

Receptor-Ligand Rebinding Kinetics in Confinement

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In this study, we investigate initial release and rebinding of ligands to their binding sites grafted on a planar surface, a situation commonly observed in single-molecule experiments and that occurs *in vivo*, e.g., during exocytosis. Via scaling arguments and molecular dynamic simulations, we analyze the dependence of nonequilibrium rebinding kinetics on two intrinsic length scales: the average separation distance between the binding sites and the total diffusible volume (i.e., height of the experimental reservoir in which diffusion takes place or average distance between receptor-bearing surfaces). We obtain time-dependent scaling laws for on rates and for the cumulative number of rebinding events. For diffusion-limited binding, the (rebinding) on rate decreases with time via multiple power-law regimes before the terminal steady-state (constant on-rate) regime. At intermediate times, when particle density has not yet become uniform throughout the diffusible volume, the cumulative number of rebindings exhibits a novel, to our knowledge, plateau behavior because of the three-dimensional escape process of ligands from binding sites. The duration of the plateau regime depends on the average separation distance between binding sites. After the three-dimensional diffusive escape process, a one-dimensional diffusive regime describes on rates. In the reaction-limited scenario, ligands with higher affinity to their binding sites (e.g., longer residence times) delay entry to the power-law regimes. Our results will be useful for extracting hidden timescales in experiments such as kinetic rate measurements for ligand-receptor interactions in microchannels, as well as for cell signaling via diffusing molecules.

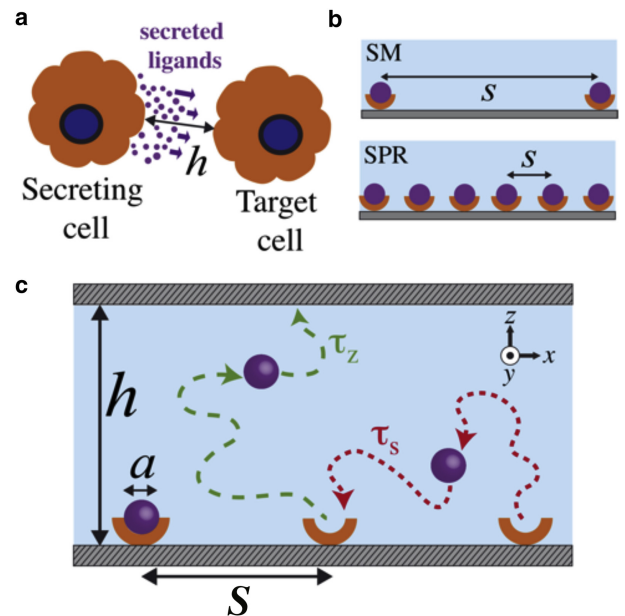


Figure: (a) Schematics of cell communication via secretion of small ligands into intercellular space of characteristic size of h . (b) In single-molecule (SM) experiments, binding sites (orange) saturated by ligands (purple spheres) are more sparsely distributed compared to SPR experiments. The binding sites are separated by a distance s . (c) An illustration of diffusion of ligand particles of size a initially located at their binding sites is shown.