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Supporting Material

Precision of sensing cell length via concentration gradients

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Supplementary Material for "Precision of sensing cell length via concentration gradients"

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Numerical simulations and density fluctuations

To verify that the assumed forms for the density fluctuations are valid, stochastic simulations of the model of Padte et al. (1) were performed.

The cell membrane was modelled as a two-dimensional square lattice with separation δx between adjacent lattice sites. The number of lattice sites was $N_x = L/\delta x$ in the longitudinal (x) direction, extending from $x = -L/2$ to $x = L/2$, and $N_y = L_\perp/\delta x$ in the transverse (y) direction, extending from $y = 0$ to $y = L_\perp$. Periodic boundary conditions were applied to diffusing proteins in the y direction, while hard-wall (zero-flux) boundaries were applied to diffusion in the x direction at the two ends of the cell. The cytoplasmic compartment was modelled as a one-dimensional lattice aligned along the $x-$direction with identical spacing δx. Hard-wall boundaries were again applied at $x = \pm L/2$.

The system was updated with a constant time step δt. In each time step each protein molecule could undergo one reaction or movement event. Cytoplasmic protein could diffuse one lattice site left or right with probability $(\delta t)D_c/(\delta x)^2$ for each direction. Alternatively, cytoplasmic proteins could associate with the membrane with probability $(\delta t)r_{\text{assoc}}$ if they were located in one the N_{assoc} sites nearest to either cell pole (i.e. if $-L/2 \leq x < -L/2 + N_{\text{assoc}}(\delta x)$ or $L/2 - N_{\text{assoc}}(\delta x) < x \leq L/2$). Upon association the protein was removed from the cytoplasm and added to the membrane at the same x position but at a position in the $y-$direction chosen uniformly at random. Membrane proteins could diffuse with probability $(\delta t)D/(\delta x)^2$ to each of the four neighbouring lattice sites, or dissociate with probability $(\delta t)\mu$. To simulate protein production, at each time step a number of protein molecules to add to the system was chosen from a Poisson distribution with mean $(\delta t)r_{\text{prod}}$. These proteins were then added to the cytoplasm at random positions. There was no protein degradation in the simulations.

To simulate polar cell growth the size of the system in the x direction was increased by two lattice sites at intervals of $\tau_{\text{grow}} = 2(\delta x)/r_{\text{grow}}$, where r_{grow} is the cell growth rate, which was taken to be constant independent of length. The additional lattice sites were added symmetrically to the two ends of the cell. The $x-$positions of proteins which were already present within the system was not changed during growth. In effect, therefore, at each growth event the

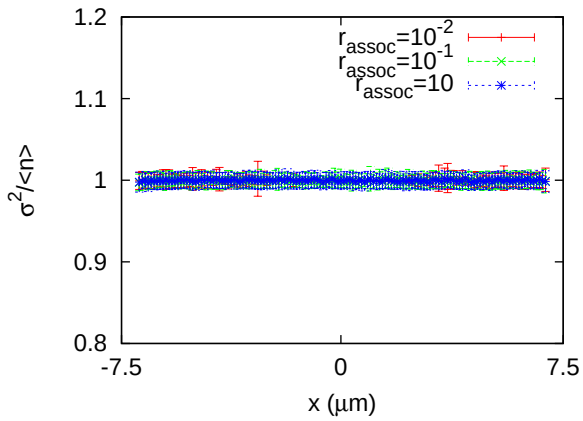

Figure 1: Instantaneous density fluctuations have $\sigma^2 \approx \langle n(x,L)\rangle$. The variance in the number of proteins at each lattice site, n, was calculated over the time for which the cell was at length $L = 14\mu m$. For each lattice site the Fano factor, $\sigma^2/\langle n\rangle$, was then calculated. Plotted is the mean of the Fano factor over all sites at a particular x position, with error bars of one standard deviation. Results are shown for simulations with three different values of $r_{\rm assoc}$. In all cases we find a Fano factor of 1.

proteins within the cell are translated by one lattice site relative to the origin pole of the cell, but their position relative to the cell mid-plane is unchanged.

Simulations were initialised with the cell of length $L = 5\mu m$ and $N = 1330$ proteins distributed uniformly in the cytoplasm, and run for a time of $1000s$ without growth to allow the protein distribution to reach steady state. Parameter values used in the simulations were as follows: $L_\perp = 10\mu m$, $\delta x = 0.1\mu m$, $\delta t = 10^{-4}s$, $D = 0.2\mu m^2 s^{-1}$, $D_c = 10\mu m^2 s^{-1}$, $\mu = 0.05s^{-1}$, $N_{\rm assoc} = 5$, $r_{\rm grow} = 10^{-3}\mu m s^{-1}$. $r_{\rm prod} = 0.267s^{-1}$ was chosen such that the mean protein concentration within the cell remained constant with growth and he mean protein copy number would be $N = 4000$ at $L = 15\mu m$. Simulations were performed with a range of values for $r_{\rm assoc}$, as described below.

These simulations were used to estimate fluctuations in the membrane protein density. First, the variability of protein density at a single detector site was quantified. To do this, the variance in the protein number while the system was of length L was calculated for each lattice site on the cell membrane. Simulations were performed with values of $r_{\rm assoc}$ ranging from 10^{-3} to 100. In all cases it was found that $\sigma^2_{n(x,L)} \approx \langle n(x,L)\rangle = \langle \rho(x,L)\rangle(\delta x)^2$. Figure 1 shows a representative example.

Finally we examined fluctuations in the time-averaged density. The density at each detector site was integrated from a time $t_{\rm initial}$ to $t_{\rm initial} + \tau$, and the resulting variance between different sites at the same $x-$position was calculated. This procedure was then repeated over ten independent simulations.

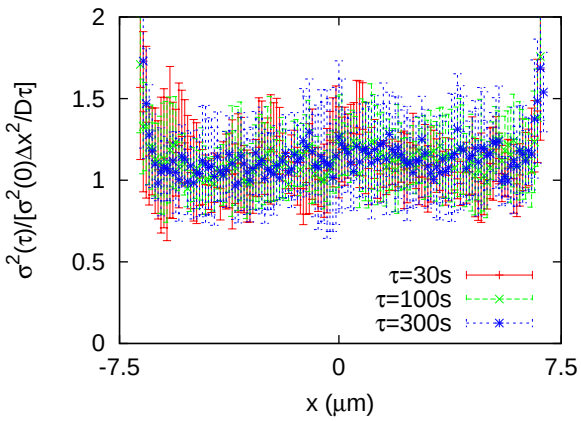

Figure 2: Time-averaged density fluctuations follow $\sigma^2(\tau) \sim \sigma^2(0)/\tau$. The occupancy of each lattice site was averaged over a time interval τ. The variance in the time-averaged occupancies between different lattice sites at the same $x-$position was then calculated. Each point shows the mean and error bar of one standard deviation of this variance over 10 simulation runs, scaled by the expected variance, $\langle n(x,L)\rangle(\Delta x)^2/(D\tau)$, with error bars of one standard deviation over the different simulations. Results for different integration periods τ are shown in different colours. In each case $t_{\rm initial}$ was during the period when $L = 13.8\mu m$. The value $r_{\rm assoc} = 1s^{-1}$ was used.

An example is shown in Figure 2. Near the mid-cell positions with which we are primarily concerned we find good agreement with the expected result, $\sigma^2(t_{\rm initial},\tau) \approx \sigma^2(t_{\rm initial},0)(\Delta x)^2/(D\tau)$, where $\sigma^2(t_{\rm initial},0) = \langle n(x, L(t_{\rm initial})\rangle$, up to a constant numerical factor of order ~ 1.1. At the cell ends significant deviations from the expected result can be found. However, these do not affect the conclusions of the paper.

References

1. Padte, N. N., S. G. Martin, M. Howard, and F. Chang, 2006. The Cell-End Factor Pom1p Inhibits Mid1p in Specification of the Cell Division Plane in Fission Yeast. *Curr. Biol.* 16:2480–2487.