Theory of GPCR motion

Meeting I

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- Note: Markovian state-switching does NOT allow for anomalous diffusion or localization over long timescales
- Observe heterogeneous behaviours in GPCRs – switching between immobile/confined/free – so the picture that seems the most tempting is 4

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  2. Our numerical simulations have shown that anomalous diffusion seems to be uniquely due to κ being bounded
- Tried to rectify both of these by introducing a drift such that $p_\infty(x) \propto e^{-\beta\kappa(x)}$, however this still did not give rise to anomalous diffusive behaviour

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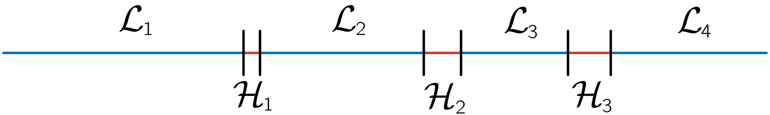

$$\mathcal{H} = \bigcup_i \mathcal{H}_i \qquad \mathcal{L} = \bigcup_i \mathcal{L}_i$$

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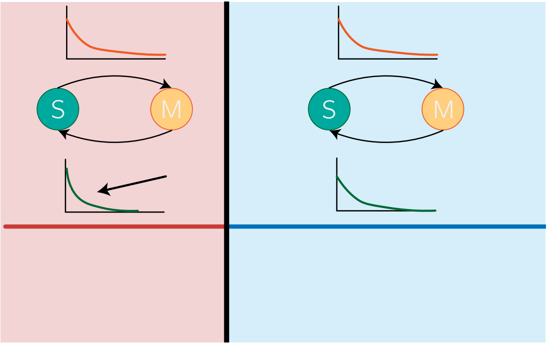
- Rate of conversion to the immobile phase is increased in $\mathcal{H}$ domains, leading to an decrease in α in these regions



References

[1] D. Krapf, in *Current Topics in Membranes*, Vol. 75 (Elsevier, 2015) pp. 167–207.

[2] A. W. C. Lau and T. C. Lubensky, Physical Review E **76**, 011123 (2007).

[3] A. G. Cherstvy and R. Metzler, Physical Review E **90**, 012134 (2014).

[4] P. Massignan, C. Manzo, J. A. Torreno-Pina, M. F. García-Parajo, M. Lewenstein, and G. J. Lapeyre, Physical Review Letters **112**, 150603 (2014), arXiv:1401.6110 [cond-mat].

The unique steady state for heterogeneous diffusion

- As in the presentation, consider the steady-state equation of the heterogeneous diffusion equation

$$\nabla \cdot [\kappa(x) \nabla p_\infty(x)] = 0 \tag{2}$$

- Let $\tilde{p}_\infty(x) = C$. Clearly $\nabla \tilde{p}_\infty(x) = 0$ so $\tilde{p}_\infty(x)$ is a steady-state solution. Normalization enforces that $C = 1/\left|\mathcal{M}\right|$, which specifies $\tilde{p}_\infty$ as the Lebesgue measure on $\mathcal{M}$
- Let ρ_∞ be any sufficiently smooth solution of Eq. (2) with periodic BC (as in the case of a closed manifold) that is not the Lebesgue measure
- Define the fluctuation field about the mean $\psi(x) := p_\infty(x) - \overline{p}_\infty$. ψ also satisfies Eq. (2) with the same BC

The unique steady state for heterogeneous diffusion

- Multiplying by Eq. (2) by ψ and using integration by parts,

$$\int_{\mathcal{M}} \psi(x)\nabla \cdot [\kappa(x)\nabla\psi(x)]\, dx = -\int_{\mathcal{M}} \kappa(x)\,|\nabla\psi(x)|^2\, dx = 0, \tag{3}$$

  since ψ is periodic and hence vanishes on the boundary.
- But the second representation of the integral is strictly positive since κ is bounded. Therefore the only steady state is $\tilde{p}_\infty$