**Table S1 Description of Simulation Parameters**

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| **Parameter description** | **Symbol** | **Value / Range of values / Calculation** |
| *Monte Carlo parameters* |  |  |
|  | Lattice step size |  | $1nm$  |
|  | Simulation box |  | $2μm×2μm$  |
|  | Observation area |  | $$1.6μm×1.6μm$$ |
|  | Total simulated time |  | $>40 sec$  |
|  | Number of molecules in frame for FCS |  | $$100\pm 20 $$ |
| *Parameters to match simulation to experimental conditions*  |
|  | Free diffusion coefficient | $$D^{out}$$ | in supported lipid bilayer $2.5{μm^{2}}/{sec}$; on cells $1.3{μm^{2}}/{sec} $  |
|  | 2D Gaussian width of PSF | $$σ$$ | $108.8nm$  |
|  | Camera pixel size |  | $64 nm$  |
|  | Effective waist of detection spot | $$ω$$ |  |
|  | Camera frame time  |  | 1.5ms; or 1000 MCS steps |
|  | Number of molecules in each frame |  | $$100\pm 20$$ |
| *Specific parameters for nano-domains* |  |  |
|  | Edge length of domains | $$l$$ | $20-75 nm$  |
|  | Fraction of area covered by domains | $$d$$ | $$0.1-0.3$$ |
|  | Relative diffusion coefficient inside domains | $$D\_{rel}$$ | $0.1-1$; ${D^{in}}/{D^{out}}$ |
|  | Probability of entering a domain | $$P\_{in}$$ | $1$  |
|  | Probability of exiting a domain | $$P\_{out}$$ | $0.01-0.04, 0.1-0.2$  |
| *Specific parameters for membrane fences* |  |  |
|  | Spacing of square-grid fences | $$a$$ | $50-500 nm$  |
|  | Hopping over probability for molecules | $$P$$ | $$0.01-0.1$$ |
| *Simulation observables* |  |  |
|  | Partition of molecules into domains | $$α$$ | (molecules inside domains) / total molecules |
|  | Confinement strength | $$S\_{conf}$$ |  |
|  | Effective diffusion coefficient | $$D\_{eff}$$ | ${1 }/{(4\*(slope of t\_{D} versus ω^{2}plot))}$  |
|  | Time-axis intercept of the FCS diffusion law | $$t\_{0}$$ | y-intercept |