

# 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  $\sigma^2$  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