

## Supplementary

Assume a population of  $n$  mitochondria, which for our purposes form discrete elements, with no fission or fusion. Consider the elements which exist independently, outside of clusters – we will call these *monomers*. We denote by  $n_m$  the number of elements which exist as monomers: hence, the number of elements in clusters is  $(n - n_m)$ . The number  $n_m$  can change in three ways: A) increasing due to breakup of a cluster, B) decreasing due to two monomers forming a cluster, and C) decreasing due to a monomer joining an existing cluster.

We define three kinetic parameters:  $\lambda_{mm}$ , the rate of collisions between a monomer and a monomer;  $\lambda_{mc}$ , the rate of collisions between a monomer and a cluster;  $\nu$ , the rate with which a monomer in a cluster departs the cluster. We make three assumptions: 1. Monomers and clusters are freely diffusing. 2. Clusters break up by piecewise loss of monomers (although different mechanisms can be addressed by adapting the associated kinetic constant  $\nu$ ). 3.  $\lambda_{mc}$  does not depend on the size distribution of clusters (but see later).

Under our assumptions, the three mechanisms through which  $n_m$  can vary give an equation for the time evolution of  $n_m$ :

$$\frac{dn_m}{dt} = A - B - C \quad (1)$$

$$= \nu(n - n_m) - 2\lambda_{mm}n_m^2 - \lambda_{mc}n_m(n - n_m) \quad (2)$$

Setting  $\frac{dn_m}{dt} = 0$  and requiring non-negative  $n_m$  gives us an expression for the steady-state number of elements that exist as monomers:

$$n_m = \frac{\nu + \lambda_{mc}n + \sqrt{\nu^2 + 8n\nu\lambda_{mm} - 2n\nu\lambda_{mc} + n^2\lambda_{mc}^2}}{2\lambda_{mc} - 4\lambda_{mm}} \quad (3)$$

We can approximate the association time  $\tau$  by considering the half-life of a dimeric cluster, immediately giving  $\tau = \ln 2/\nu$ . If we set  $\lambda_{mm} \rightarrow 1$ , so that other parameters are scaled by this value, the proportion of mitochondria in clusters  $c = (n - n_m)/n$  is given by:

$$c = \frac{n(\lambda_{mc} - 4)\tau - \ln 2 + \tau\sqrt{n^2\lambda_{mc}^2 - 2n\tau^{-1}(\lambda_{mc} - 4)\ln 2 + \tau^{-2}\ln^2 2}}{2n(\lambda_{mc} - 2)\tau} \quad (4)$$

As shown in Fig. 1,  $c(\tau)$  is a monotonically increasing function of  $\tau$  for all values of  $\tau$  and  $\lambda_{mc}$  within an extended range of magnitudes. The proportion of mitochondria in clusters therefore universally increases with association regardless of the specific parameters describing interactions between monomers and clusters.

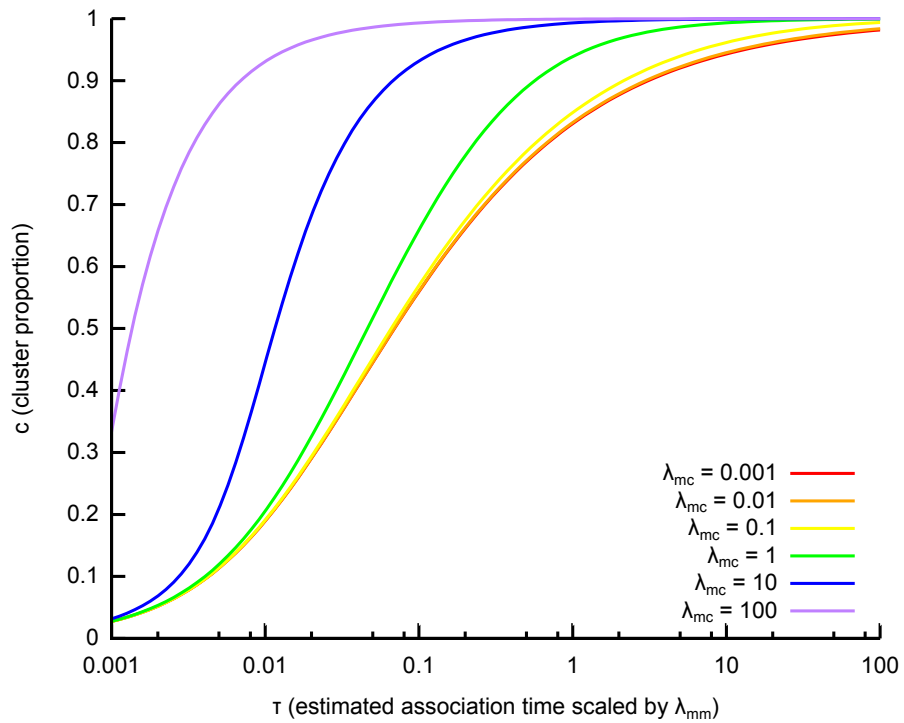


Figure 1: **Monotonic increase of proportion of clustered mitochondria with association time.** Proportion of mitochondria existing in clusters as association time, estimated using  $\tau = \ln 2/\nu$ , varies, with different  $\lambda_{mc}$  values. Other parameter values are  $n = 10$ ,  $\lambda_{mm} = 1$ .