## S8 The calculation of volume changes over time

This section describes a method for calculating the time evolution of an initial volume in the phase space. We used this method to determine the extent of variance reduction in single-nucleus gene circuits (Fig. 4C,D).

Given the diffusionless gap gene dynamical system in the nucleus at A-P position $x$ (Eq. 2)

$$
\frac{d v^{a}}{d t}=R^{a} g\left(\sum_{b=1}^{N} T^{a b} v^{b}+m^{a} v^{\mathrm{Bcd}}(x)+\sum_{\beta=1}^{N_{e}} E^{a \beta} v^{\beta}(x, t)+h^{a}\right)-\lambda^{a} v^{a}
$$

we want to calculate the volume $V_{t}$ at time $t$ of a box of initial conditions $\mathcal{B}_{0}$. Let us represent the right hand side as $f\left(v_{t}, t\right)$, where $v_{t}=\left(v_{t}^{1}, v_{t}^{2}, v_{t}^{3}, v_{t}^{4}\right)$ is the four-dimensional state vector at time $t$.

The ODE is discretized into a map,

$$
\begin{equation*}
v_{t+d t}=\gamma\left(v_{t}, t\right) \tag{S1}
\end{equation*}
$$

where $\gamma\left(v_{t}, t\right)=v_{t}+f\left(v_{t}, t\right) d t$. Regard the map at time $t+(n-1) d t$,

$$
v_{t+n d t}=\gamma\left(v_{t+(n-1) d t}, t+(n-1) d t\right),
$$

as a curvilinear coordinate transformation of the phase space, then the infinitesimal volume at time $t+n d t$,

$$
d V_{t+n d t}=d v_{t+n d t}^{1} d v_{t+n d t}^{2} d v_{t+n d t}^{3} d v_{t+n d t}^{4}
$$

can be written as,

$$
\begin{equation*}
d V_{t+n d t}=J\left(v_{t+(n-1) d t}, t+(n-1) d t\right) d V_{t+(n-1) d t} . \tag{S2}
\end{equation*}
$$

Here, $d V_{t+(n-1) d t}$ is the infinitesimal volume at $t+(n-1) d t$, and $J\left(v_{t}, t\right)$ is the Jacobian of the map at time $t$. Applying Eq. (S2) repeatedly, the infinitesimal volume at $t, d V_{t}$, can be written in terms of the initial infinitesimal volume, $d V_{0}$ as

$$
d V_{t}=J\left(v_{t-(n-1) d t}, t-(n-1) d t\right) J\left(v_{t-(n-2) d t}, t-(n-2) d t\right) \ldots J\left(v_{0}, 0\right) d V_{0}
$$

If the initial box $\mathcal{B}_{0}$ evolves to $\mathcal{B}_{t}$ at time $t, \mathcal{B}_{t}$ 's volume is

$$
\begin{aligned}
V_{t} & =\iiint \int_{\mathcal{B}_{t}} d V_{t} \\
& =\iiint \int_{\mathcal{B}_{0}}\left[J\left(v_{t-(n-1) d t}, t-(n-1) d t\right) \ldots J\left(v_{0}, 0\right)\right] d v_{0}^{1} d v_{0}^{2} d v_{0}^{3} d v_{0}^{4} .
\end{aligned}
$$

The integral on the right hand side was evaluated using the multidimensional trapezoidal rule [1], successively refining the grid on the initial box $\mathcal{B}_{0}$ until the integral converged. The time-step for the discretized map $\gamma\left(v_{t}, t\right)$ was chosen small enough such that the Euler-method solution of Eq. (2) converged.

## References

[1] Press WH, Teukolsky SA, Vetterling WT, Flannery BP (1992) Numerical Recipes in C. Cambridge, U.K.: Cambridge University Press, second edition.

