

### S3 CME for discrete model

Let  $q(n_1, n_2, t)$  be the density for  $n_1$  sensitive cells and  $n_2$  resistant cells. Let  $\lambda_i$  denote the proliferation rate of each cell population, and  $\delta_i$  denote the death rate of each cell population (one of which will be zero). We have that

$$\begin{aligned} \frac{dq(n_1, n_2, t)}{dt} = & (n_1 - 1)\lambda_1 q(n_1 - 1, n_2, t) + (n_1 + 1)\delta_1 q(n_1 + 1, n_2, t) \\ & + (n_2 - 1)\lambda_2 q(n_1, n_2 - 1, t) + (n_2 + 1)\delta_2 q(n_1, n_2 + 1, t) \\ & + n_1 r_{12} q(n_1 + 1, n_2 - 1, t) + n_2 r_{21} q(n_1 - 1, n_2 + 1, t) \\ & - (n_1 \lambda_1 + n_1 \delta_1 + n_2 \lambda_2 + n_2 \delta_2) q(n_1, n_2, t). \end{aligned} \quad (1)$$

To obtain the mass function for the total cell count,  $q(n, t)$ , we consider that

$$q(n, t) = \sum_{n_1=0}^{\infty} q(n_1, n - n_1, t). \quad (2)$$

In practice, we consider a partial sum truncated at  $n_1 = 50$ , which we find to be sufficient given the maximum cell counts observed in Fig. 8 of the main text.