1

bacterial chemosensors

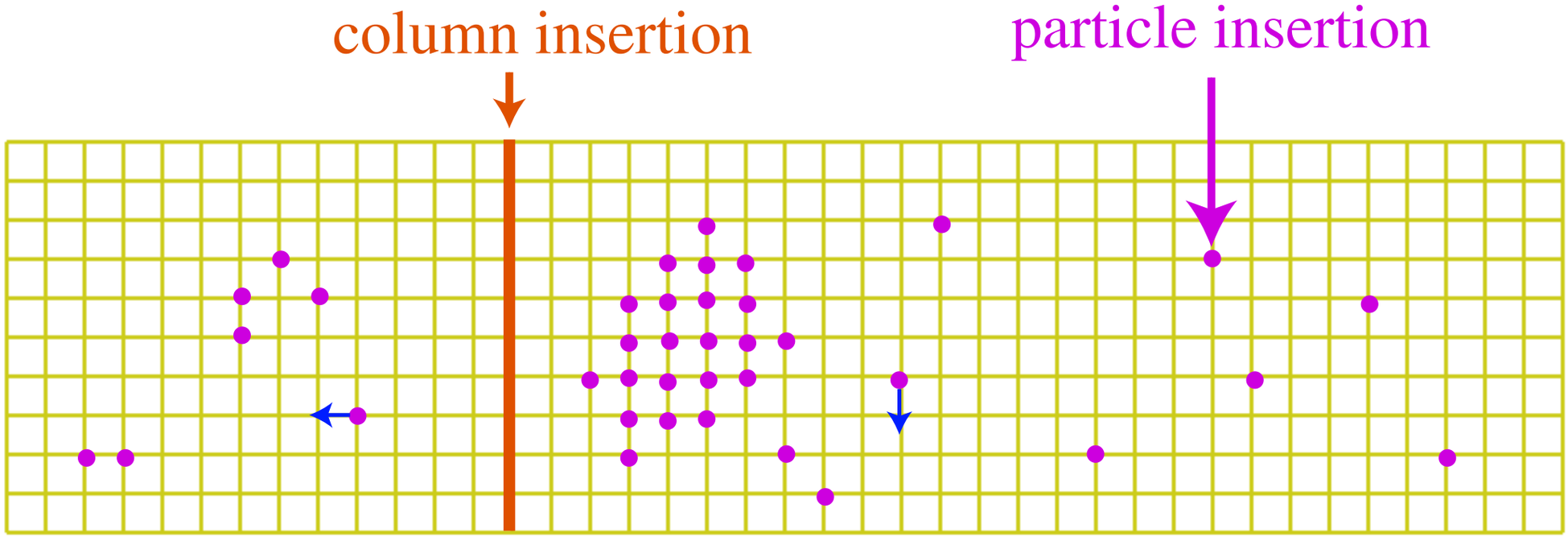
assembly model

spatial distribution of clusters

a simple spatial model

clusters are motionless

singles move on a grid



insertion: kon

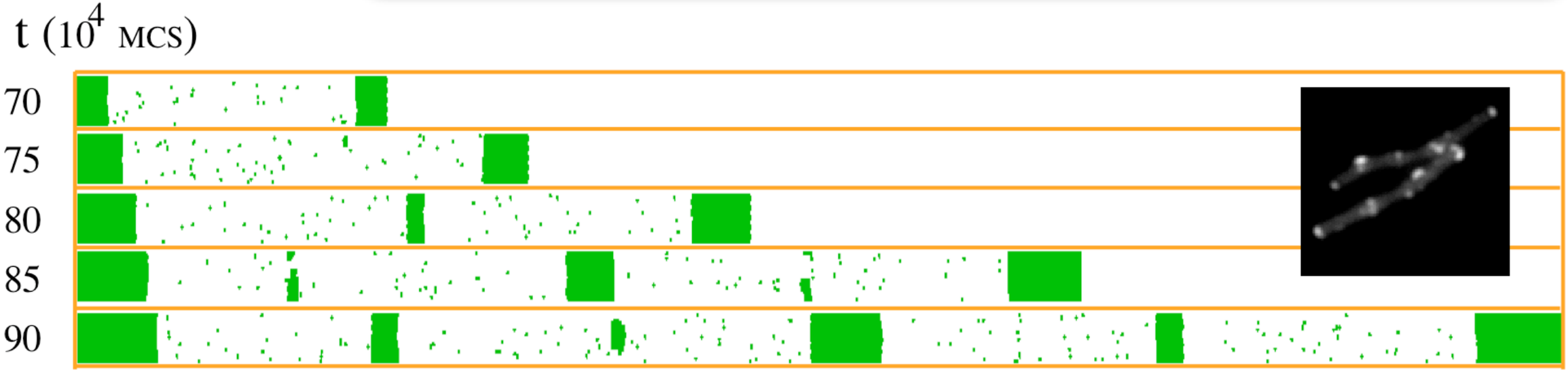
diffusion: D

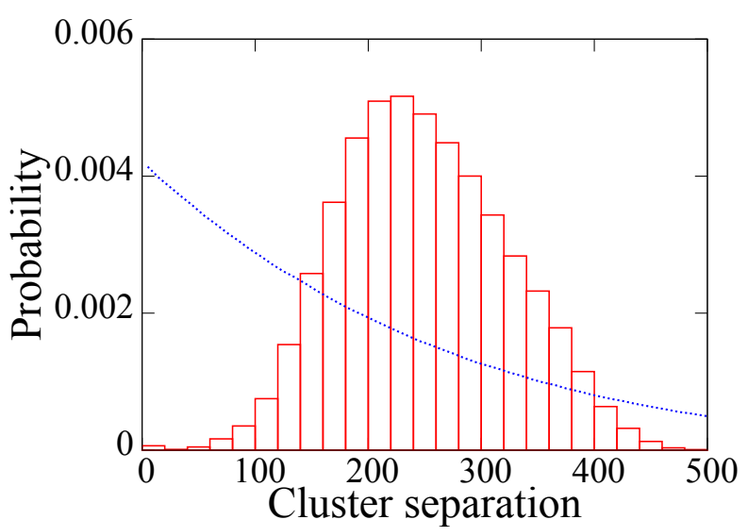
binding/unbinding: J, alpha

growth: gamma

reasonable parameters reproduce spatial arrangement of chemo-sensors

Self-organized periodicity of protein clusters in growing bacteria -PRL 2008





size seems to depend on age

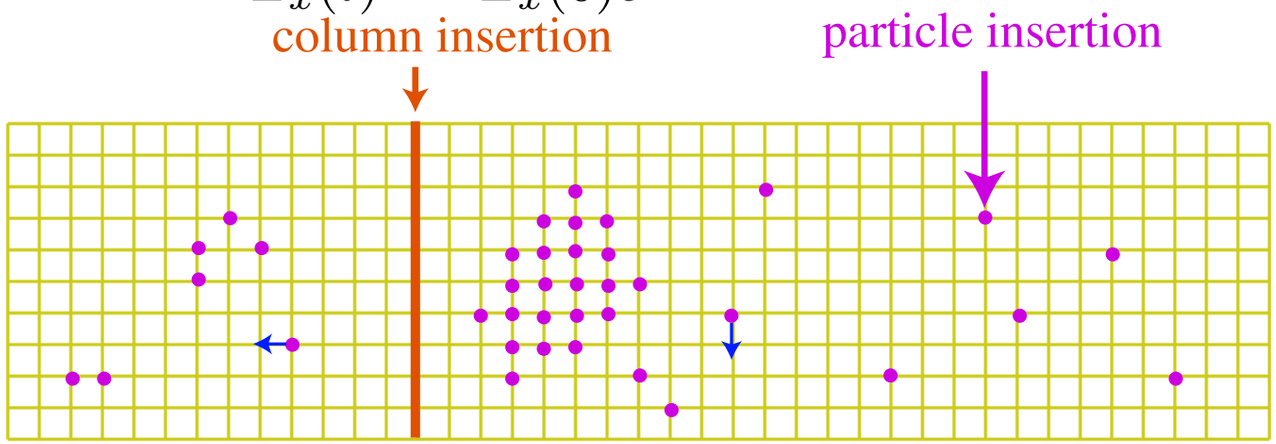
Metropolis simulation

Simple Ising model

With entropic penalty, alpha=0.5: "the price of lost freedom"

$$E = -J \sum_{<i,j>} \sigma_i \sigma_j \; + \; \alpha J n_{\mathrm{c}}$$

$$L_x(t) \; \approx \; L_x(0) e^{\gamma t}$$



E(X) only depends on degree distribution [*]

2

Metropolis algorithm

general definition

general principle

We assume:
- an energy function $E : X \to \mathbb{R}$ on a countable state space X
- an *a priori* symmetric irreflexive ($\alpha(x,x) = 0$) Markov kernel α on X

With this data, we can define a dtMC as a process that mostly but not always follows lines of decreasing energy (gradient-driven). The idea is that α will select a candidate transition which we then might accept with a certain probability. If energy diminishes along that transition *[why not with a probability that increases as a function of the $-\Delta E$??]* we take it certainly; if it increases we take it with a decreasing probability (as we are reluctant to climb up the energy landscape).

Note that the α kernel defines the transition graph.

Define for $\alpha(x,y) > 0$ (equivalently $\alpha(y,x) > 0$):

$$\begin{array}{lcll} \beta(x,y) & = & \min(1, e^{E(x)}\alpha(x,y)^{-1} \cdot e^{-E(y)}\alpha(y,x)) & \text{acceptance prob} \\ p(x,y) & = & \alpha(x,y)\beta(x,y) & \text{total motion prob} \end{array}$$

In case of a rejection we stay at x, which completes the definition of the transition function:

$$p(x,x) = 1 - \textstyle\sum_{y \neq x} \alpha(x,y)\beta(x,y) \quad \text{null event prob}$$

So - supposing wlog $\beta(x,y) \leq 1$ - we do get detailed balance wrt E:

$$\begin{aligned} p(y,x)/p(x,y) &= \alpha(y,x)/\alpha(x,y) \cdot \beta(y,x)/\beta(x,y) \\ &= \alpha(y,x)/\alpha(x,y) \cdot e^{-E(x)}\alpha(x,y) \cdot e^{E(y)}\alpha(y,x)^{-1} \\ &= e^{E(y)} \cdot e^{-E(x)} \end{aligned}$$

Note that this probability equipment preserves the underlying transition graph defined by α - as $\beta(x,y)$ is never zero. In particular it is still symmetric. Only the transition probabilities are altered. Unless x is a local max for E, $\sum_{y \neq x} p(x,y) < 1$, and the remaining mass is converted into staying put at x.

If α is uniform and the underlying transition graph is regular (with finite and non-zero degree), then $\beta(x,y)$ accepts certainly if $\Delta E := E(y) - E(x) \leq 0$ - or else with probability $\exp(-\Delta E) \leq 1$. This case is called Metropolis?

One can extend the above to $\Delta E = +\infty$ - then $\beta(x,y) = 0$ for infinite ys, ie rejection is certain. The underlying transition graph gets restricted (eg one can refuse to jump off a domain in the plane).

extensions

One can also extend this to non-symmetric α, in which case one needs to reject certainly if $\alpha(y, x) = 0$ (meaning β corrects the lack of symmetry by cancelling assymetric jumps).

One can also deal with non irreflexive α, but this seems idiotic.

One can use α to localize the moves, optimize the price of computing ΔE, and favour a priori y with lower energy if possible.

caveat!

A common mistake is to repeat without incrementing time - ie go *ostinato*. Eg write until($\omega_i, 0 \leq w_i \leq 1$) for the obstinate 2-step postselection (comme une boucle for en fait plutot puisque ca termine toujours), where:
- 1) one draws uniformly an i (in a finite non-empty set) and
- 2) accepts ω_i with probability w_i, or else goto 1 and advance time.

This picks up ω_i with probability $p(\omega_i) = w_i / \sum_j w_j$, as this probability $p(\omega_i)$ satisfies the recursive relation (supposing $|\Omega| = m < \infty$):

$$p(\omega_i) = w_i/m + 1/m(\sum_j (1 - w_j))p(\omega_i)$$

Getting to pick ω_i will happen after some mean time which one can also compute - this will increase as w_i decreases.

Now, supposing $E(x) \geq E(y)$ ie $w(x,y) = 1$:

$$\begin{aligned} p(y,x)/p(x,y) &= w(y,x)/\sum_{y'} w(y,y') \cdot \sum_{y'} w(x,y')/w(x,y) \\ &= \exp(E(y) - E(x)) \cdot \sum_{y'} w(x,y')/\sum_{y'} w(y,y') \end{aligned}$$

so that - if $\sum_{y'} w(x,y') = \sum_{y'} w(y,y')$ for any two neighbours x, y - E is an equilibrium for $p(x,y)$ (on the initial component). But there is no reason why this should be true in general with this assignment! Eg if x is the center of a star and has energy zero, while peripheral nodes ahev energy 1, then this is saying that $d(x) = 1/e$ which is absurd - perhaps in the limit where many neighbours have lower energy, therefore contributing a 1, the equation is approximately satisfied?

3

return to the model

event types

We have events of the following type:
- *growth* at rate γ, a grid column is duplicated
- *insertion* of new receptors, at rate k, one receptor is added to a free site on the grid
- *diffusion* of single receptors, at rate δ, one free receptor diffuses to a nearby free site on the grid
- *binding/unbinding* with energy ∂E defined by a coupling term J and an entropy cost for loss of freedom αJ - eg implemented by a Metropolis algorithm.

numerical values

Numerics:

- $L_y, J, \alpha = 50, 4, 0.5$;
- $\gamma, k = 8 \times 10^{-6}, 2 \times 10^{-6}$
- $D = 0.018 \mu m^2 s^{-1}$ which is related to δ by $h^2 \delta = D$, $h = \ell_y / L_y$, ℓ_y the actual dimension along y (we could take x as well) approximately $\ell_y = 3 \mu m$ (after Moran et al. SnapShot: key numbers in biology. Cell (2010) vol. 141 (7) pp. 1262).

NB: the state space $L_x(t) \times L_y \to \{0, 1\}$ grows with time; can we extend Spatial Kappa to do this?

diffusion

§diffusion - 1D case

$x \geq 0$, finite amount of stuff, $\partial_x n(0^+, t) = 0$:

$$n(x,t) \propto t^{-1/2} e^{-x^2/4Dt} \tag{7}$$

which verifies indeed $\partial_t n(x,t) = D\partial_{x^2} n(x,t)$ as both sides of the equation are equal to :

$$(e^{-x^2/(4Dt)}(x^2 - 2Dt))/(4Dt^{5/2})$$

(from alpha)

The diffusion length $\sqrt{4Dt}$ is the mean distance from origin after t time units, eg if $D = 0.018\mu m^2 s^{-1}$, then after $2.5s$, a particle has moved $\sqrt{0.18}\mu m \simeq 0.4\mu m$ so about $1/5$ of EColi's length.

Growth

Exercise: Write a Kappa model of this system without growth - how would you model growth?

We define a few simple observables:
- $N(t)$ for the total number of receptors
- $n(t)$ for the total number of free receptors (with no neighbouring receptor)
- $\rho(t) = n(t)/N(t)$ for the receptor 'density'

By the growth law, the average cell length is (we have exponential growth):

$$L_x(t) = L_x(0)e^{\gamma t} \tag{6}$$

keeping a nearly constant density

By the growth law, the average cell length is (we have exponential growth):

$$L_x(t) = L_x(0)e^{\gamma t}$$

and so the average total number of places (or sites) is:

$$N(t) = N(0)e^{\gamma t}$$

On the other hand, still on average:

$$\partial_t n(t) = k(N(t) - n(t))$$

with solution (C a constant):

$$n(t) = Ce^{-kt} + \frac{k}{k+\gamma}N(t)$$

So we can start at invariant density k/(k+gamma)

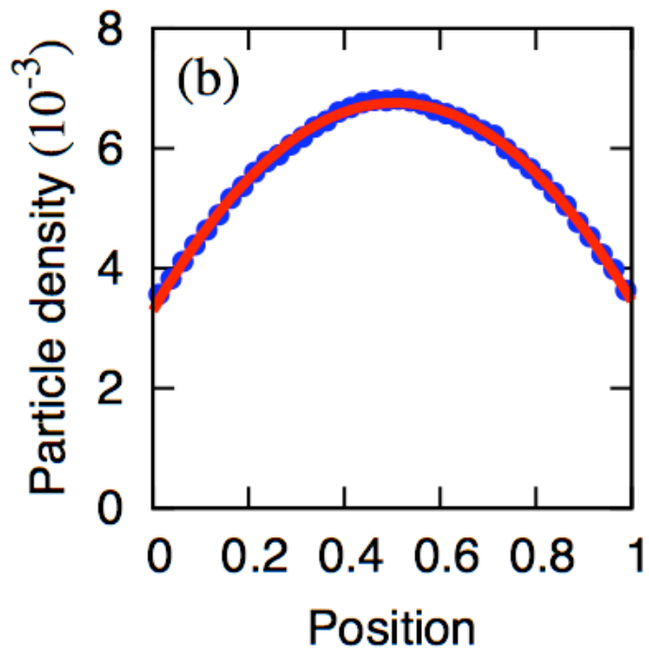
diffusion 2

§diffusion - 1D case with sinks

It is easy to see that the steady state solution to diffusion $\partial^{x^2} n(x) = 0$ with two sinks (clusters on each side are considered as sinks) separated by ℓ is:

$$n(x) = k/2D((x - \ell/2)^2 + (\ell/2)^2) \tag{11}$$

So max density is in the middle



Clusters will appear there