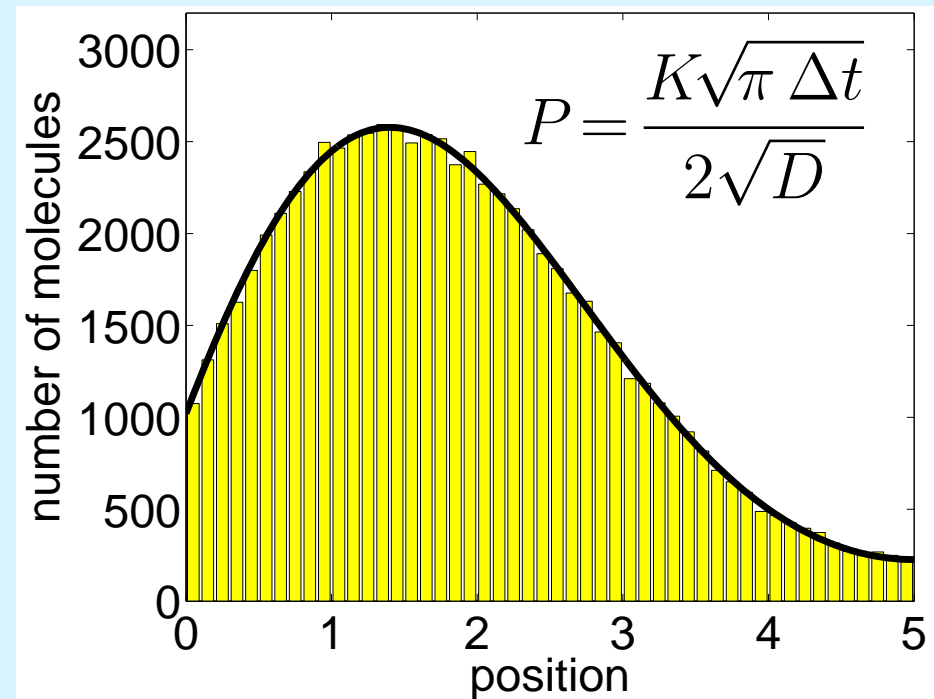
Correct choice of P for different stochastic models

whenever a molecule hits the boundary, it is adsorbed with probability P , and otherwise reflected

Compartment-based model



Discretized Brownian motion



Relations between P and K for four different stochastic simulation algorithms are derived in *RE and J. Chapman, Physical Biology, 2007*. Both position and velocity jump processes are analyzed.

In this talk, I will discuss the derivation for the discretized Brownian motion.



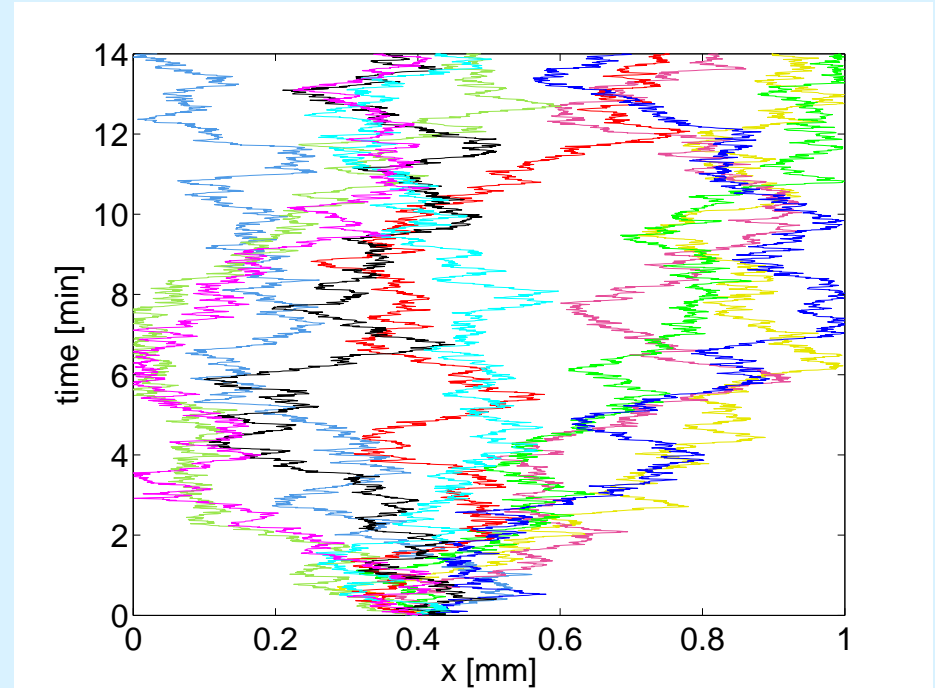
Discretized Brownian motion

Stochastic model of diffusion:

$$X(t + \Delta t) = X(t) + \sqrt{2D \Delta t} \zeta_x$$

ζ_x ... normally distributed random variable with zero mean and unit variance

D ... diffusion constant



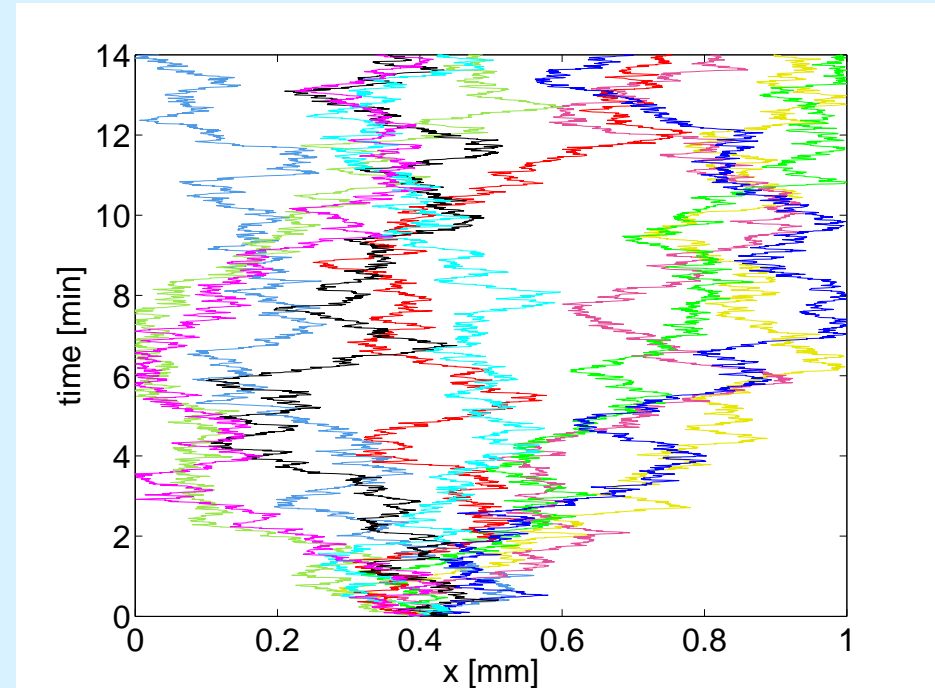
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Remarks:

- $X(t + \Delta t) = X(t) + \sqrt{2D \Delta t} \zeta_x$ is the Euler-Maruyama discretization of the stochastic differential equation (SDE) $X(t + dt) = X(t) + \sqrt{2D} dW$
- the Fokker-Planck equation corresponding to this SDE is the diffusion equation

$$\frac{\partial c}{\partial t}(x, t) = D \frac{\partial^2 c}{\partial x^2}(x, t)$$

- however, we want to analyse the algorithm which uses the finite time step Δt
=> we will analyse a suitable integral equation

Derivation of reactive boundary condition

Diffusion in half-line $[0, \infty)$. Reactive boundary at $x = 0$.

$$X(t + \Delta t) = X(t) + \sqrt{2D \Delta t} \zeta_x \quad (*)$$

Boundary condition at $x = 0$: **whenever a molecule hits the boundary, it is adsorbed with probability $P = \bar{P}\sqrt{\Delta t}$, and otherwise it is reflected.**

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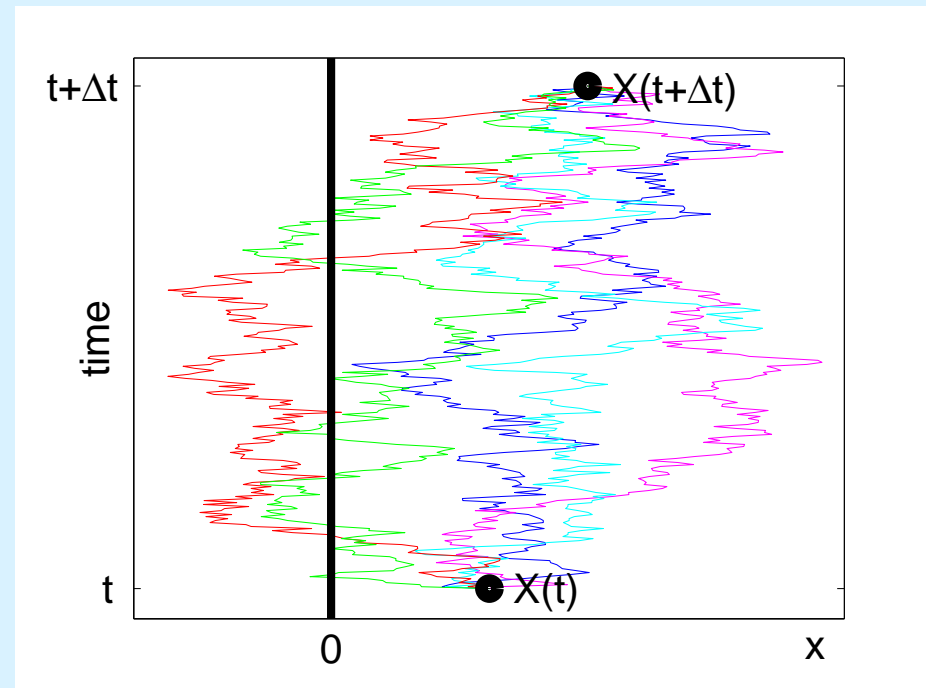
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This can be interpreted in two ways:

(a) If $X(t + \Delta t)$ computed by (*) is negative, then $X(t + \Delta t) = -X(t) - \sqrt{2D \Delta t} \zeta_x$ with probability $1 - \bar{P}\sqrt{\Delta t}$, otherwise we remove the molecule from the system.

(b) If $X(t + \Delta t)$ computed by (*) is positive, then we remove the molecule from the system with probability

$$\exp[-X(t)X(t + \Delta t)/(D\Delta t)]\bar{P}\sqrt{\Delta t}.$$



We can use either (a), or (a)–(b). The analysis is the same. The results differ by a factor of two.

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Let $p_{\Delta t} \equiv p_{\Delta t}(x, t) : [0, \infty) \times \Delta t \mathbb{N}_0 \rightarrow [0, \infty)$ be the probability density function of this process, so that $p_{\Delta t}(x, i\Delta t)dx$ is the probability of finding a molecule in the interval $[x, x + dx]$ at time $t = i\Delta t$.

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$$p_{\Delta t}(x, t + \Delta t) = \int_0^\infty p(x, t + \Delta t | y, t) p_{\Delta t}(y, t) dy,$$

where $p(x, t + \Delta t | y, t)$ is the conditional probability distribution function of finding a molecule at point x at time $t + \Delta t$ given that it is at point y at time t .

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$$p(x, t + \Delta t | y, t) = \frac{1}{\sqrt{4\pi D \Delta t}} \left(\exp \left[-\frac{(x - y)^2}{4D \Delta t} \right] + (1 - \bar{P}\sqrt{\Delta t}) \exp \left[-\frac{(x + y)^2}{4D \Delta t} \right] \right)$$

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for the case (a). If (a)–(b) is used, then \bar{P} is replaced by $2\bar{P}$.

Boundary layer analysis

Our algorithm is equivalent to the integral equation:

$$p_{\Delta t}(x, t + \Delta t) = \int_0^{\infty} \frac{p_{\Delta t}(y, t)}{\sqrt{4\pi D \Delta t}} \left(\exp \left[-\frac{(x - y)^2}{4D \Delta t} \right] + (1 - \bar{P}\sqrt{\Delta t}) \exp \left[-\frac{(x + y)^2}{4D \Delta t} \right] \right) dy$$

We want to relate \bar{P} with the rate constant K of the boundary chemical reaction.

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$$p_{\Delta t}(x, t + \Delta t) = \int_0^\infty \frac{p_{\Delta t}(y, t)}{\sqrt{4\pi D \Delta t}} \left(\exp \left[-\frac{(x-y)^2}{4D \Delta t} \right] + (1 - \bar{P}\sqrt{\Delta t}) \exp \left[-\frac{(x+y)^2}{4D \Delta t} \right] \right) dy$$

We want to relate \bar{P} with the rate constant K of the boundary chemical reaction.

- Away from the boundary, a steepest descent approximation to the integral as

$$\Delta t \rightarrow 0 \text{ leads to the diffusion equation } \frac{\partial c}{\partial t}(x, t) = D \frac{\partial^2 c}{\partial x^2}(x, t).$$

- Close to the boundary, there is a boundary layer of width $\sqrt{\Delta t}$: we change variables from x to η by setting $x = \sqrt{\Delta t} \eta$ and define the inner solution $p_{inner}(\eta, t) = p_{\Delta t}(\sqrt{\Delta t} \eta, t)$. Expanding p_{inner} in the powers of $\sqrt{\Delta t}$, we obtain $p_{inner}(\eta, t) \sim p_{i,0}(\eta, t) + \sqrt{\Delta t} p_{i,1}(\eta, t) + \Delta t p_{i,2}(\eta, t) + \dots$

Using this expansion in the integral equation and matching with the outer

expansion, we get $p_{i,0}(t) = c(0, t)$ and $\lim_{\eta \rightarrow \infty} \frac{\partial p_{i,1}}{\partial \eta}(\eta, t) = \frac{\partial c}{\partial x}(0, t)$.

Boundary layer analysis

We get the Robin boundary condition by computing

$$D \frac{\partial c}{\partial x}(0, t) = D \lim_{\eta \rightarrow \infty} \frac{\partial p_{i,1}}{\partial \eta}(\eta, t) = D \lim_{\eta \rightarrow \infty} g(\eta) \text{ where } g \text{ is the solution of the}$$

$$\text{integral equation: } g(\eta) = \phi(\eta) + \frac{1}{\sqrt{4\pi D}} \int_{-\infty}^{\infty} g(\xi) \exp \left[-\frac{(\xi - \eta)^2}{4D} \right] d\xi$$

$$\text{where } \phi(\eta) = \frac{\bar{P} p_{i,0}}{\sqrt{2\pi D}} \exp \left[-\frac{\eta^2}{8D} \right] \left(\operatorname{erf} \left[\frac{\eta}{\sqrt{8D}} \right] - \operatorname{erf} \left[-\frac{\eta}{\sqrt{8D}} \right] \right).$$

Boundary layer analysis

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Applying the Fourier transform and Cauchy's residue theorem, we get

$$D \lim_{\eta \rightarrow \infty} g(\eta) = \frac{\bar{P} \sqrt{D}}{\sqrt{\pi}} p_{i,0}. \text{ Since } p_{i,0}(t) = c(0, t), \text{ we obtain } K = \frac{\bar{P} \sqrt{D}}{\sqrt{\pi}}.$$



Boundary layer analysis

We get the Robin boundary condition by computing

$$D \frac{\partial c}{\partial x}(0, t) = D \lim_{\eta \rightarrow \infty} \frac{\partial p_{i,1}}{\partial \eta}(\eta, t) = D \lim_{\eta \rightarrow \infty} g(\eta) \text{ where } g \text{ is the solution of the}$$

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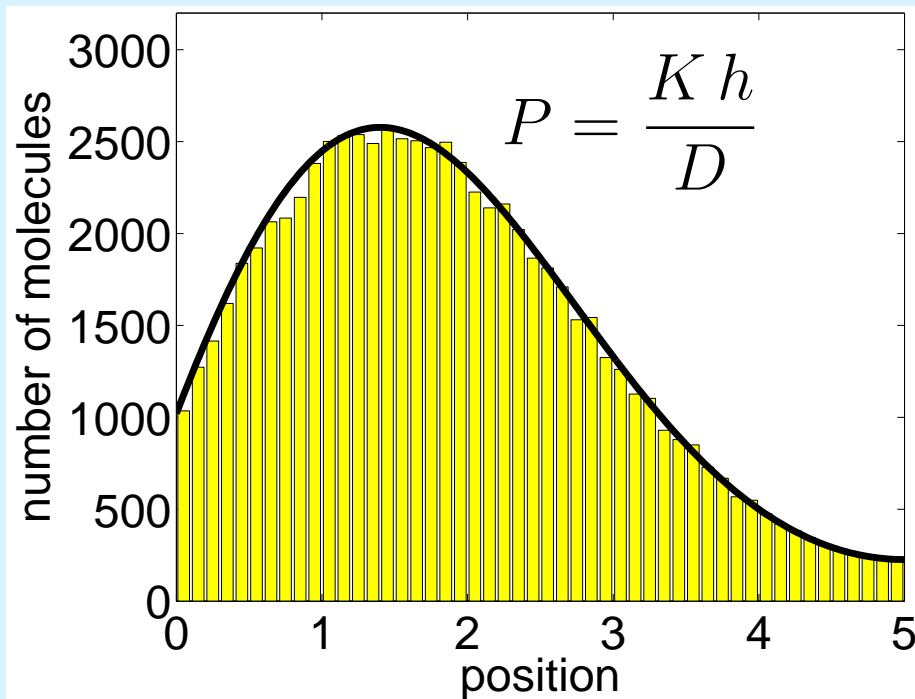
$$\text{If the boundary condition (a)–(b) is used instead of (a), we have } K = \frac{2\bar{P} \sqrt{D}}{\sqrt{\pi}}$$

$$\text{which implies } P = \bar{P} \sqrt{\Delta t} = \frac{K \sqrt{\pi} \Delta t}{2\sqrt{D}}.$$

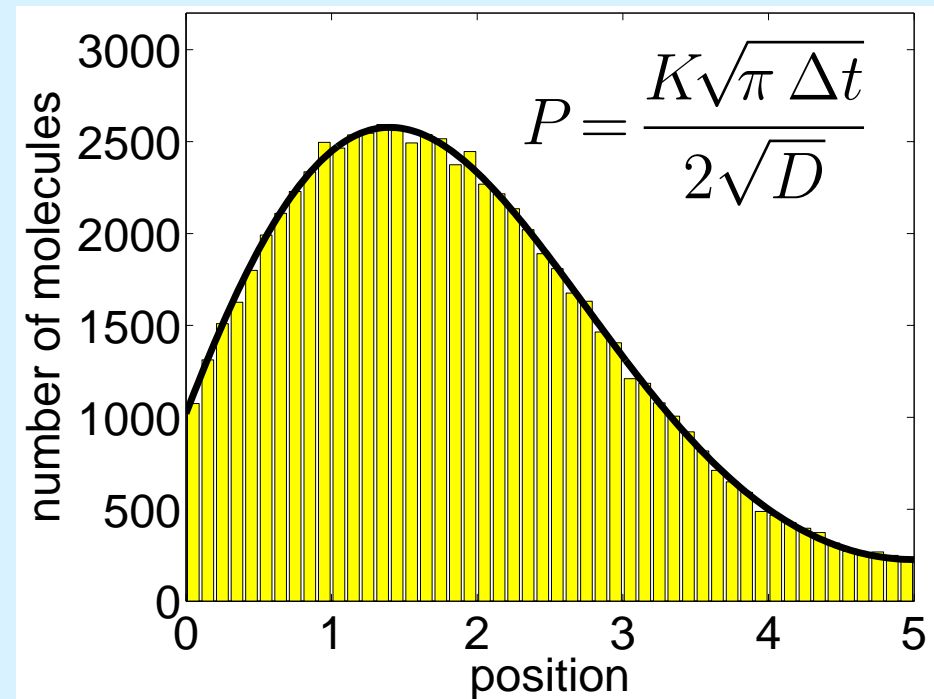
Correct choice of P for different stochastic models

whenever a molecule hits the boundary, it is adsorbed with probability P , and otherwise reflected

Compartment-based model



Discretized Brownian motion

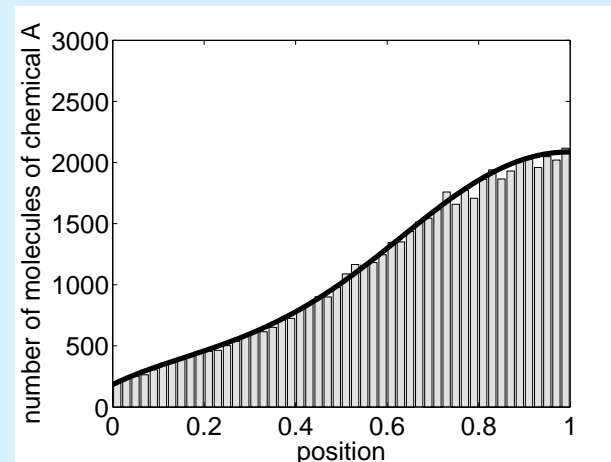
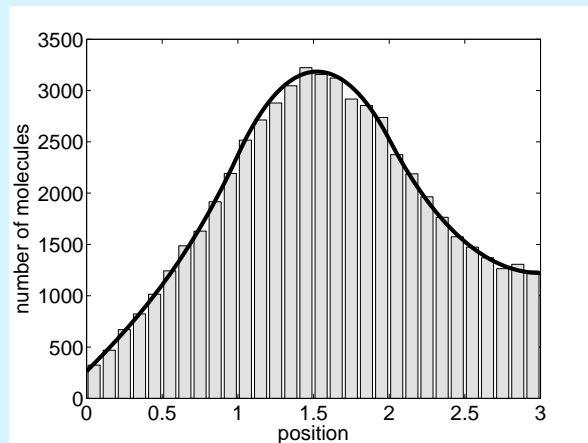


Relations between P and K for four different stochastic simulation algorithms are derived in *RE and J. Chapman, Physical Biology, 2007*. Both position and velocity jump processes are analyzed.

Boundary conditions for reaction-diffusion-taxis processes

We discussed diffusion so far, but:

- the boundary conditions for stochastic models of reaction, diffusion and taxis only depend on the corresponding model of the diffusion
- chemical reactions (e.g. modelling gene regulatory networks) or taxis/advection (e.g. modelling ion channels, chemotaxis) do not influence the boundary conditions

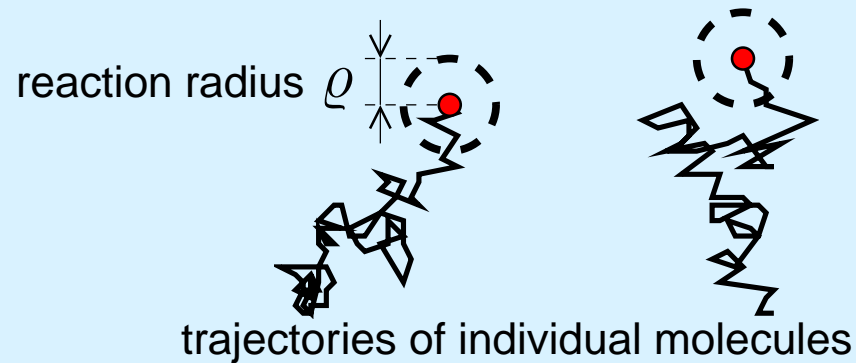


- the results can also be used for coupling detailed (stochastic) models of the boundary with continuum (PDE) models of the interior

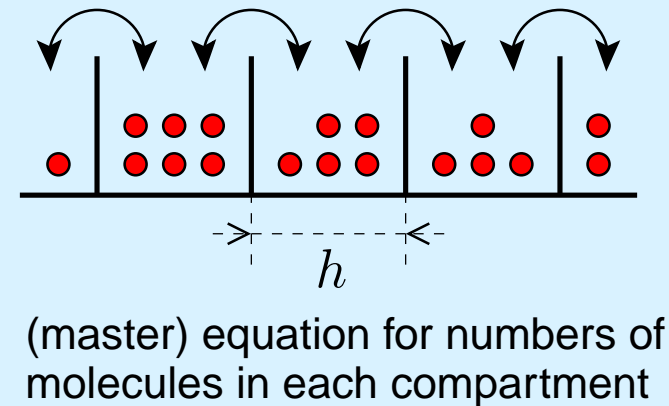
Overview of my talk

I introduced two classes of stochastic reaction-diffusion models:

Molecular-based modelling



Compartment-based modelling



In this talk, I discuss analysis of both stochastic reaction-diffusion approaches.

There are three situations which have to be handled with care:

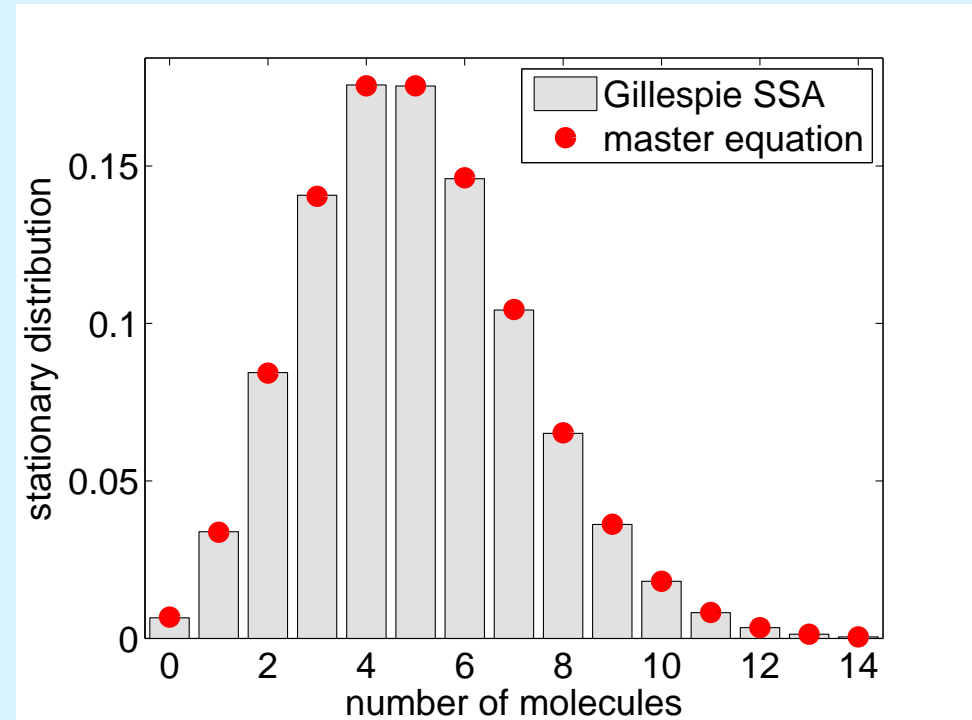
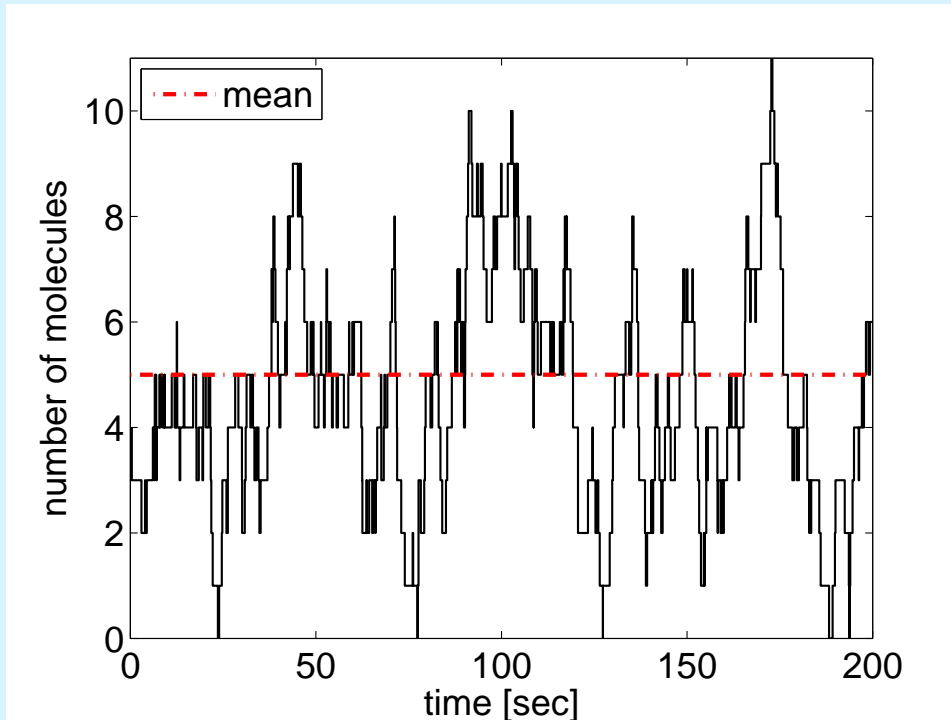
(i) modelling reactive boundaries

(ii) modelling bimolecular reactions



(iii) modelling reversible reactions

Bimolecular reactions – well-stirred systems



Propensity functions: $\alpha_1(t) = A(t)B(t)k_1/V$ $\alpha_2(t) = k_2V$

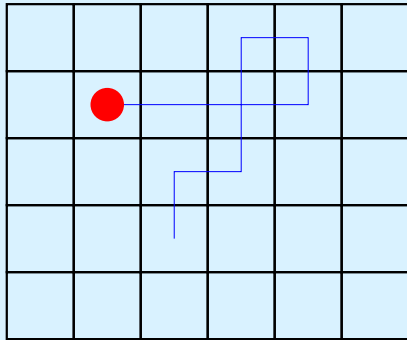
Probability that the i -th reaction occurs in the infinitesimally small time interval $[t, t + dt)$ is equal to $\alpha_i(t) dt$. \Rightarrow Gillespie stochastic simulation algorithm

Stationary distribution:
$$\phi(n) = \frac{1}{n!} \left(\frac{k_2 V^2}{k_1 B} \right)^n \exp \left[-\frac{k_2 V^2}{k_1 B} \right]$$

Stochastic simulation algorithms of diffusion

Compartment-based model:
lattice points a distance h apart

$$[X(t + \Delta t), Y(t + \Delta t), Z(t + \Delta t)] =$$



$$\left\{ \begin{array}{ll} [X(t), Y(t), Z(t)] & \text{with prob. } 1 - 6D\Delta t/h^2 \\ [X(t) - h, Y(t), Z(t)] & \text{with probab. } D\Delta t/h^2 \\ [X(t) + h, Y(t), Z(t)] & \text{with probab. } D\Delta t/h^2 \\ [X(t), Y(t) - h, Z(t)] & \text{with probab. } D\Delta t/h^2 \\ [X(t), Y(t) + h, Z(t)] & \text{with probab. } D\Delta t/h^2 \\ [X(t), Y(t), Z(t) - h] & \text{with probab. } D\Delta t/h^2 \\ [X(t), Y(t), Z(t) + h] & \text{with probab. } D\Delta t/h^2 \end{array} \right.$$

D ... diffusion constant, Δt ... time step

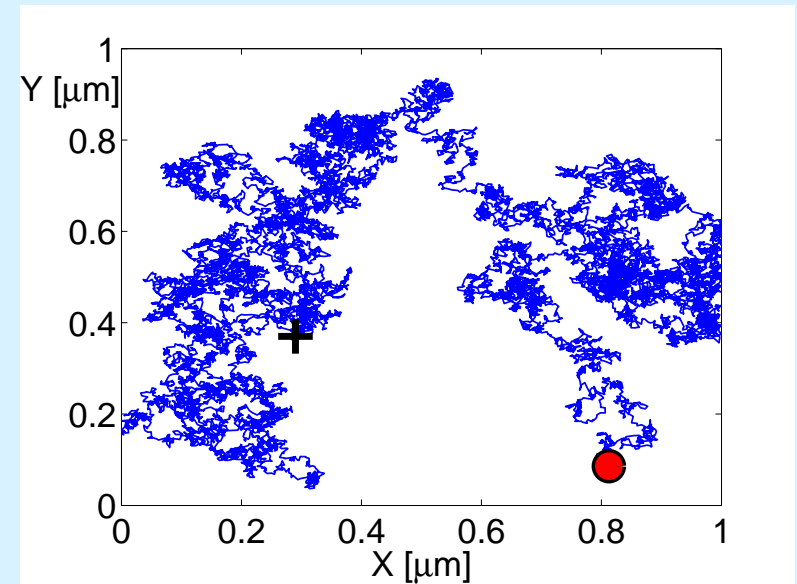
Discretized Brownian motion: off-lattice model

$$X(t + \Delta t) = X(t) + \sqrt{2D \Delta t} \zeta_x$$

$$Y(t + \Delta t) = Y(t) + \sqrt{2D \Delta t} \zeta_y$$

$$Z(t + \Delta t) = Z(t) + \sqrt{2D \Delta t} \zeta_z$$

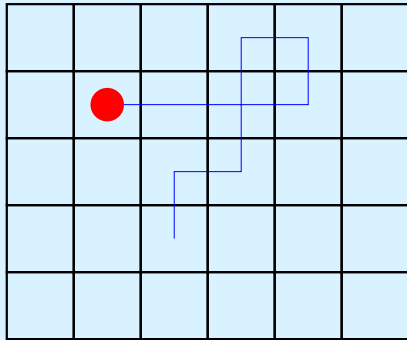
$\zeta_x, \zeta_y, \zeta_z$... normally distributed random variables with zero mean and unit variance



Compartment-based reaction-diffusion algorithm

Compartment-based model:
lattice points a distance h apart

$$[X(t + \Delta t), Y(t + \Delta t), Z(t + \Delta t)] =$$



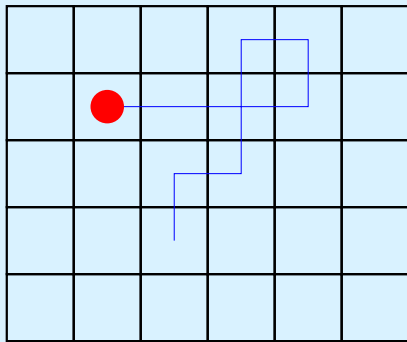
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D ... diffusion constant, Δt ... time step

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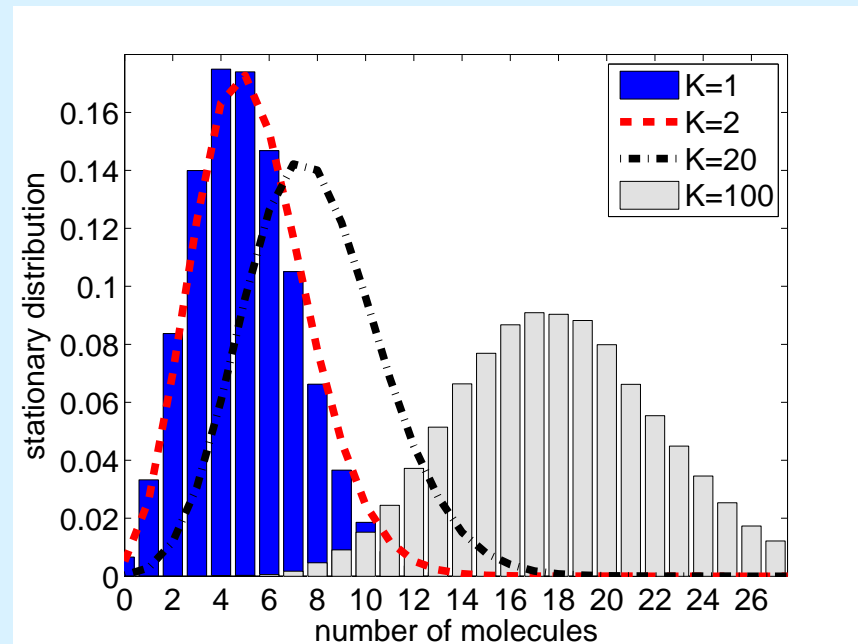
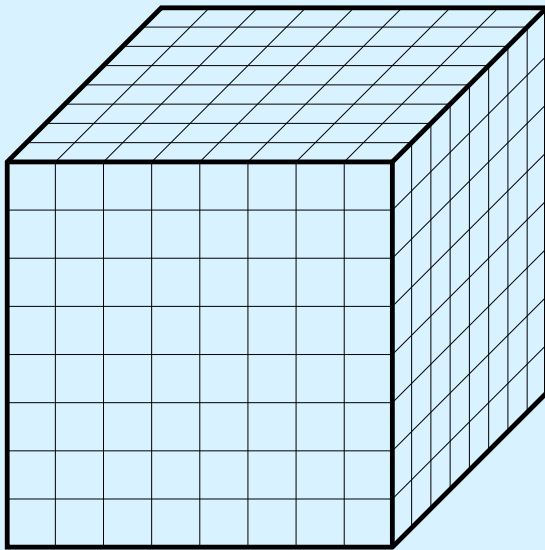
Modelling chemical reactions: cubic compartments of volume h^3 ; only molecules in the same compartment can react with each other

$A_{ijk}(t), B_{ijk}(t)$... numbers of molecules in the (i, j, k) -th compartment



Bimolecular reactions - compartment-based model

divide cubic domain $[0, L] \times [0, L] \times [0, L]$ into K^3 (well-mixed) compartments of volume h^3 where $h = L/K$



Conclusions:

- bimolecular reaction $A + B \rightarrow B$ is lost in the limit $h \rightarrow 0$
- the value of h should not be too small
(but h must be chosen small enough to get the desired spatial resolution)

Correcting compartment-based model

Bimolecular reaction $A + B \xrightarrow{k_1} B$

New "reactions": $A_{ijk} + B_{ijk} \xrightarrow{k_1} B_{ijk}$

Original propensity functions:

$$\alpha_{ijk,1}(t) = A_{ijk}(t)B_{ijk}(t) \frac{k_1}{h^3}$$

Solution: increase rate of bimolecular reaction per compartment =>

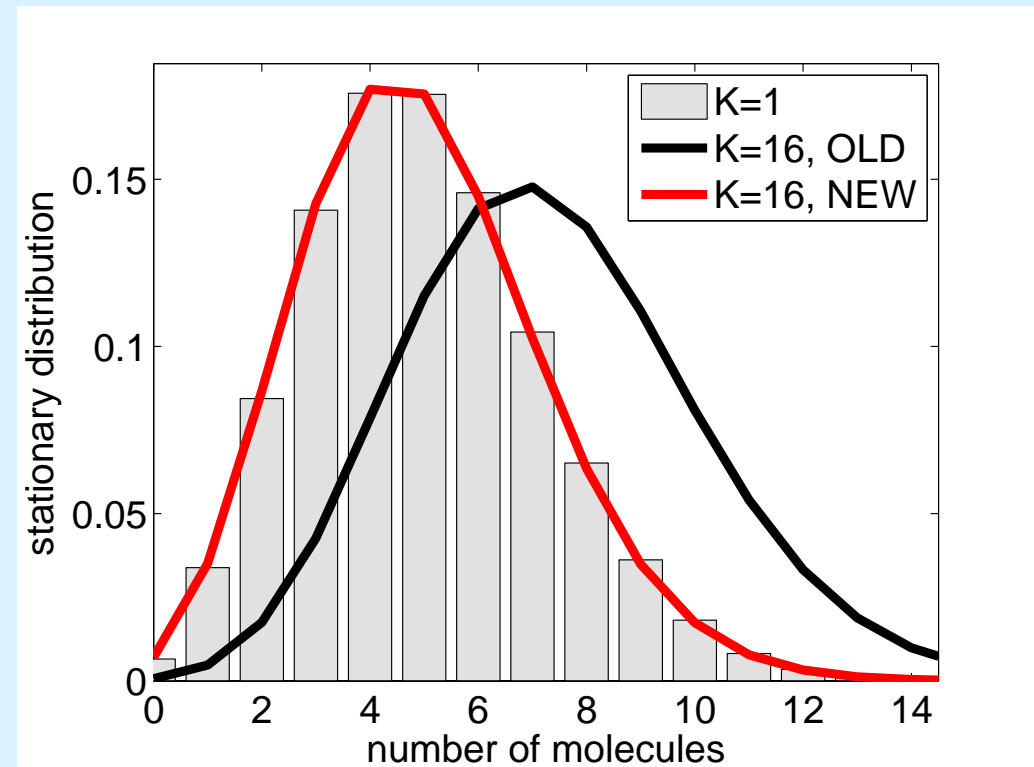
New propensity functions:

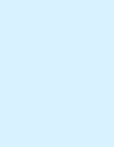
$$\alpha_{ijk,1}(t) = A_{ijk}(t)B_{ijk}(t) \frac{(D_A + D_B)k_1}{(D_A + D_B)h^3 - \beta h^2 k_1}$$

where $\beta \approx 0.25$

Compartment-based model can be corrected for $h \geq h_{crit} = \frac{\beta k_1}{D_A + D_B}$

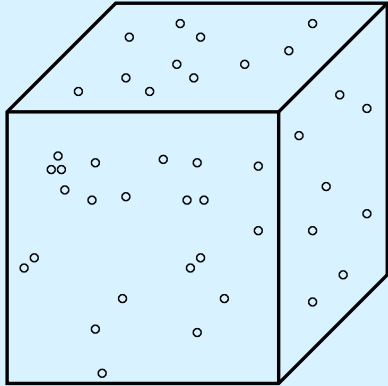
RE and J. Chapman, *Physical Biology*, 2009





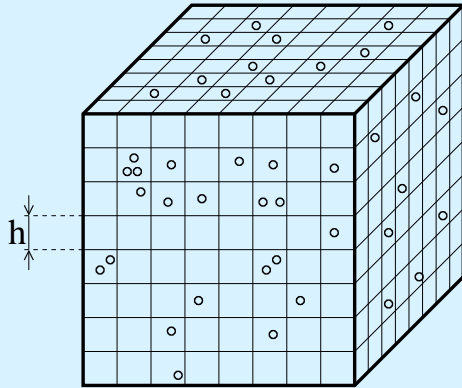
Stochastic reaction-diffusion modelling

Compartment-based model



Stochastic reaction-diffusion modelling

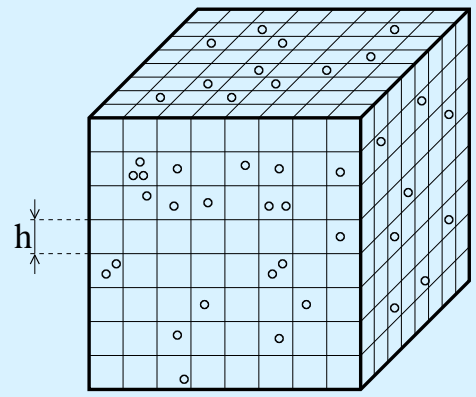
Compartment-based model



small compartments are assumed to be well-mixed
software: MesoRD (Hattne et al, Bioinformatics, 2005)

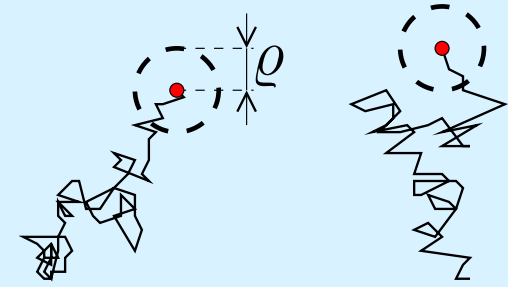
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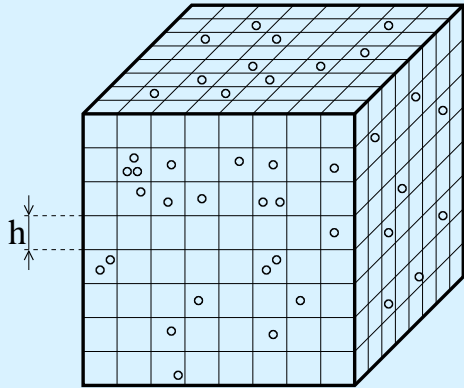
Molecular-based model



reaction radius ρ
Smoldyn (Andrews and Bray, Phys. Biol., 2004)

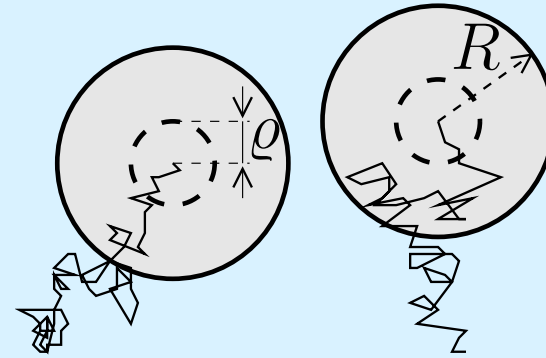
Stochastic reaction-diffusion modelling

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Molecular-based models

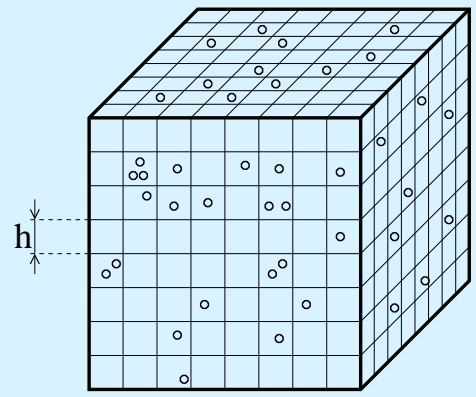


reaction radius ρ , molecular radius R
Smoldyn (Andrews and Bray, Phys. Biol., 2004)

Reaction radius ρ is unrealistically small for typical values of bimolecular rate constants and diffusion coefficients.

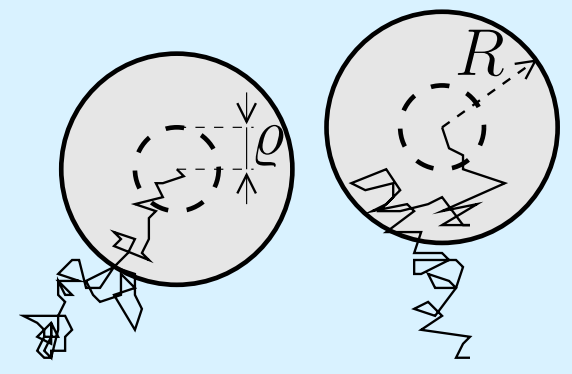
$\lambda-\bar{\varrho}$ stochastic reaction-diffusion algorithm

Compartment-based model



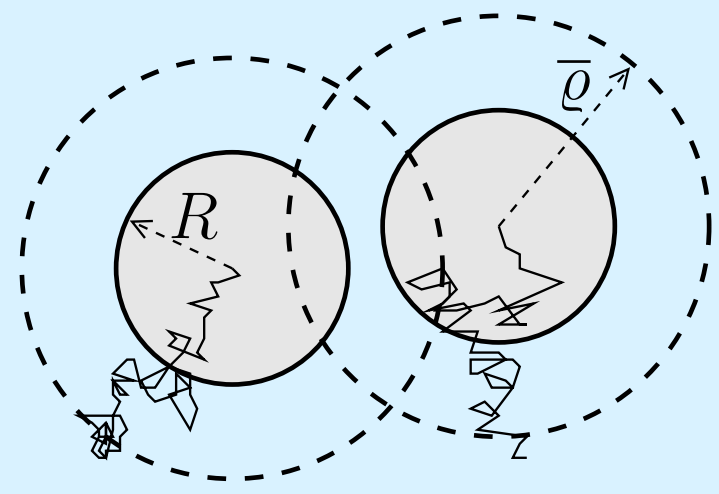
small compartments are assumed to be well-mixed
software: MesoRD (Hattne et al, Bioinformatics, 2005)

Molecular-based models



reaction radius ϱ , molecular radius R
Smoldyn (Andrews and Bray, Phys. Biol., 2004)

$\lambda-\bar{\varrho}$ model:



An “intermediate” model: whenever the distance between two molecules (which are subject to a bimolecular reaction) is less than $\bar{\varrho}$, they will react with with rate λ

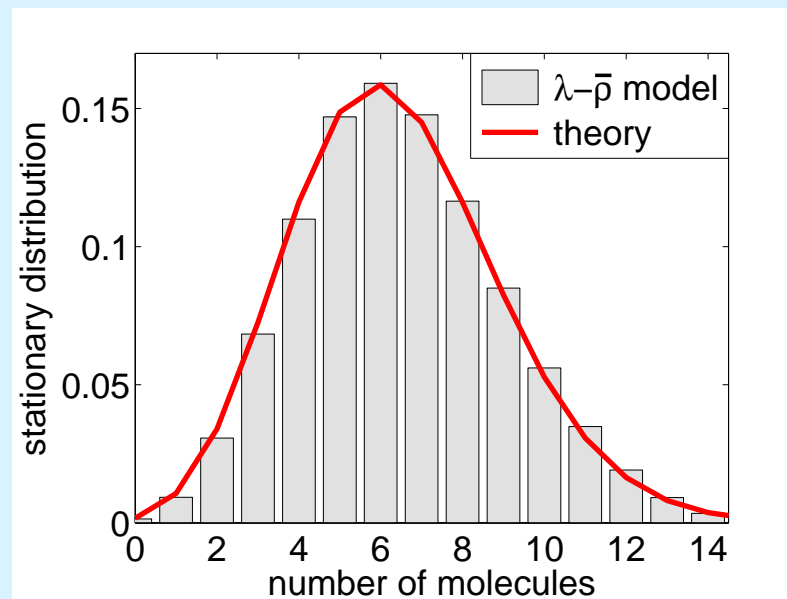
λ - $\bar{\varrho}$ stochastic reaction-diffusion algorithm

The relation between $\bar{\varrho}$ and λ and experimentally measurable parameters (kinetic rate constant k_1 , diffusion constants D_A and D_B):

$$k_1 = 4\pi(D_A + D_B) \left(\bar{\varrho} - \sqrt{\frac{D_A + D_B}{\lambda}} \tanh \left(\bar{\varrho} \sqrt{\frac{\lambda}{D_A + D_B}} \right) \right)$$

This formula is correct for a very small time step Δt (in the theoretical limit $\Delta t \rightarrow 0$). If the average jump length during one time step is comparable to $\bar{\varrho}$, then the relation between $\bar{\varrho}$, λ , k_1 , D_A and D_B also depends on Δt .

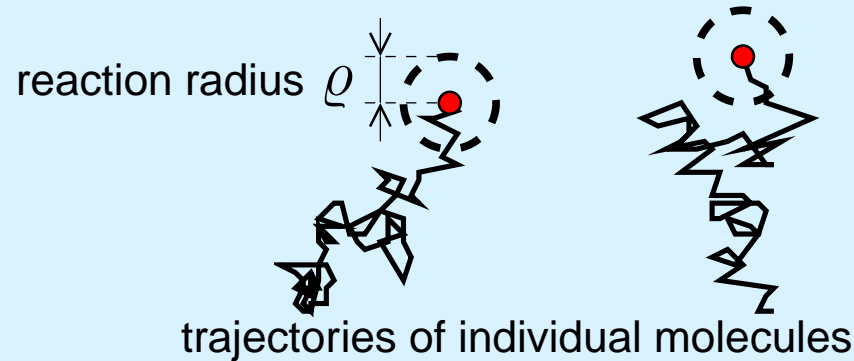
RE and J. Chapman, Physical Biology, 2009



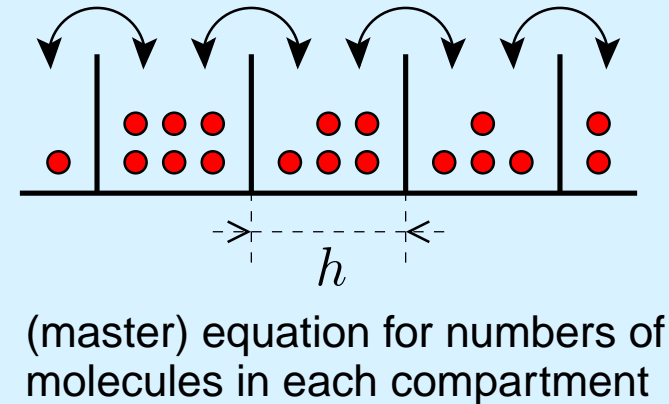
Overview of my talk

I introduced two classes of stochastic reaction-diffusion models:

Molecular-based modelling



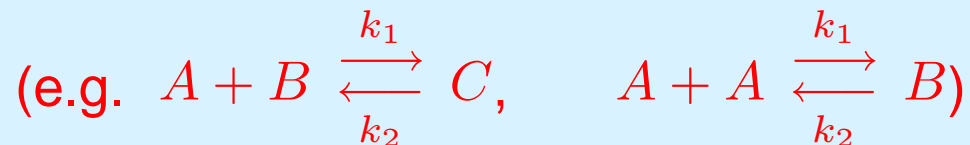
Compartment-based modelling



In this talk, I discuss analysis of both stochastic reaction-diffusion approaches.

There are three situations which have to be handled with care:

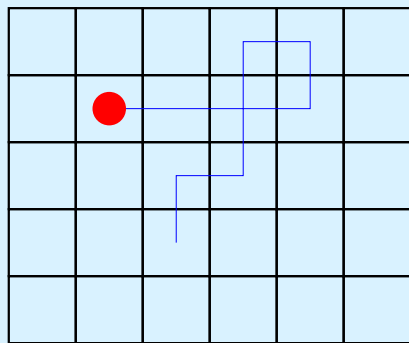
- (i) modelling reactive boundaries
- (ii) modelling bimolecular reactions
- (iii) modelling reversible reactions**



Diffusion models in reaction-diffusion algorithms

Compartment-based model:
lattice points a distance h apart

$$[X(t + \Delta t), Y(t + \Delta t), Z(t + \Delta t)] =$$



$$\left\{ \begin{array}{ll} [X(t), Y(t), Z(t)] & \text{with prob. } 1 - 6D\Delta t/h^2 \\ [X(t) - h, Y(t), Z(t)] & \text{with probab. } D\Delta t/h^2 \\ [X(t) + h, Y(t), Z(t)] & \text{with probab. } D\Delta t/h^2 \\ [X(t), Y(t) - h, Z(t)] & \text{with probab. } D\Delta t/h^2 \\ [X(t), Y(t) + h, Z(t)] & \text{with probab. } D\Delta t/h^2 \\ [X(t), Y(t), Z(t) - h] & \text{with probab. } D\Delta t/h^2 \\ [X(t), Y(t), Z(t) + h] & \text{with probab. } D\Delta t/h^2 \end{array} \right.$$

D ... diffusion constant, Δt ... time step

software MesoRD: <http://mesord.sourceforge.net>

Discretized Brownian motion: off-lattice model

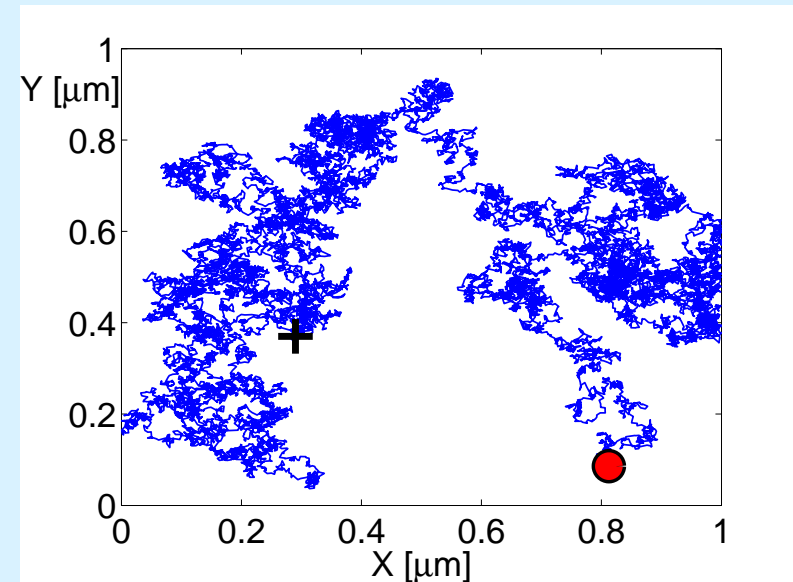
$$X(t + \Delta t) = X(t) + \sqrt{2D \Delta t} \zeta_x$$

$$Y(t + \Delta t) = Y(t) + \sqrt{2D \Delta t} \zeta_y$$

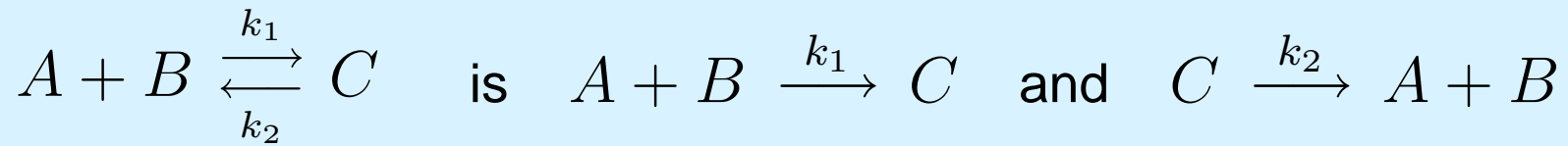
$$Z(t + \Delta t) = Z(t) + \sqrt{2D \Delta t} \zeta_z$$

$\zeta_x, \zeta_y, \zeta_z$... normally distributed random variables with zero mean and unit variance

software Smoldyn: <http://www.smoldyn.org>

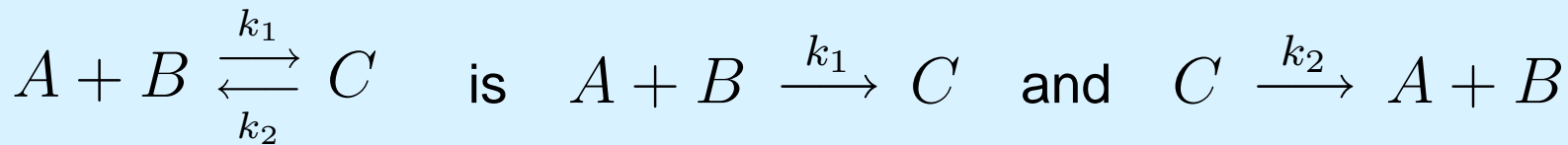


Reversible reactions – molecular-based modelling

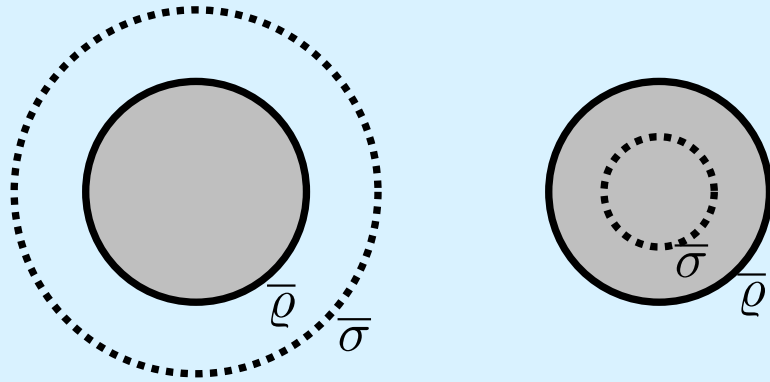


software Smoldyn introduces reaction radius ϱ and unbinding radius σ

Reversible reactions – molecular-based modelling



λ - $\bar{\rho}$ algorithm: two cases



reaction radius $\bar{\rho}$
unbinding radius $\bar{\sigma}$

$$\bar{\rho} > \bar{\sigma}: \quad k_1 = \frac{4\pi\bar{\sigma}(D_A + D_B) \left(\bar{\rho} \sqrt{\frac{\lambda}{D_A + D_B}} - \tanh \left(\bar{\rho} \sqrt{\frac{\lambda}{D_A + D_B}} \right) \right)}{\bar{\sigma} \sqrt{\frac{\lambda}{D_A + D_B}} - \bar{\rho} \sqrt{\frac{\lambda}{D_A + D_B}} + \tanh \left(\bar{\rho} \sqrt{\frac{\lambda}{D_A + D_B}} \right)}$$

$\bar{\rho} \leq \bar{\sigma}$:

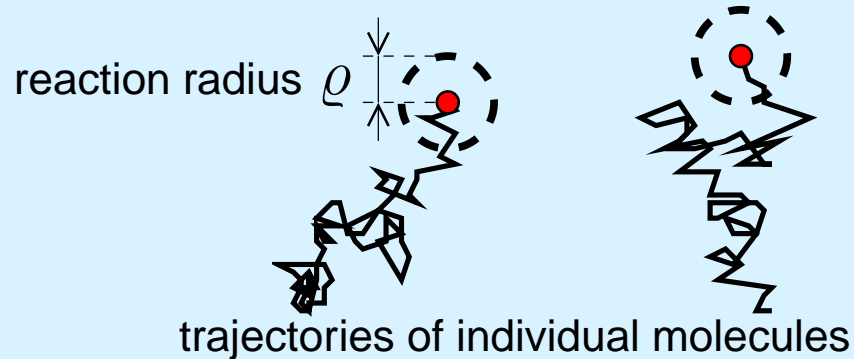
$$k_1 = \frac{4\pi\bar{\sigma}(D_A + D_B) \left(\bar{\rho} \sqrt{\frac{\lambda}{D_A + D_B}} - \tanh \left(\bar{\rho} \sqrt{\frac{\lambda}{D_A + D_B}} \right) \right)}{\cosh \left((\bar{\rho} - \bar{\sigma}) \sqrt{\frac{\lambda}{D_A + D_B}} \right) \tanh \left(\bar{\rho} \sqrt{\frac{\lambda}{D_A + D_B}} \right) - \sinh \left((\bar{\rho} - \bar{\sigma}) \sqrt{\frac{\lambda}{D_A + D_B}} \right)}$$

=> unbinding radius is not needed for $\bar{\rho}$ equal to a typical protein radius (nm)

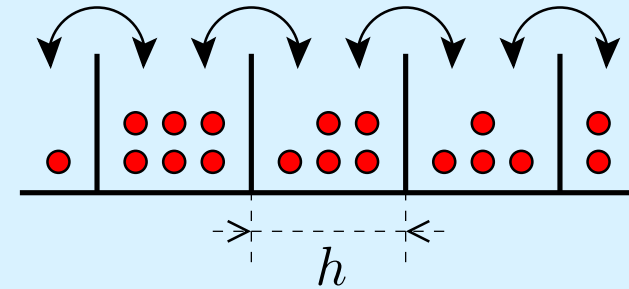
Summary

- stochastic modelling of chemical reactions and molecular diffusion:

Molecular-based modelling



Compartment-based modelling



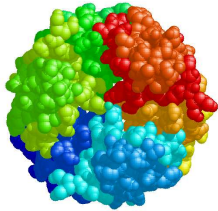
(master) equation for numbers of molecules in each compartment

- there are three situations which have to be handled with care:
 - reactive boundaries
 - bimolecular reactions
 - reversible reactions

Related problems

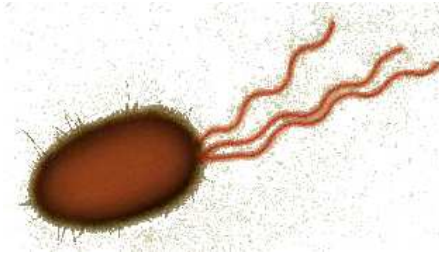
individual-level (microscopic) behaviour is often stochastic (fluctuations, noise)

macromolecules



genes and proteins

unicellular organisms



bacteria

animals



locusts

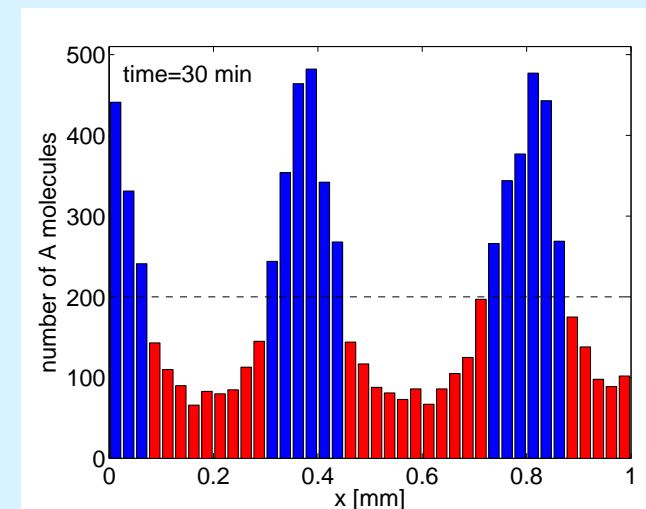
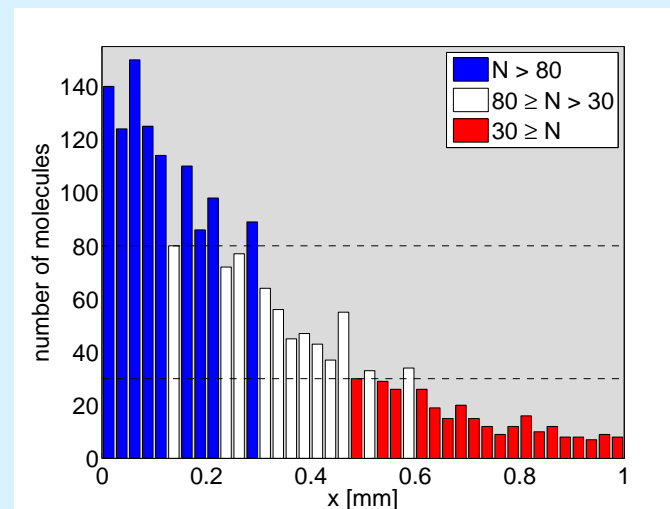
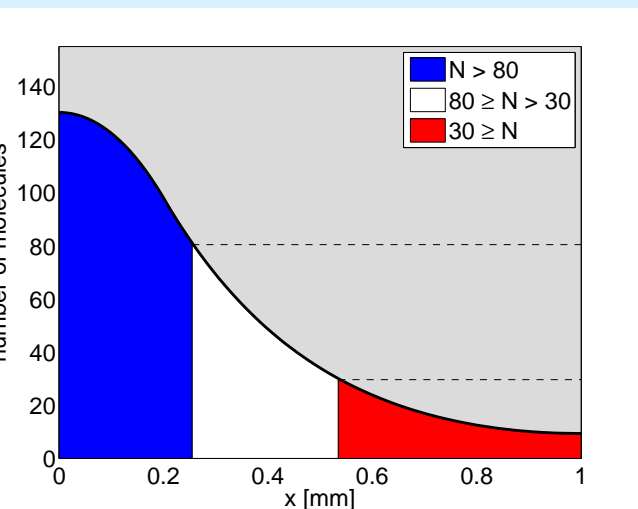
- derivation of macroscopic equations from individual-based models, understanding collective behaviour of interacting individuals
- **bacterial chemotaxis:** individual-based model is a velocity jump process with internal variables, each cell is described by its position x , velocity v and internal variables y
- **locusts:** self-propelled particle (individual-based) model

Buhl et al, Science, 2006; Yates et al, PNAS, 2009

Summary and open problems

I presented analysis of on-lattice and off-lattice stochastic reaction-diffusion models. Our goal is to answer the following questions:

- How do the parameters of algorithms relate to experimentally measurable quantities? What is the correct choice of the algorithm parameters?
- Under which conditions are the stochastic reaction-diffusion models equivalent? Can we use different models in different parts of the domain?
- What is the role of noise in biological systems? Pattern formation in developmental biology? Turing patterns? Intracellular concentration gradients?



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Preprints:

<http://people.maths.ox.ac.uk/erban>

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