Stochastic survival of the densest in neurons

May 17, 2023

1 Glossary

variables:
W_s = number of wildtype mtDNA molecules in the soma
M_s = number of mutant mtDNA molecules in the soma
W_a = number of wildtype mtDNA molecules in the axon
M_a = number of mutant mtDNA molecules in the axon

parameters:
μ = death rate or degradation rate
γ = transport rate between two units
δ_m = mutant deficiency ratio
C_b = adaptive birth rate control strength parameter
C_t = adaptive transport rate control strength parameter
NSS_A = carrying capacity of axon
NSS_S = carrying capacity of soma

2 Equations governing per capita reaction rates and rates of change in the model

2.1 Per capita rates:

All per capita reaction rates are identical for wildtype (wt) and mutant (mt) mtDNA molecules, and defined as follows:

2.1.1 Birth rates:

mtDNA is produced in the soma only. The rate of production is sufficient to supply both the soma and the axon.

$$Birth_{soma} = 2\mu + C_b \times (Nss_S - W_s - \delta_m M_s) \tag{1}$$

$$Birth_{axon} = 0 \tag{2}$$

2.1.2 Death rates:

mtDNA is degraded with equal rates in the soma and axon.

$$Death_{soma} = \mu \tag{3}$$

$$Death_{axon} = \mu \tag{4}$$

2.1.3 Transport rates:

mtDNA is transported between the soma and the axon. At steady state, anterograde (soma to axon) transport is 2x the rate of retrograde transport.

$$Move_{soma-axon} = 2\gamma + C_t \times (Nss_A - W_a - \delta_m M_a) \tag{5}$$

$$Move_{axon-soma} = \gamma \tag{6}$$

2.2 Absolute rates of change:

Thus the absolute rates of change for the four model variables are:

$$\frac{dW_s}{dt} = W_s \times ([2\mu + C_b \times (Nss_S - W_s - \delta_m M_s)] - [\mu] - [2\gamma + C_t \times (Nss_A - W_a - \delta_m M_a)]) + W_a \times [\gamma] \tag{7}$$

$$\frac{dM_s}{dt} = M_s \times ([2\mu + C_b \times (Nss_S - W_s - \delta_m M_s)] - [\mu] - [2\gamma + C_t \times (Nss_A - W_a - \delta_m M_a)]) + M_a \times [\gamma] \tag{8}$$

$$\frac{dW_a}{dt} = W_a \times ([0] - [\mu] - [\gamma]) + W_s \times [2\gamma + C_t \times (Nss_A - W_a - \delta_m M_a)] \tag{9}$$

$$\frac{dM_a}{dt} = M_a \times ([0] - [\mu] - [\gamma]) + M_s \times [2\gamma + C_t \times (Nss_A - W_a - \delta_m M_a)] \tag{10}$$

3 Steady states and simplification

A crucial steady state for the system occurs when both the soma and the axon are at carrying capacity, and the ratio of wild-type to mutant molecules, and the absolute number of molecules is identical in both units:

$$W_s = W_a \wedge M_s = M_a \wedge Nss_S = Nss_A \wedge Nss_S - W_s - \delta_m M_s = 0 \wedge Nss_A - W_a - \delta_m M_a = 0 \tag{11}$$

In such cases, the adaptive birth rate and transport rate terms are both 0:

$$C_b \times (Nss_S - W_s - \delta_m M_s) = 0 \wedge C_t \times (Nss_A - W_a - \delta_m M_a) = 0 \tag{12}$$

Thus, the system is reduced such that the rates are:

$$Birth_{soma} = 2\mu \tag{13}$$

$$Birth_{axon} = 0 \tag{14}$$

$$Death_{soma} = \mu \tag{15}$$

$$Death_{axon} = \mu \tag{16}$$

$$Move_{soma-axon} = 2\gamma \tag{17}$$

$$Move_{axon-soma} = \gamma \tag{18}$$

Thus the absolute rates of change for the four model variables are:

$$\frac{dW_s}{dt} = W_s \times [2\mu - \mu - 2\gamma] + W_a \times [\gamma] = 0 \tag{19}$$

$$\frac{kdM_s}{dt} = M_s \times [2\mu - \mu - 2\gamma] + M_a \times [\gamma] = 0 \tag{20}$$

$$\frac{dlW_a}{dt} = W_a \times [-\mu - \gamma] + W_s \times [2\gamma] = 0 \tag{21}$$

$$\frac{dM_a}{dt} = M_a \times [-\mu - \gamma] + M_s \times [2\gamma] = 0 \tag{22}$$

Thus $\mu = \gamma$.

4 simplified model

4.1 glossary

variables:
W_s = number of wildtype mtDNA molecules in the soma
M_s = number of mutant mtDNA molecules in the soma
W_a = number of wildtype mtDNA molecules in the axon
M_a = number of mutant mtDNA molecules in the axon

parameters:
λ = death/degradation rate and transport rate (replacing μ and γ)
δ_m = mutant deficiency ratio
C_b = adaptive birth rate control strength parameter
C_t = adaptive transport rate control strength parameter
NSS = carrying capacity of axon and carrying capacity of soma

4.2 equations with explicit birth, death and transport rates

$$\frac{dW_s}{dt} = W_s \times ([2\lambda + C_b \times (Nss - W_s - \delta_m M_s)] - [\lambda] - [2\lambda + C_t \times (Nss - W_a - \delta_m M_a)]) + W_a \times [\lambda] \tag{23}$$

$$\frac{dM_s}{dt} = M_s \times ([2\lambda + C_b \times (Nss - W_s - \delta_m M_s)] - [\lambda] - [2\lambda + C_t \times (Nss - W_a - \delta_m M_a)]) + M_a \times [\lambda] \tag{24}$$

$$\frac{dW_a}{dt} = W_a \times ([0] - [\lambda] - [\lambda]) + W_s \times [2\lambda + C_t \times (Nss - W_a - \delta_m M_a)] \tag{25}$$

$$\frac{dM_a}{dt} = M_a \times ([0] - [\lambda] - [\lambda]) + M_s \times [2\lambda + C_t \times (Nss - W_a - \delta_m M_a)] \tag{26}$$