

Mitochondria distribution with localized glucose sources

Summary of model

- One-dimensional domain, length L
- Glucose behavior:
 - Concentration is fixed to c_0 at the boundaries
 - Spreads diffusively with diffusivity D
 - Consumed by mitochondria with Michaelis-Menten kinetics (K_M, k_g). Consumption rate (concentration change per unit time) is given by:

$$\frac{k_g K_M G(x) H(x)}{G(x) + K_M}$$

where $H(x)$ is mitochondrial density (unitless, integrates to total length of mitochondria in cell), $G(x)$ is glucose concentration.

- Mitochondria behavior:
 - Initiate processive walks with rate k_w . Assumed to move in random direction for each processive walk.
 - Stop processive walks with rate

$$r_s(x) = \frac{k_s K_M G(x)}{G(x) + K_M}$$

where k_s is a rate constant (units of per concentration per time). Note that this assumes the K_M is the same for mitochondria stopping and glucose consumption (ie: assuming that glucose hexokinase is the limiting step for both processes)

- Equations at steady state:

$$D \frac{\partial^2 G}{\partial x^2} - \frac{k_g K_M G}{G + K_M} H(x) = 0$$

$$H(x) = \frac{f [k_w + r_s(x)]}{k_w + \frac{1}{L} \int_0^L r_s(x) dx}$$

where f is fraction of domain length occupied by mitochondria.

- Dimensionless parameters defining model behavior

$$\hat{\lambda} = \sqrt{\frac{D}{k_g f L^2}}, \quad \text{length-scale of glucose decay, relative to } L$$

$$\hat{c}_0 = \frac{c_0}{K_M}, \quad \text{boundary concentration, relative to } K_M$$

$$\hat{k}_s = \frac{k_s K_M}{k_w}, \quad \text{equilibrium stopping constant at high glucose}$$

- Approximate parameter estimates:
 - Assume sugar consumption by 1 mitochondrion is $2.5 \times 10^5 \text{ s}^{-1}$ (from yeast)
 - Assume mitochondrion length $1\mu\text{m}$, axon diameter $2\mu\text{m}$, axon length $500\mu\text{m}$.
 - Assume 75 mitochondria in the axon
 - Assume $K_M = 0.1\text{mM}$
 - Assume glucose diffusivity $140\mu\text{m}^2/\text{s}$ (from ATP diffusivity)
 - Dimensionless length scale of glucose decay: $\hat{\lambda} \approx 0.06$
- Variation metric used to quantify how localized the mitochondria are:

$$V = 6\sigma^2/L^2 - 0.5$$

where σ^2 is the variance in the mitochondrial distribution. This gives $V = 0$ for uniform distribution and $V = 1$ for two peaks at the domain edges.

Results