A. Particle interactions in the simulation algorithm

The Min reaction scheme as introduced in equations (1a – 1e) of the main text consists of five molecular reactions, which can be classified into three different types of reactions.

(i) First-order unimolecular reactions of the type $A \xrightarrow{k_1} B$. These kind of reactions have no dependence on the spatial coordinates of the system. In the Min reaction scheme the nucleotide exchange reaction ($\lambda$) in the bulk and the membrane detachment ($\sigma_{off}$) are of this type.

(ii) Simple membrane attachment reactions are also first-order unimolecular reactions of the above type $A \xrightarrow{k_{1,m}} B$, but with the additional constraint that a particle must be in close proximity to a membrane to be able to attach to it. The binding of MinD in its ATP-bound state to the membrane ($\sigma_D$) is a reaction of this type.

(iii) Bimolecular membrane attachment reactions. This reaction type is of second-order

$$A + B \xrightarrow{k_{2,m}} \text{product(s)}$$

and describes the bimolecular association of a particle in the bulk with an already membrane-bound particle. The cooperative MinD recruitment ($\sigma_{dD}$) and the MinE recruitment ($\sigma_E$) by membrane-bound MinD are reactions of this type.

To create a consistent particle-based simulation algorithm for the above introduced types of reactions, we compare our reactive Brownian dynamics algorithm with the corresponding mean-field partial differential equations, as they are for example studied in [1]. For this we consider each of the three reaction types individually using only a simplified minimal setting.

(i) First-order unimolecular reactions

For the first reaction type the corresponding differential equation is a simple Poisson process

$$\partial_t \rho = -k_1 \rho,$$
where \( \rho \) denotes the free particle density and \( k_1 \) is the corresponding first-order reaction rate constant. Introducing a concrete system size \( V \) we can equally convert particle densities into particle numbers \( N \) and have equivalently \( \partial_t N = -k_1 N \) with the standard exponential solution

\[
\rho(t) = \rho_0 e^{-k_1 t}, \quad N(t) = N_0 e^{-k_1 t}.
\]

In a particle-based simulation framework with a total of \( N_0 \) particles of a generic species \( A \) we are interested in the reaction probability \( p_{\text{react,1}}(\Delta t) \), that a particle of type \( A \) undergoes such a first-order reaction within a fixed, finite time step of length \( \Delta t \). After a time \( t = \Delta t \) the solution of the linear degradation equation (3) tells us that \( n_r \) particles will have reacted

\[
n_r = N_0 - N(\Delta t) = N_0 (1 - e^{-k_1 \Delta t}).
\]

This means that a single particle has a probability of

\[
p_{\text{react,1}}(\Delta t) = 1 - \exp(-k_1 \Delta t),
\]

to react during a time step \( \Delta t \).

(ii) First-order membrane attachment

For this second reaction type we consider a setting with a membrane at the bottom surface at \( z = 0 \) of a rectangular simulation volume \( V \) to which a generic species \( A \) can attach. In this scenario the lateral displacements in both the \( x \)- and \( y \)- direction can be integrated out in a straightforward way allowing us to reduce the system to an effective one-dimensional system where \( z \) is the only spatial dependency that remains. In the resulting one-dimensional domain we have a membrane at \( z = 0 \) and impose a reflecting no-flux boundary condition at \( z = L_z \). The corresponding differential equation for the particle density \( \rho(z,t) \) now reads

\[
\partial_t \rho(z,t) = D \partial_{zz} \rho(z,t) - \sigma \delta(z) \rho(z,t) \quad \text{with} \quad 0 \leq z \leq L_z
\]

subject to \( \partial_z \rho(z,t) \mid_{z=L_z} = 0 \). In the particle-based simulation framework we again want to implement this first-order process using a Poisson rate \( k_{1,m} \) to come up with a reaction probability \( p_{\text{react,1m}}(\Delta t) \) that a particle has attached to the membrane within a fixed, finite time step \( \Delta t \). Since we want only particles that are in close proximity to the membrane to be able to attach to it, we introduce a finite distance \( d \) to encode this spatial confinement (see figure 1). In this way only particles within a distance \( z < d \) to the bottom surface at \( z = 0 \) can attempt this first
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order attachment reaction. In this picture the actual system boundary at \( z = 0 \) is also treated as a reflective no-flux boundary like the opposite boundary at \( z = L_z \), since the adsorption step can now happen anywhere in the layer of thickness \( d \) above the bottom surface.

To relate the Poisson-rate \( k_{1,m} \) to the rate constant \( \sigma \) of the mean-field equation (6) we approximate the \( \delta \)-functional in equation (6) by a \( \Theta \)-function of width \( d \)

\[
\delta(z) \rightarrow \frac{1}{d} \Theta(d - z) \quad \text{with} \quad z > 0,
\]

mimicking our scenario in the particle-based framework. Using \( \rho = \rho(z,t) \) and the approximation from above we obtain

\[
\partial_t \rho = D \partial_{zz} \rho - \frac{\sigma}{d} \Theta(d - z) \rho.
\]

Integrating once over the full domain we get

\[
\int_0^{L_z} \partial_t \rho \, dz = \int_0^{L_z} \left[ D \partial_{zz} \rho - \frac{\sigma}{d} \Theta(d - z) \rho \right] \, dz.
\]

The term on the left hand side of the above expression

\[
\int_0^{L_z} \partial_t \rho \, dz = \partial_t \int_0^{L_z} \rho \, dz = \partial_t N
\]

is the time derivative of the total amount of particles, while the term

\[
\int_0^{L_z} \Theta(d - z) \rho \, dz =: N_d
\]

denotes all particles \( N_d \) that are less than \( d \) away from the membrane at \( z = 0 \). The term \( \int_0^{L_z} D \partial_{zz} \rho \, dz \) vanishes because of the reflecting boundary conditions (\( \partial_z \rho(0) = \partial_z \rho(L_z) = 0 \)). With this we obtain

\[
\partial_t N = - \frac{\sigma}{d} N_d.
\]

Since in this setting \( N \) can only change by membrane attachment of the particles \( N_d \), we can identify \( \sigma/d \) as the desired Poisson rate

\[
k_{1,m} = \frac{\sigma}{d}
\]

for the first-order reaction step that we wish to implement. This means that a single particle that is within distance \( d \) of a reactive surface of the system has a probability of

\[
p_{\text{react},1m}(\Delta t) = 1 - \exp(-k_{1,m} \Delta t) = 1 - \exp\left(-\frac{\sigma}{d} \Delta t\right)
\]

to react during each time step of length \( \Delta t \).

To compare our simulation algorithm with the mean-field equation (6), we solved the PDE numerically using an explicit time-stepping scheme for a finite-difference discretization using the Min-system parameter set A as introduced in table 1 of the main text. For this given parameter choice the numerical solutions for the density profiles \( \rho(z,t) \) were approximately homogeneous along \( z \), due to fast diffusion in comparison to other competing timescales. Therefore we approximated the solution of equation (6) as a spatially homogeneous density \( \rho(z,t) = \rho(t) \) allowing us to obtain an analytical solution for this specific parameter set and system size. Under
this assumption equation (6) simplifies to
\[ \partial_t \rho(t) = -\sigma \delta(z) \rho(t), \]
which after integrating once over the entire domain gives
\[ L_z \partial_t \rho(t) = -\sigma \rho(t) \]
with the standard solution
\[ \rho(t) = \rho_0 \exp \left(-\frac{\sigma}{L_z} t \right). \]

Simulation results from the particle-based algorithm are in good agreement with this analytical solution, as depicted in figure 2, where we chose the intrinsic algorithm parameter \( d = 0.02 \mu\text{m} \). This choice is also sufficiently small compared to the full domain size of \( L_z \) (4% of \( L_z \) for \( L_z = 0.5 \mu\text{m} \)).

(iii) Bimolecular membrane attachment

The third reaction type we consider here describes the bimolecular association of a freely diffusing bulk particle with already membrane-bound particles. The corresponding mean-field differential equation for this type of reactions reads
\[ \partial_t \rho = D \nabla^2 \rho - \sigma \delta(z) \tilde{\rho}_b \rho, \]
where \( \rho \) denotes the density of free particles of species \( A \) and \( \tilde{\rho}_b \) is the density of membrane-bound particles. In the particle-based framework we adopt an algorithm used in the software package Smoldyn [2]. The treatment for irreversible bimolecular association reactions follows the spirit of the classical Smoluchowski-model for irreversible diffusion-limited reactions [3]. Here two particles instantaneously react upon collision, leading to the diffusion-limited on-rate
for bimolecular association of

\[ k_S = 4\pi Dr_S, \]  

where \( D \) denotes the mutual diffusion coefficient of the reacting pair and \( r_S \) the effective collision distance which in the most naive picture is taken to be the sum of the molecular radii. To also address activation-limited or only partially diffusion-influenced reactions Collins and Kimball [4] proposed to impose a radiation-boundary condition which nicely conveys the picture of a finite activation-limited reaction probability once a pair of reactants has met via diffusional encounter. For the sake of simplicity and algorithmic speed, Andrews and Bray [2] came up with an algorithm which keeps the spirit of the original idea by Smoluchowski by introducing a binding radius \( \sigma_r \) and letting particles react instantaneously once they are separated by \( r < \sigma_b \). To account for activation-limited effects the sum of the molecular radii is in this picture replaced by this effective binding radius \( \sigma_r \leq r_S \). They propose an algorithm which calculates \( \sigma_r \) for a given diffusion coefficient \( D \), time step \( \Delta t \) and a forward rate constant \( k \). In fact the algorithm solves the forward problem of determining the effective simulated forward rate constant \( k \) for a given time step \( \Delta t \), diffusion coefficient \( D \) and binding radius \( \sigma_b \) and stores these results in a look-up table, which is then inverted to interpolate a binding radius for a given reaction rate \( k \). The forward problem itself is solved numerically by propagating an initial radial distribution function (RDF) \( f(r) \) forward in time, by carrying out alternating diffusion and irreversible reaction steps. The diffusive steps are implemented by convolving the full radial distribution function with a three-dimensional Gaussian and in each reaction step the RDF is set to zero in the range \( 0 \leq r \leq \sigma_b \) to account for the irreversible reactions that have taken place. In each iteration the effective reaction rate is then given by integrating the area under the RDF from \( [0, \sigma_b] \) after the diffusive step. This procedure is repeated iteratively until convergence is achieved. By inverting the tabulated relation between the \( k \)'s and the \( \sigma_b \)'s one solves the inverse problem and can thus obtain \( \sigma_b = \sigma_b(D, \Delta t, k) \) as a function of the diffusion coefficient \( D \), the time step \( \Delta t \) and the forward rate constant \( k \). The radial distribution functions \( f(r) \) one obtains using this algorithm reduce to the radial distribution function of the Smoluchowski model \( f_s(r) \) in the limit of small time steps \( \Delta t \to 0 \), as to be expected for infinitely detailed Brownian motion.

For irreversible bimolecular reactions the RDF in the Smoluchowski model reads

\[ f_s(r) = \begin{cases} 
1 - \frac{\sigma_b}{r} & \text{for } r \geq \sigma_b \\
0 & \text{for } r < \sigma_b.
\end{cases} \]  

(20)

In general however, the RDFs qualitatively resemble the functional form of the radial distribution function according to the Collins and Kimball [4] model.

For a quantitative test of our algorithm with the corresponding mean-field results we solve equation (18) numerically. In order to do so we make further simplifying assumptions. For arbitrary distributions of the bound particles \( \tilde{\rho}_b \) the differential equation (18) can not be reduced to one dimension as before, however, it is possible to do so for evenly distributed bound particles. We numerically solved this PDE using the Min-system parameter set A as introduced in table 1 of the main text and assuming evenly distributed bound particles \( \tilde{\rho}_b = \text{const.} \) on the bottom surface of a rectangular simulation box of volume \( V \). To match this scenario of the mean-field model in the particle-based framework, we consider a molecular species \( A \) of freely diffusing particles in a simulation volume \( V \) which can react with membrane-bound particles of another species \( B \). For the sake of simplicity we remove particles of species \( A \) after a successful reaction step with a membrane-bound particle, while the bound-particles are not removed after the reaction step to keep \( \tilde{\rho}_b = \text{const.} \). The results of this comparison using the Min-systems’ parameters and several different values for \( \tilde{\rho}_b \) are shown in figure 3.
Figure 3 Simulation of 6003 free particles that are removed upon reaction with evenly distributed bound particles on the bottom surface of a rectangular simulation volume. \( N \) denotes number of remaining free particles in the system. Blue rectangles depict the values from the numerical solution of equation (18) and red triangles represent the results from the particle-based simulation algorithm. The parameters from the main text are used. Those are \( D = 2.5 \mu m^2/s \), \( L_z = 0.5 \mu m \) and \( \sigma = 0.0149 \mu m^3/s \). In the four figures different values for the density of the bound particles were used: top left \( \tilde{\rho}_b = 4 \mu m^{-2} \), top right \( \tilde{\rho}_b = 25 \mu m^{-2} \), bottom left \( \tilde{\rho}_b = 100 \mu m^{-2} \) and bottom right \( \tilde{\rho}_b = 225 \mu m^{-2} \).

B. Supplementary Movies

All supplementary movies are visualizations of simulation trajectories that were obtained using parameter set A.

- **S1 Stochastic switching**
  Time-course data of surface-bound MinD and MinDE complexes of a simulation trajectory that undergoes both transverse striped oscillations and longitudinal pole-to-pole oscillations and stochastically switches between them. Shown are only membrane-bound particles of the 10\( \mu m \times 5 \mu m \times 0.5 \mu m \) compartment in geometry A. Additionally the projected \( x \)- and \( y \)-density histograms of both particle densities individually and their sum is shown in the corresponding subplots. This trajectory corresponds to the density kymographs shown in figure 2 of the main text.

- **S2 Longitudinal striped mode**
  Time-course data of surface-bound MinD and MinDE complexes of a simulation trajectory with the same parameters as movie S1 that exhibits stable longitudinal striped oscillations. The compartment size is again 10\( \mu m \times 5 \mu m \times 0.5 \mu m \). The top histogram depicts the projected density in \( x \)-direction of the two membrane-bound species and their sum, respectively.

- **S3 Transverse pole-to-pole mode**
  Time-course data of surface-bound MinD and MinDE complexes of a simulation trajectory with the same parameters as movie S1 that exhibits stable transverse pole-to-pole oscillations. The compartment size is again 10\( \mu m \times 5 \mu m \times 0.5 \mu m \). The right histogram depicts the projected density in \( y \)-direction of the two membrane-bound species and their sum, respectively.

- **S4 Edge oscillation**
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Time-course data of surface-bound MinD and MinDE complexes in geometry B. The centered rectangular area, delimited by dashed lines, is the bottom surface of the $5\mu m \times 2.5\mu m \times 4\mu m$ compartment while the other rectangular regions are the down-projected side walls of the full three-dimensional simulation volume. Shown are again only membrane-bound particles of MinD and MinDE, respectively. This movie corresponds to figure 7A of the main text with a compartment height of $z = 4\mu m$ (green color) and shows an edge-oscillation.

References


