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Citation for published version:
Popovic, N, Carsten, M & Swain, P 2015, 'A geometric analysis of fast-slow models for stochastic gene expression' Journal of Mathematical Biology. DOI: 10.1007/s00285-015-0876-1

Digital Object Identifier (DOI):
10.1007/s00285-015-0876-1

Published In:
Journal of Mathematical Biology

ELECTRONIC SUPPLEMENTARY MATERIAL TO A GEOMETRIC ANALYSIS OF FAST-SLOW MODELS FOR STOCHASTIC GENE EXPRESSION (JOURNAL OF MATHEMATICAL BIOLOGY)

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A. Geometric singular perturbation theory

The perturbation technique for the study of singularly perturbed systems of (ordinary) differential equations that is known as geometric singular perturbation theory was initiated by Fenichel in a series of groundbreaking articles [5, 6]. We present a brief overview here, referring to [8] for an accessible review and to [7] for a survey of applications, with a focus on the life sciences.

A.1. **Fast-slow systems.** We consider systems of first-order autonomous ordinary differential equations in the general ('standard') form

$$\varepsilon\dot{\mathbf{u}} = \mathbf{f}(\mathbf{u}, \mathbf{v}, \varepsilon), \tag{A.1a}$$

$$\dot{\mathbf{v}} = \mathbf{g}(\mathbf{u}, \mathbf{v}, \varepsilon); \tag{A.1b}$$

here, $(\mathbf{u}, \mathbf{v}) \in \mathbb{R}^k \times \mathbb{R}^l$, with $k, l \in \mathbb{N}$, $0 < \varepsilon \ll 1$ is a real 'small' parameter, and the overdot denotes differentiation with respect to the 'slow' independent variable τ. Moreover, and without loss of generality, the functions $\mathbf{f} :\ \mathbb{R}^k \times \mathbb{R}^l \times \mathbb{R}^+ \to \mathbb{R}^k$ and $\mathbf{g} :\ \mathbb{R}^k \times \mathbb{R}^l \times \mathbb{R}^+ \to \mathbb{R}^l$ are assumed to be $\mathcal{C}^\infty$-smooth in all of their arguments.

Rescaling (A.1) by introducing the new, 'fast' time $t = \frac{\tau}{\varepsilon}$, we obtain the system of equations

$$\mathbf{u}' = \mathbf{f}(\mathbf{u}, \mathbf{v}, \varepsilon), \tag{A.2a}$$

$$\mathbf{v}' = \varepsilon\mathbf{g}(\mathbf{u}, \mathbf{v}, \varepsilon). \tag{A.2b}$$

Equations (A.1) and (A.2) are equivalent for ε positive; however, the singular limit as $\varepsilon \to 0$ yields two entirely different systems: setting $\varepsilon = 0$ in (A.1), one obtains the 'reduced problem'

$$\mathbf{0} = \mathbf{f}(\mathbf{u}, \mathbf{v}, 0), \tag{A.3a}$$

$$\dot{\mathbf{v}} = \mathbf{g}(\mathbf{u}, \mathbf{v}, 0), \tag{A.3b}$$

while Equation (A.2) implies the 'layer problem'

$$\mathbf{u}' = \mathbf{f}(\mathbf{u}, \mathbf{v}, 0), \tag{A.4a}$$

$$\mathbf{v}' = \mathbf{0}. \tag{A.4b}$$

In both cases, the fast-slow formulation affords a dimension reduction: Equation (A.3) represents an algebro-differential system, whereby the flow of $\mathbf{v}$ is constrained to lie on the (l-dimensional) 'critical manifold' $\mathcal{S}_0$ that is defined by $\mathbf{f}(\mathbf{u}, \mathbf{v}, 0) = \mathbf{0}$; similarly, the analysis of (A.4) is simplified by the observation that $\mathbf{v}$ is merely a parameter which parametrizes the (k-dimensional) flow of (A.4a), the equilibria of which are located on $\mathcal{S}_0$. Correspondingly, $\mathbf{u}$ and $\mathbf{v}$ are referred to as the fast and the slow variables, respectively.

Date: March 6, 2015.

A.2. **Fenichel's Theorems.** The aim of geometric singular perturbation theory is to infer the flow of the 'slow' system, Equation (A.1) – or, alternatively, of the equivalent 'fast' formulation in (A.2) – from the simplified dynamics of the corresponding limiting systems, Equations (A.3) and (A.4). Typically, the following two assumptions are made for the manifold $\mathcal{S}_0$ [6, 7, 8]:

(1) $\mathcal{S}_0$ is compact and 'normally hyperbolic,' *i.e.*, the eigenvalues of the Jacobian $D_{\mathbf{u}}\mathbf{f}(\mathbf{u}, \mathbf{v}, 0)$, evaluated on $\mathcal{S}_0$, are uniformly bounded away from the imaginary axis;
(2) $\mathcal{S}_0$ can be written as the graph of a (smooth) function $\mathbf{U}_0 : \mathbb{R}^l \to \mathbb{R}^k$, with $\mathbf{u} = \mathbf{U}_0(\mathbf{v})$ for $\mathbf{v}$ in some compact domain $\mathcal{V} \subset \mathbb{R}^l$.

***Remark* S.1.** A manifold is called hyperbolic if the local linearisation about it is structurally stable; it is *normally* hyperbolic if, in addition, the expansion or contraction near the manifold in the transversal ($\mathbf{u}$-)direction is stronger than in the tangential ($\mathbf{v}$-)direction. □

Three theorems due to Fenichel [6] then hold; see also [7, 8]. The first of these theorems concerns the persistence of the critical manifold $\mathcal{S}_0$ for ε positive, but small, as a slow manifold $\mathcal{S}_\varepsilon$:

Theorem A.1 (Fenichel's First Theorem)**.** *Under the above assumptions, there exists a manifold $\mathcal{S}_\varepsilon$, for $\varepsilon > 0$ sufficiently small, that is $\mathcal{O}(\varepsilon)$-close, and diffeomorphic, to $\mathcal{S}_0$. Moreover, $\mathcal{S}_\varepsilon$ is (locally) invariant under the flow of* (A.1)*, and can be written as the graph of a (smooth) function $\mathbf{U}(\mathbf{v}, \varepsilon)$, with $\mathbf{U}(\mathbf{v}, 0) = \mathbf{U}_0(\mathbf{v})$.*

Theorem A.1 implies, in particular, that the (slow) dynamics on $\mathcal{S}_\varepsilon$ can be obtained as a regular perturbation of the reduced flow on the critical manifold $\mathcal{S}_0$; specifically, the latter is described by $\dot{\mathbf{v}} = \mathbf{g}(\mathbf{U}(\mathbf{v}, 0), \mathbf{v}, 0)$, while the former is given by $\dot{\mathbf{v}} = \mathbf{g}(\mathbf{U}(\mathbf{v}, \varepsilon), \mathbf{v}, \varepsilon)$.

While Fenichel's First Theorem is local, in that it is restricted to the manifold $\mathcal{S}_0$ itself, the Second Theorem addresses the surrounding phase space. We assume that the Jacobian $D_{\mathbf{u}}\mathbf{f}(\mathbf{u}, \mathbf{v}, 0)$ has k_{u} eigenvalues with negative real parts and k_{s} eigenvalues with positive real parts, where $k_{\mathrm{s}} + k_{\mathrm{u}} = k$; since any point on the critical manifold $\mathcal{S}_0$ is an equilibrium point for the layer problem, Equation (A.4), it then follows that each such point admits a k_{s}-dimensional stable manifold and a k_{u}-dimensional unstable manifold. Taking the union of these 'fibres' over all 'base points' on $\mathcal{S}_0$, we may define corresponding stable and unstable manifolds $\mathcal{W}^{\mathrm{s}}(\mathcal{S}_0)$ and $\mathcal{W}^{\mathrm{u}}(\mathcal{S}_0)$, respectively, for $\mathcal{S}_0$, which have dimension $k_{\mathrm{s}} + l$ and $k_{\mathrm{u}} + l$, respectively. Fenichel's Second Theorem implies the persistence of these manifolds:

Theorem A.2 (Fenichel's Second Theorem)**.** *Under the above assumptions, there exist manifolds $\mathcal{W}^{\mathrm{s}}(\mathcal{S}_\varepsilon)$ and $\mathcal{W}^{\mathrm{u}}(\mathcal{S}_\varepsilon)$, for $\varepsilon > 0$ sufficiently small, that are $\mathcal{O}(\varepsilon)$-close, and diffeomorphic, to $\mathcal{W}^{\mathrm{s}}(\mathcal{S}_0)$ and $\mathcal{W}^{\mathrm{u}}(\mathcal{S}_0)$, respectively. Moreover, $\mathcal{W}^{\mathrm{s}}(\mathcal{S}_\varepsilon)$ and $\mathcal{W}^{\mathrm{u}}(\mathcal{S}_\varepsilon)$ are (locally) invariant under the flow of* (A.1).

Finally, by Fenichel's Third Theorem, the fibres that constitute $\mathcal{W}^{\mathrm{s}}(\mathcal{S}_0)$ and $\mathcal{W}^{\mathrm{u}}(\mathcal{S}_0)$ also persist for ε sufficiently small. While the perturbed counterparts of individual fibres are certainly not invariant, as their base points on $\mathcal{S}_\varepsilon$ evolve under the flow of (A.1), one may prove the invariance of appropriately defined families of such fibres; details can be found in [7, 8].

***Remark* S.2.** Equation (A.1) would be classified as 'singularly perturbed' in the parlance of asymptotic analysis, as neither of the two 'singular' systems, Equations (A.3) and (A.4), can yield a uniformly valid approximation for the 'perturbed' flow of (A.1) when ε is positive, but small; in fact, the reduction in the order of the differential equation in (A.1a) – from one to zero – as $\varepsilon \to 0$ is a classical warning sign of singularly perturbed behaviour [10]. □

B. Generalised initial conditions

The geometric framework developed in the main text can be applied to approximate the propagator probabilities $P_{mn|m_0n_0}$ for general (albeit deterministic) initial numbers of mRNA and protein, *i.e.*, for non-zero values of m_0 and n_0, respectively, in Equation (6). Here, we give a representative sample of results which can thus be obtained; see, in particular, Propositions B.2 through B.4 below.

B.1. **Leading-order asymptotics.** In this section, we discuss the leading-order asymptotics of the propagator probabilities $P_{mn|m_0n_0}(t,0)$ and $P_{mn|m_0n_0}(\tau,0)$ on the fast and the slow time-scales, respectively, for arbitrary values of $m_0, n_0 \in \mathbb{N}_0$.

B.1.1. *Fast dynamics.* Given Equation (14), it is straightforward to obtain the leading-order asymptotics of F: recalling that $\mathcal{F}_0(u_0,v_0,t) = (1+u_0)^{m_0}(1+v_0)^{n_0}$, by Equation (17), and substituting in $(u_0,v_0)(u,v,t,\varepsilon)$ from (23) – truncated at leading order in ε – we find

$$\text{(B.1)} \qquad \mathcal{F}_0(u,v,t) \equiv F(u,v,t,0) = \left[\frac{1}{1-bv} + \Big(u - \frac{bv}{1-bv}\Big)\mathrm{e}^{-(1-bv)t}\right]^{m_0}(1+v)^{n_0},$$

which satisfies the normalisation condition $F(0,0,t,0) = 1$, as required. (A similar expression for F is given in Equation (21) of [3].)

***Remark* S.3.** The large-t limit in Equation (B.1) yields

$$\text{(B.2)} \qquad \lim_{t\to\infty} F(u,v,t,0) = \frac{(1+v)^{n_0}}{(1-bv)^{m_0}} = \lim_{\tau\to 0^+} F(U_0(v),v,\tau,0),$$

which depends on v only. (Here, $U_0(v) = \frac{bv}{1-bv}$ is defined as in (10).) Correspondingly, the probability-generating function F will again be independent of u – to lowest order in ε – once the fast (transient) flow has subsided, as observed previously in Section 4.2.2; see also [12]. ☐

The relation between $F(u,v,t,\varepsilon)$ and $P_{mn|m_0n_0}(t,\varepsilon)$ in Equation (32), in combination with the differentiability of the fast expansion for F with respect to (u,v), recall Equation (14b), gives the following result on the large-time asymptotics of $P_{mn|m_0n_0}$ on the fast t-scale. (Here, we note that we may take the limit as $t\to\infty$, both in F and in its derivatives: while (14b) is *a priori* only valid on finite t-intervals, the application of the transformation in Equation (23) effectively reverses the direction of time, making that limit well-defined; see also Section B.1.3 below.)

Proposition B.1. *Let $m, n, m_0, n_0 \in \mathbb{N}_0$, where m_0 and n_0 denote initial numbers of mRNA and protein, respectively, with $P_{mn|m_0n_0}(0,0) = \delta_{mm_0}\delta_{nn_0}$. Then, the stationary probability distribution $P^\infty_{mn|m_0n_0}(0) := \lim_{t\to\infty} P_{mn|m_0n_0}(t,0)$ is given as follows:*

(i) *for $m \in \mathbb{N}$ and arbitrary n, m_0, $n_0 \in \mathbb{N}_0$, $P^\infty_{mn|m_0n_0}(0) = 0$;*

(ii) *for $m = 0$ and $m_0 = 0$,*

$$P^\infty_{0n|0n_0}(0) = \begin{cases} 0 & \textit{when } n_0 = 0, \\ \delta_{nn_0} & \textit{when } n_0 \in \mathbb{N} \end{cases}$$

(irrespective of $n \in \mathbb{N}$), while

$$P^\infty_{00|0n_0}(0) = \begin{cases} 1 & \textit{when } n_0 = 0, \\ 0 & \textit{when } n_0 \in \mathbb{N}; \end{cases}$$

(iii) *finally, when $m = 0$, $m_0 \in \mathbb{N}$, and n, $n_0 \in \mathbb{N}_0$,*

$$\text{(B.3)} \qquad P^\infty_{0n|m_0n_0}(0) = \begin{cases} 0 & \textit{for } n_0 > n, \\ \binom{m_0-n_0+n-1}{m_0-1}\frac{b^{n-n_0}}{(1+b)^{m_0-n_0+n}} & \textit{for } n_0 \le n. \end{cases}$$

Proposition B.1 confirms that the bivariate distribution $P_{mn|m_0n_0}$ is approximated to leading order by the marginal distribution $P_{0n|m_0n_0}$ of protein for large values of t, *i.e.*, that the distribution of mRNA peaks at zero. (Specifically, it follows from the corresponding proof that $P_{mn|m_0n_0}(t,0)$ decays exponentially in time whenever $m \in \mathbb{N}$; cf. Section C.3 below for details.) Moreover, we remark that Equation (B.3) agrees with [3, Equation (23)], where only the case of non-zero m_0 was considered; as argued there, (B.3) implies, in particular, that the initial number n_0 of protein is conserved on the fast t-scale, with each of the m_0 initial mRNAs giving rise to geometrically distributed protein numbers.

***Remark* S.4.** Alternatively, the expression for $P^{\infty}_{0n|m_0n_0}(0)$ in (B.3) can be found by taking the limit as $t \to \infty$ in $F(u,v,t,0)$ first – which eliminates any u-dependence to the order considered here – and by differentiating the resulting expression with respect to v; in other words, the large-t limit in Equation (B.1) commutes with differentiation of $F(u,v,t,0)$ with respect to u and v. □

***Remark* S.5.** An explicit expression for $P_{0n|m_0n_0}(t,0)$ for arbitrary $n \in \mathbb{N}$ can, in principle, be obtained by applying Faà Di Bruno's formula [11, Theorem 2]

$$\frac{d^n}{dx^n} f(g(z)) = \sum \frac{n!}{k_1!k_2!\cdots k_n!}\, f^{(k_1+k_2+\cdots+k_n)}(g(z)) \prod_{j=1}^{n} \left(\frac{g^{(j)}(z)}{j!}\right)^{k_j}$$

to Equation (C.8) below, where the sum is taken over all n-tuples $(k_1,k_2,\ldots,k_n)$ such that $\sum_{j=1}^{n} jk_j = n$. However, the resulting formulae are cumbersome, and are hence omitted here; see also [2, Section 3]. □

B.1.2. *Slow dynamics.* Given the definition of $P_{0n|m_0n_0}(\tau,\varepsilon)$ in Equation (37), as well as the lowest-order approximation

$$F_0(v,\tau) \equiv F(U_0(v),v,\tau,0) = \frac{(1+v\mathrm{e}^{-\tau})^{n_0}}{(1-bv\mathrm{e}^{-\tau})^{m_0}}\Big(\frac{1-bv\mathrm{e}^{-\tau}}{1-bv}\Big)^{a} \tag{B.4}$$

for F on this slow τ-scale, asymptotic formulae for the leading-order slow propagator $P_{0n|m_0n_0}(\tau,0)$ can now be derived via several different routes. (Here, we again allow for arbitrary initial numbers m_0 and n_0 of mRNA and protein, respectively, in Equation (B.4); moreover, we have applied the matching condition in (B.2) to fix the constant C_0 in Equation (21) accordingly. Finally, we have made use of the fact that $v_0(v,\tau) = v\mathrm{e}^{-\tau}$ in the resulting expression.) Conceptually, the most straightforward procedure involves the direct differentiation of the above leading-order approximation for F, which yields

Proposition B.2. *Let $n, m_0, n_0 \in \mathbb{N}_0$, let $\varepsilon \in [0,\varepsilon_0]$, with $\varepsilon_0 > 0$ sufficiently small, and assume that $\tau \gg \varepsilon$. Then, the propagator probabilities $P_{0n|m_0n_0}(\tau,\varepsilon)$ are given by*

$$\begin{aligned} P_{0n|m_0n_0}(\tau,0) = {} & \frac{(1-\mathrm{e}^{-\tau})^{n_0}}{(1+b\mathrm{e}^{-\tau})^{m_0}} \frac{\Gamma(a+n)}{\Gamma(n+1)\Gamma(a)} \Big(\frac{b}{1+b}\Big)^{n} \Big(\frac{1+b\mathrm{e}^{-\tau}}{1+b}\Big)^{a} \\ & \times \sum_{k=0}^{n} \frac{\Gamma(n+1)}{\Gamma(k+1)\Gamma(n-k+1)} \frac{\Gamma(a+n-k)}{\Gamma(a+n)} \frac{\Gamma(m_0+k)}{\Gamma(m_0)} \Big(\frac{1+b}{\mathrm{e}^{\tau}+b}\Big)^{k} \\ & \times {}_2F_1\big(-k,-n_0;1-m_0-k;\tfrac{\mathrm{e}^{\tau}+b}{b(1-\mathrm{e}^{\tau})}\big)\, {}_2F_1\big(-n+k,-a;1-a-n+k;\tfrac{1+b}{\mathrm{e}^{\tau}+b}\big) \end{aligned} \tag{B.5}$$

for any $m_0 \geq 2$*, whereas*

$$\text{(B.6)}\quad P_{0n|0n_0}(\tau,0) = (1-\mathrm{e}^{-\tau})^{n_0}\frac{\Gamma(a+n)}{\Gamma(n+1)\Gamma(a)}\Big(\frac{b}{1+b}\Big)^n\Big(\frac{1+b\mathrm{e}^{-\tau}}{1+b}\Big)^a \times\sum_{k=0}^{n}(-1)^k\frac{\Gamma(n+1)}{\Gamma(k+1)\Gamma(n-k+1)}\frac{\Gamma(a+n-k)}{\Gamma(a+n)}\frac{\Gamma(n_0+1)}{\Gamma(n_0-k+1)}\Big[\frac{1+b}{b(1-\mathrm{e}^{\tau})}\Big]^k \times {}_2F_1\big(-n+k,-a;1-a-n+k;\tfrac{1+b}{\mathrm{e}^{\tau}+b}\big)$$

for $m_0 = 0$ *and*

$$\text{(B.7)}\quad P_{0n|1n_0}(\tau,0) = \frac{(1-\mathrm{e}^{-\tau})^{n_0}}{1+b\mathrm{e}^{-\tau}}\frac{\Gamma(a+n)}{\Gamma(n+1)\Gamma(a)}\Big(\frac{b}{1+b}\Big)^n\Big(\frac{1+b\mathrm{e}^{-\tau}}{1+b}\Big)^a \times\sum_{k=0}^{n}\frac{\Gamma(n+1)}{\Gamma(n-k+1)}\frac{\Gamma(a+n-k)}{\Gamma(a+n)}\Big(\frac{1+b}{\mathrm{e}^{\tau}+b}\Big)^k\bigg\{(-1)^{n_0}\Big[\frac{\mathrm{e}^{\tau}(1+b)}{b(1-\mathrm{e}^{\tau})}\Big]^{n_0} + \frac{(-1)^k}{\Gamma(k+2)}\frac{\Gamma(n_0+1)}{\Gamma(n_0-k)}\Big[\frac{\mathrm{e}^{\tau}+b}{b(1-\mathrm{e}^{\tau})}\Big]^{k+1}{}_2F_1\big(1,1-n_0+k;2+k;\tfrac{\mathrm{e}^{\tau}+b}{b(1-\mathrm{e}^{\tau})}\big)\bigg\} \times {}_2F_1\big(-n+k,-a;1-a-n+k;\tfrac{1+b}{\mathrm{e}^{\tau}+b}\big)$$

for $m_0 = 1$*, to leading order in* ε*. (Here,* ${}_2F_1$ *denotes the standard hypergeometric function* [1, Section 15]*, as before.)*

For $m_0 = 0 = n_0$ in Equation (B.6), the only non-zero contribution in the sum therein is obtained for $k = 0$, as the reciprocal Gamma function $\frac{1}{\Gamma}$ is zero whenever its argument is a non-positive integer. Hence, (B.6) then agrees with Equation (8) of [12], which we quote for future reference here:

$$\text{(B.8)}\qquad P_n(\tau,0) = \frac{\Gamma(a+n)}{\Gamma(n+1)\Gamma(a)}\Big(\frac{b}{1+b}\Big)^n\Big(\frac{1+b\mathrm{e}^{-\tau}}{1+b}\Big)^a{}_2F_1\big(-n,-a;1-a-n;\tfrac{1+b}{\mathrm{e}^{\tau}+b}\big),$$

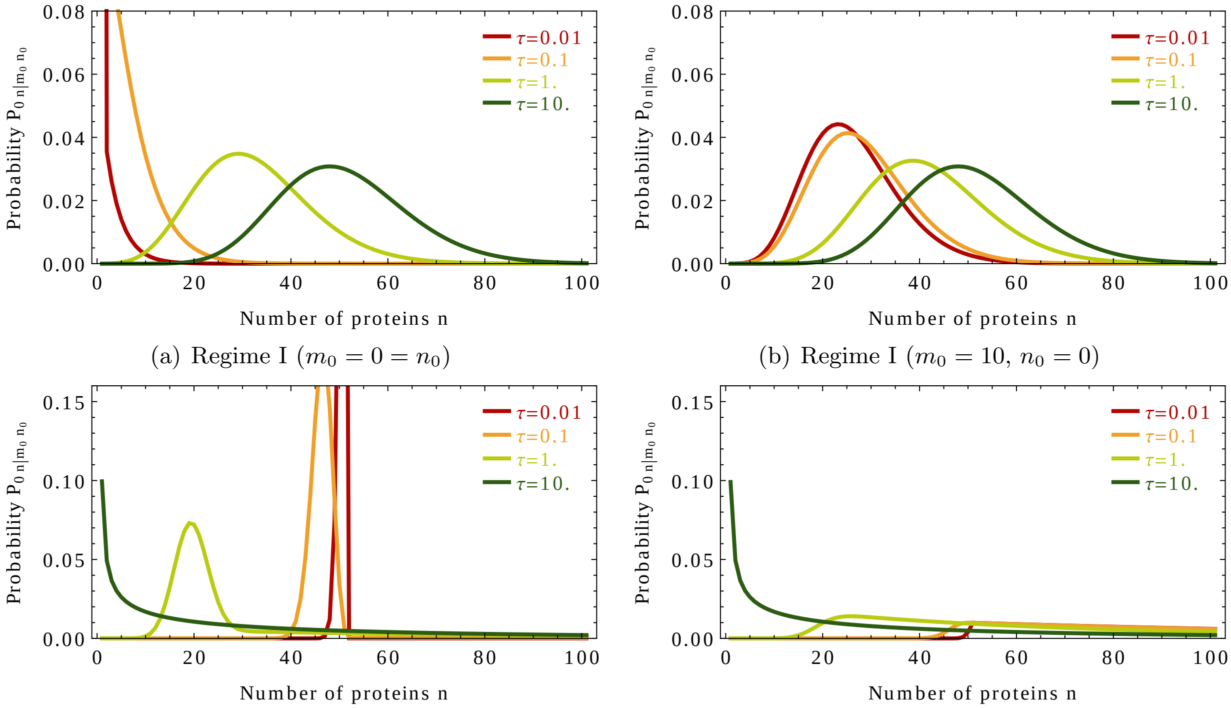
where we have defined $P_n \equiv P_{0n|00}$. Moreover, one easily verifies that Equations (B.5) through (B.7) reduce to [12, Equation (9)] in the (stationary) limit as $\tau \to \infty$, irrespective of the chosen values of m_0 and n_0. (To that end, one observes that the only contribution in the corresponding sums is obtained for $k = 0$ in that limit, as the hypergeometric functions occurring therein reduce to ${}_2F_1(0,-n_0;1-m_0;-\frac{1}{b}) = 1 = {}_2F_1(-n,-a;1-a-n;0)$ and as

$${}_2F_1(1,1-n_0;2;-\tfrac{1}{b}) = \begin{cases}\frac{b}{n_0}\big[\big(\frac{1+b}{b}\big)^{n_0}-1\big] & \text{when } n_0 \in \mathbb{N},\\ b\ln\frac{1+b}{b} & \text{when } n_0 = 0,\end{cases}$$

respectively, all of which are bounded for any choice of (a,b), (m_0,n_0), and n; in particular, in (B.7), the terms in curly brackets then combine to 1 for $\tau \to \infty$, as required.) Finally, we note that the stationary limit now does not commute with differentiation with respect to z, in contrast to the situation encountered on the fast t-scale; recall Remark S.4.

The leading-order expansion for the propagator $P_{mn|m_0n_0}(\tau,0)$, as given in Proposition B.2, is illustrated in Figure S.1 for varying initial numbers m_0 and n_0 of mRNA and protein, respectively. One observes that the dependence of $P_{mn|m_0n_0}$ on (m_0,n_0) diminishes rapidly with increasing τ; in other words, the effects of non-zero initial mRNA and protein numbers are only relevant for short times.

Specifically, for $m_0 \neq 0$, the corresponding propagator probabilities differ markedly for small values of τ, as the initial presence of mRNA translates into higher protein numbers initially; see Figures S.1(b) and S.1(d). However, for τ large, mRNA has decayed to a sufficient degree for the probabilities to be indiscernible from those found for $m_0 = 0$; recall Figure 3. Similarly, it



(a) Regime I ($m_0 = 0 = n_0$)

(b) Regime I ($m_0 = 10$, $n_0 = 0$)

(c) Regime II ($m_0 = 0$, $n_0 = 50$)

(d) Regime II ($m_0 = 1$, $n_0 = 50$)

FIGURE S.1. The zeroth-order propagator probabilities $P_{0n|m_0n_0}(\tau, 0)$ defined in Equation (B.5) for varying values of m_0 and n_0; here, $a = 20$ and $b = 2.5$ in panels 1(a) and 1(b) ('regime I'), while $a = 0.5$ and $b = 100$ in panels 1(c) and 1(d) ('regime II'). (We note that, for $\tau = 10$, the curves almost coincide with the stationary probability distribution obtained in [12, Equation (9)]; see also Equation (B.8).)

follows from Figures S.1(a) and S.1(c) that a change in n_0 results in a shift of the peak of the initial distribution away from zero, which again merely alters the transient dynamics, *i.e.*, the convergence behaviour of the propagator probabilities to the stationary marginal protein distribution P_n^∞ that is obtained in the limit as $\tau \to \infty$; cf. [12, Equation (9)].

Alternatively to the differentiation procedure applied in the proof of Proposition B.2 – which is algebraically rather cumbersome, as seen in Section C.3 below – one can combine the leading-order asymptotics of P_n in Equation (B.8) with the approximation for F in (B.4) to approximate $P_{0n|m_0n_0}$ for general (non-zero) $m_0, n_0 \in \mathbb{N}$ via a summation argument. We have the following result:

Proposition B.3. *Let the assumptions of Proposition B.2 be satisfied; then, the propagator probabilities $P_{0n|m_0n_0}(\tau, \varepsilon)$ are given by*

$$\text{(B.9)}\quad P_{0n|m_0n_0}(\tau, 0) = \frac{(1 - \mathrm{e}^{-\tau})^{n_0}}{(1 + b\mathrm{e}^{-\tau})^{m_0}} \sum_{s=0}^{\infty} \binom{m_0 + s - 1}{m_0 - 1} \Big(\frac{b}{1 + b\mathrm{e}^{-\tau}}\Big)^s \times \sum_{r=0}^{n_0} \binom{n_0}{r} \frac{1}{(1 - \mathrm{e}^{-\tau})^r} P_{n-(r+s)}(\tau, 0)\mathrm{e}^{-(r+s)\tau},$$

to leading order in ε. (Here, $P_{n-(r+s)}(\tau, 0) = P_{0,n-(r+s)|00}(\tau, 0)$, with $P_{n-(r+s)}$ as defined in Equation (B.8)*.)*

As before, one easily verifies that Equation (B.9) reduces to the stationary probability distribution given in [12, Equation (9)] as $\tau \to \infty$, independent of (m_0, n_0); see also Equation (43).

Finally, we quote a representation for $P_{0n|m_0n_0}$ which is only valid under additional assumptions on the parameters a and m_0:

Proposition B.4. *Let the assumptions of Proposition B.3 be satisfied, and assume that, additionally, $\tilde{a} := a - m_0 > 0$; then, the propagator probabilities $P_{0n|m_0n_0}(\tau, \varepsilon)$ are given by*

(B.10)
$$P_{0n|m_0n_0}(\tau,0) = \frac{(1-\mathrm{e}^{-\tau})^{n_0}}{(1+b)^{m_0}} \sum_{s=0}^{\infty} \binom{m_0+s-1}{m_0-1} \Big(\frac{b}{1+b}\Big)^s \sum_{r=0}^{n_0} \binom{n_0}{r} \frac{1}{(1-\mathrm{e}^{-\tau})^r} \widetilde{P}_{n-(r+s)}(\tau,0)\mathrm{e}^{-r\tau},$$

to leading order in ε. (Here, the parameter a in $P_{n-(r+s)}$ has been replaced with the modified parameter $\tilde{a}$ in $\widetilde{P}_{n-(r+s)}$.)

While we have confirmed numerically that all formulae for $P_{0n|m_0n_0}$ derived in this subsection are in agreement as long as any potential restrictions on a and m_0 are satisfied (data not shown), numerical simulation also suggests that the implementation of Proposition B.2 involves the least computational effort. One reason is certainly that the infinite summation which needs to be performed explicitly in the evaluation of Equations (B.9) and (B.10) is avoided. (While the Gamma functions occurring in (B.5) do involve infinite sums, efficient algorithms for evaluating these functions are implemented in all commercial computer algebra packages.) A further reduction in computational effort is due to the fact that the infinite series representation for the hypergeometric function ${}_2F_1(\alpha_1, \alpha_2; \beta; z)$ terminates [1, Section 15.4] – *i.e.*, that it reduces to a polynomial of finite degree in z – when at least one of the parameters α_1 or α_2 is a negative integer, as is the case in Equations (B.5) through (B.7).

B.1.3. *Large-time limit.* Not surprisingly, the above analysis confirms our intuition that the large-time limit of the leading-order probability-generating function F, as well as of its derivatives with respect to u and v, is well-defined: on the fast t-scale, Equation (B.2) implies the existence of $\lim_{t\to\infty} F(u, v, t, 0)$, while it follows immediately from Proposition B.1 that $\lim_{t\to\infty} P_{mn|m_0n_0}(t, 0)$ exists. Similarly, on the slow τ-scale, Equation (B.4) shows that the stationary generating function $F^\infty(v) \equiv \lim_{\tau\to\infty} F_0(v, \tau) = (1 - bv)^{-a}$ is well-defined, while Proposition B.2 yields the well-definedness of the resulting probability distribution. (In particular, since $v_0 = v\mathrm{e}^{-\tau}$ is a dynamic variable on the slow τ-scale, any (m_0, n_0)-dependence in F must vanish in that limit.)

In fact, it follows from standard geometric singular perturbation theory – and, indeed, from conventional asymptotic techniques for ordinary differential equations – that $\lim_{t\to\infty} F(u, v, t, 0)$ must equal $\lim_{\tau\to 0^+} F(U_0(v), v, \tau, 0)$, where U_0 is defined as in Equation (10). While that relation cannot, in general, be expected to hold for the corresponding derivatives with respect to u and v, we do find $\lim_{t\to\infty} P_{mn|m_0n_0}(t, 0) = \lim_{\tau\to 0^+} P_{mn|m_0n_0}(\tau, 0)$ here, which is best verified by comparing the respective asymptotics of $P_{mn|m_0n_0}$, as given in Propositions B.1 and B.3. (It should be equally possible to refer to Proposition B.2; however, since the argument $\frac{\mathrm{e}^\tau + b}{b(1-\mathrm{e}^\tau)}$ in some of the hypergeometric functions therein becomes unbounded for $\tau = 0$, a detailed study of the small-τ asymptotics of Equations (B.5) through (B.7) may be required in that case.)

B.2. **First-order asymptotics.** Given the leading-order approximation for the propagator probabilities $P_{mn|m_0n_0}$ for general values of (m_0, n_0), as derived in the previous section, the corresponding first-order correction (in ε) can again be determined via the perturbative procedure developed in Section 4. We discuss one particular regime here, restricting ourselves to the case where $m_0 = 0$ and $n_0 \in \mathbb{N}$; as in Section 4, we first describe separately the asymptotics of $P_{mn|0n_0}$ on the fast and the slow time-scales, which we then combine into a 'composite' expansion for the propagator $P_{n|n_0}$ that is uniformly valid in time.

B.2.1. *Fast dynamics.* In analogy to Section 4.2.1, we consider the generating function $F(u, v, t, \varepsilon)$ on the fast t-scale, up to an $\mathcal{O}(\varepsilon^2)$-error; however, in contrast to Equation (26), we now allow for general $n_0 \in \mathbb{N}$:

$$F(z', z, t, \varepsilon) = z^{n_0}\Bigg\{1 - \varepsilon\Bigg[n_0\frac{z-1}{z}t - \frac{a}{1-b(z-1)}\Bigg(b(z-1)t + \Big[z' - \frac{1}{1-b(z-1)}\Big]\big\{1 - \mathrm{e}^{-[1-b(z-1)]t}\big\}\Bigg)\Bigg]\Bigg\} + \mathcal{O}(\varepsilon^2).$$

(Here, we have again abused notation, replacing (u, v) with (z', z); moreover, we remark that the above expansion is regular at $z = 0$ due to our restriction on n_0.) As in the proof of Proposition 4.1, the fast propagator $P_{mn|0n_0}(t, \varepsilon)$ can then be approximated by repeated differentiation of F with respect to z' and z:

Proposition B.5. *Let $m, n \in \mathbb{N}_0$ and $n_0 \in \mathbb{N}$, and let $\varepsilon \in [0, \varepsilon_0]$, with $\varepsilon_0 > 0$ sufficiently small; moreover, assume that $t \ll \varepsilon^{-1}$, i.e., let $\varepsilon t = o(1)$. Then, the propagator probabilities $P_{mn|0n_0}(t, \varepsilon)$ are given by*

(B.11)

$$P_{0n|0n_0}(t,\varepsilon) = \begin{cases} 0 & \textit{when } n < n_0 - 1, \\ \varepsilon n_0 t & \textit{when } n = n_0 - 1, \\ 1 - \varepsilon\frac{a}{1+b}\Big\{\big(\frac{1+b}{a}n_0 + b\big)t + \frac{1}{1+b}\big[1 - \mathrm{e}^{-(1+b)t}\big]\Big\} & \textit{when } n = n_0, \\ \frac{\varepsilon}{\Gamma(n-n_0+2)}ab^{n-n_0}t^{n-n_0+1} & \\ \quad\times\Big\{{}_1F_1(n-n_0+1; n-n_0+2; -(1+b)t)t & \\ \quad-\frac{n-n_0+1}{1+b}\big[{}_1F_1\big(n-n_0+1; n-n_0+2; -(1+b)t\big) - \mathrm{e}^{-(1+b)t}\big]\Big\} & \textit{when } n > n_0 \end{cases}$$

for $m = 0$ and by

(B.12)

$$P_{1n|0n_0}(t,\varepsilon) = \begin{cases} 0 & \textit{when } n < n_0, \\ \frac{\varepsilon}{\Gamma(n-n_0+2)}ab^{n-n_0}t^{n-n_0+1}{}_1F_1\big(n-n_0+1; n-n_0+2; -(1+b)t\big) & \textit{when } n \geq n_0 \end{cases}$$

for $m = 1$, up to an $\mathcal{O}(\varepsilon^2)$-error. (Here, ${}_1F_1$ denotes the confluent hypergeometric function [1], *as before.) For $m \geq 2$, $P_{mn|0n_0}(t, \varepsilon) \equiv 0$ to the order considered here.*

The proof is lengthy, but straightforward, and is based on a combination of the techniques and identities that were previously applied in proving Propositions 4.1 and B.1. (In the case where $n = n_0$, one additionally makes use of the identity ${}_1F_1(1; 2; -z) = \frac{1}{z}(1 - \mathrm{e}^{-z})$; see, *e.g.*, [1, Equation 13.6.14].) We emphasise that $P_{0n|0n_0}$ is always zero – at least to the order considered here – when $n < n_0 - 1$, as well as that the expression found for $n = 0$, which is again best derived separately, can now be subsumed under the case of general $n \in \mathbb{N}$ if one takes into account that the only non-zero contribution is obtained for $n = n_0 - 1$ then:

$$P_{00|0n_0}(t,\varepsilon) = \begin{cases} \varepsilon t & \text{when } n_0 = 1, \\ 0 & \text{when } n_0 \geq 2. \end{cases}$$

Moreover, we note that, when $n_0 = 0$, Equations (B.11) and (B.12) reduce to their respective counterparts, Equations (33) through (35), in the statement of Proposition 4.1.

Finally, given Proposition B.5, we have the following approximation for the marginal protein distribution $P_{n|n_0} = P_{0n|0n_0} + P_{1n|0n_0}$:

$$P_{n|n_0}(t,\varepsilon) = \begin{cases} 0 & \text{when } n < n_0 - 1, \\ \varepsilon n_0 t & \text{when } n = n_0 - 1, \\ 1 - \varepsilon \frac{ab}{1+b}\Big\{\big(\frac{1+b}{ab}n_0 + 1\big)t - \frac{1}{1+b}\big[1 - \mathrm{e}^{-(1+b)t}\big]\Big\} & \text{when } n = n_0, \\ \frac{\varepsilon}{\Gamma(n-n_0+2)} ab^{n-n_0} t^{n-n_0+1} & \\ \quad \times \Big\{(t+1)\,{}_1F_1\big(n-n_0+1; n-n_0+2; -(1+b)t\big) & \\ \quad -\frac{n-n_0+1}{1+b}\big[{}_1F_1\big(n-n_0+1; n-n_0+2; -(1+b)t\big) - \mathrm{e}^{-(1+b)t}\big]\Big\} & \text{when } n > n_0, \end{cases}$$

up to an $\mathcal{O}(\varepsilon^2)$-error. (As expected, the above formulae again reduce to their counterpart, Equation (36), when $n_0 = 0$.)

B.2.2. *Slow dynamics.* Next, we derive the first-order asymptotics of the propagator $P_{mn|0n_0}$ – *i.e.*, of the probability of observing m mRNAs and n proteins, given 0 and n_0 of each initially, respectively – on the slow τ-scale:

Proposition B.6. *Let $n \in \mathbb{N}_0$ and $n_0 \in \mathbb{N}$, and let $\varepsilon \in [0, \varepsilon_0]$, with $\varepsilon_0 > 0$ sufficiently small; moreover, assume that $\tau \gg \varepsilon$. Then, the propagator probabilities $P_{mn|0n_0}(\tau, \varepsilon)$ are given by*

$$\begin{aligned}
P_{0n|0n_0}(\tau,\varepsilon) &= \big(1-\mathrm{e}^{-\tau}\big)^{n_0} \frac{\Gamma(a+n)}{\Gamma(n+1)\Gamma(a)}\Big(\frac{b}{1+b}\Big)^n \Big(\frac{1+b\mathrm{e}^{-\tau}}{1+b}\Big)^a \\
&\quad \times \sum_{k=0}^{n} \frac{\Gamma(n+1)}{\Gamma(n-k+1)} \frac{\Gamma(a+n-k)}{\Gamma(a+n)} {}_2F_1\big(-n+k, -a; 1-a-n+k; \tfrac{1+b}{\mathrm{e}^\tau+b}\big) \\
&\quad \times \Bigg\{ \frac{(-1)^k}{\Gamma(k+1)} \frac{\Gamma(n_0+1)}{\Gamma(n_0-k+1)} \Big[\frac{1+b}{b(1-\mathrm{e}^\tau)}\Big]^k - \frac{\varepsilon}{2}\frac{a}{(1+b)^2}(k+1) \\
&\quad \times \Big[{}_2F_1\big(-k, -n_0; -1-k; \tfrac{1+b}{b(1-\mathrm{e}^\tau)}\big) + \Big(\frac{1+b}{\mathrm{e}^\tau+b}\Big)^{k+2} \mathrm{e}^{2\tau}\, {}_2F_1\big(-k,-n_0;-1-k; \tfrac{\mathrm{e}^\tau+b}{b(1-\mathrm{e}^\tau)}\big)\Big]\Bigg\}
\end{aligned} \tag{B.13}$$

when $m = 0$ and by

$$\begin{aligned}
P_{1n|0n_0}(\tau,\varepsilon) &= \varepsilon\big(1-\mathrm{e}^{-\tau}\big)^{n_0} \frac{\Gamma(a+n)}{\Gamma(n+1)\Gamma(a)}\Big(\frac{b}{1+b}\Big)^n \Big(\frac{1+b\mathrm{e}^{-\tau}}{1+b}\Big)^a \frac{a}{1+b} \\
&\quad \times \sum_{k=0}^{n} \frac{\Gamma(n+1)}{\Gamma(n-k+1)} \frac{\Gamma(a+n-k)}{\Gamma(a+n)} {}_2F_1\big(-n+k, -a; 1-a-n+k; \tfrac{1+b}{\mathrm{e}^\tau+b}\big) \\
&\quad \times \Bigg\{(-1)^{n_0}\Big[\frac{1+b\mathrm{e}^\tau}{b(1-\mathrm{e}^\tau)}\Big]^{n_0} + (-1)^k \frac{\Gamma(n_0+1)}{\Gamma(k+2)\Gamma(n_0-k)} \Big[\frac{1+b}{b(1-\mathrm{e}^\tau)}\Big]^{k+1} {}_2F_1\big(1, 1-n_0+k; 2+k; \tfrac{1+b}{b(1-\mathrm{e}^\tau)}\big)\Bigg\}
\end{aligned} \tag{B.14}$$

when $m = 1$, up to an $\mathcal{O}(\varepsilon^2)$-error. For $m \geq 2$, $P_{mn|0n_0}(\tau, \varepsilon) \equiv 0$ to the order considered here.

The proof of Proposition B.6 is largely analogous to that of Proposition 4.2, and is hence omitted here. (While the two hypergeometric functions occurring in the last line of Equation (B.13) may be eliminated via the relation ${}_2F_1(-k, -n_0; -1-k; z) = -\frac{1}{k+1}(1-z)^{n_0-1}[(-n_0+k+1)z - (k+1)]$, the resulting expression seems unnecessarily cumbersome.) We remark that, for $n_0 = 0$, (B.13) and (B.14) reduce to Equations (38) and (39), respectively, in the statement of Proposition 4.2; see the discussion below Proposition B.2 for details.

Finally, we emphasise that the marginal protein distribution on this slow τ-scale is again defined as $P_{n|n_0} = P_{0n|0n_0} + P_{1n|0n_0}$, to first order in ε.

B.2.3. *Uniform (fast-slow) dynamics.* We conclude our discussion with the first-order asymptotics of the uniform (composite) propagator $P_{n|n_0}$ that is valid both on the fast and the slow time-scales, for arbitrary $n_0 \in \mathbb{N}_0$; cf. Equation (44):

Proposition B.7. *Let $n \in \mathbb{N}_0$, let $\varepsilon \in [0, \varepsilon_0]$, with $\varepsilon_0 > 0$ sufficiently small, let $t_* > 0$ be arbitrary, but fixed, and let $\tau_* = \varepsilon t_*$. Up to an $\mathcal{O}(\varepsilon^2)$-error, the uniform marginal protein distribution $P_{n|n_0}(\tau, t, \varepsilon)$ is then given by $P_{n|n_0}(\tau, t, \varepsilon) \equiv P_{n|n_0}(\tau, \varepsilon)$ when $n < n_0$ and by*

$$\begin{aligned} P_{n|n_0}(\tau, t, \varepsilon) &= P_{n|n_0}(\tau, \varepsilon) + \varepsilon a \frac{b^{n-n_0}}{(1+b)^{n-n_0+2}} \big[n - n_0 - b - (1+b)t\big] \\ &+ \frac{\varepsilon}{\Gamma(n-n_0+2)} a b^{n-n_0} t^{n-n_0+1} \Big\{ {}_1F_1\big(n-n_0+1; n-n_0+2; -(1+b)t\big) t \\ &- \frac{1}{1+b}\big[(n-n_0-b) {}_1F_1\big(n-n_0+1; n-n_0+2; -(1+b)t\big) - (n-n_0+1)\mathrm{e}^{-(1+b)t}\big] \Big\} \end{aligned} \tag{B.15}$$

when $n \geq n_0$, for any $t \in (0, t_*]$ and $\tau \in (0, \tau_*]$. (Here, $P_{n|n_0}(\tau, \varepsilon)$ is defined as in the previous subsection.)

The proof is analogous to that of Proposition 4.3, and is hence omitted here. (The restriction to positive times in Equation (B.15) is necessitated by the fact that the expressions in Equations (B.13) and (B.14) are *a priori* undefined at $\tau = 0$; however, their validity may be extended asymptotically to that point via the formulae found in Section 15.12 of [4].)

C. Full mathematical proofs

In this section, we collect the mathematical proofs that underlie the asymptotic analysis presented in Sections 3 and 4 of the main text, as well as in Section B above.

C.1. **Proofs for Section 3.**

Proof of Proposition 3.1. The first statement follows directly from Theorem A.1.

The second statement can be obtained by making the Ansatz in (11) for $\mathcal{S}_\varepsilon$; since the manifold $\mathcal{S}_\varepsilon$ is (locally) invariant, $u = U(v, \varepsilon)$ must then satisfy Equation (8a): by the Chain Rule, $\dot{u} = \frac{\partial U}{\partial v}(v, \varepsilon)\dot{v}$, which, together with $\frac{\partial U}{\partial v}(v, \varepsilon) = \frac{dU_0}{dv} + \frac{dU_1}{dv}\varepsilon + \cdots + \frac{dU_K}{dv}\varepsilon^K + \mathcal{O}(\varepsilon^{K+1})$ and (8b), yields

$$\begin{aligned} \varepsilon\left[\frac{dU_0}{dv} + \frac{dU_1}{dv}\varepsilon + \cdots + \frac{dU_K}{dv}\varepsilon^K + \mathcal{O}(\varepsilon^{K+1})\right] v &= U_0 + U_1\varepsilon + \cdots + U_K\varepsilon^K + \mathcal{O}(\varepsilon^{K+1}) \\ &\quad - b\big[1 + U_0 + U_1\varepsilon + \cdots + U_K\varepsilon^K + \mathcal{O}(\varepsilon^{K+1})\big] v. \end{aligned}$$

Comparing terms in like powers of ε in the above relation, we find a system of recursive equations for $U_k(v)$, $k = 0, \ldots, K$:

$$\mathcal{O}(1): \quad 0 = U_0 - b(1 + U_0)v, \tag{C.1a}$$

$$\mathcal{O}(\varepsilon^k): \quad \frac{dU_{k-1}}{dv} v = U_k - bU_k v \qquad \text{for } k = 1, \ldots K. \tag{C.1b}$$

To leading order in ε, we hence recover the expression for $\mathcal{S}_0$ in Equation (10) from (C.1a), as required. Next, given $\frac{dU_0}{dv} = \frac{b}{(1-bv)^2}$, we find $U_1 = \frac{bv}{(1-bv)^3}$ for $k = 1$, as claimed. The general expression for U_k when $k \in \mathbb{N}$ then follows from (C.1b) in combination with an induction argument, which implies the second statement.

The third statement follows trivially from (8b) and (8c), in combination with (11).

The fourth statement is evident from the fact that any point on ℓ is an equilibrium state for Equation (8) irrespective of ε; hence, the line ℓ itself must be contained in the invariant manifold $\mathcal{S}_\varepsilon$.

Finally, the fifth statement is an immediate consequence of Theorem A.2. $\square$

C.2. **Proofs for Section 4.**

Proof of Proposition 4.1. Rewriting Equation (26) in terms of $z' = 1+u$ and $z = 1+v$, one finds

(C.2)
$$F(z', z, t, \varepsilon) = 1 + \varepsilon \frac{a}{1-b(z-1)}\left(b(z-1)t + \left[z' - \frac{1}{1-b(z-1)}\right]\left\{1 - \mathrm{e}^{-[1-b(z-1)]t}\right\}\right) + \mathcal{O}(\varepsilon^2);$$

hence, $\frac{\partial^m}{\partial (z')^m} F(z', z, t, \varepsilon) = 0$ for $m \geq 2$, at least to first order in ε, which implies $P_{mn}(t, \varepsilon) \equiv 0$ then. Thus, it only remains to consider the cases where $m = 0$ or $m = 1$.

We first present the proof for $m = 0$: evaluating (C.2) at $z' = 0$, we have

$$F(0, z, t, \varepsilon) = 1 + \varepsilon \frac{ab(z-1)}{1-b(z-1)} t - \varepsilon \frac{a}{[1-b(z-1)]^2}\left\{1 - \mathrm{e}^{-[1-b(z-1)]t}\right\} + \mathcal{O}(\varepsilon^2).$$

Setting $z = 0$ in the above expression, we immediately obtain P_{00}, as given in Equation (33).

To derive the asymptotics of P_{0n} for $n \geq 1$, we differentiate $F(0, z, t, \varepsilon)$ repeatedly with respect to z; recall Equation (32). The derivative of the first (t-dependent) term can be evaluated by noting that $\frac{\partial^n}{\partial z^n}\frac{b(z-1)}{1-b(z-1)}\big|_{z=0} = n!\frac{b^n}{(1+b)^{n+1}}$, where $n \in \mathbb{N}$. Writing $[1-b(z-1)]^{-2} = (1+b)^{-2}(1 - \frac{b}{1+b}z)^{-2}$, we then have $\frac{\partial^k}{\partial z^k}[1-b(z-1)]^{-2}\big|_{z=0} = (1+b)^{-2}\Gamma(k+2)(\frac{b}{1+b})^k$ for any $k \in \mathbb{N}_0$, which implies, in particular, $\frac{\partial^n}{\partial z^n}[1-b(z-1)]^{-2}\big|_{z=0} = (n+1)!\frac{b^n}{(1+b)^{n+2}}$. Next, we make use of the fact that $\frac{\partial^k}{\partial z^k}\mathrm{e}^{-[1-b(z-1)]t}\big|_{z=0} = b^k t^k \mathrm{e}^{-(1+b)t}$ for $k \in \mathbb{N}_0$ as well as of the Product Rule, obtaining

$$\begin{aligned}\frac{\partial^n}{\partial z^n}\left\{\frac{1}{[1-b(z-1)]^2}\mathrm{e}^{-[1-b(z-1)]t}\right\}\bigg|_{z=0} &= \frac{1}{(1+b)^2}\sum_{k=0}^n \binom{n}{k}\frac{\partial^k}{\partial z^k}\frac{1}{\left(1-\frac{b}{1+b}z\right)^2}\cdot\frac{\partial^{n-k}}{\partial z^{n-k}}\mathrm{e}^{-[1-b(z-1)]t}\bigg|_{z=0} \\ &= \frac{b^n}{(1+b)^2}\sum_{k=0}^n \binom{n}{k}(k+1)!\frac{t^{n-k}}{(1+b)^k}\cdot\mathrm{e}^{-(1+b)t}\end{aligned}$$

and, hence, in sum

$$P_{0n}(t,\varepsilon) = \varepsilon\frac{ab^n}{(1+b)^{n+2}}\left[(1+b)t - (n+1) + \sum_{k=0}^n \frac{k+1}{(n-k)!}(1+b)^{n-k}t^{n-k}\cdot\mathrm{e}^{-(1+b)t}\right] + \mathcal{O}(\varepsilon^2). \quad \text{(C.3)}$$

Finally, we note that

$$\sum_{k=0}^n \frac{k+1}{(n-k)!}z^{n-k} = \frac{1}{n!}\left[(n+1-z)\Gamma(n+1,z)\mathrm{e}^z + z^{n+1}\right]$$

and

$$\Gamma(n+1,z) = n! - \frac{z^{n+1}}{n+1}\,{}_1F_1(n+1;n+2;-z); \quad \text{(C.4)}$$

cf. [1, Equation 6.5.12]; here, $\Gamma(\alpha, z)$ and ${}_1F_1(\alpha;\beta;z)$ denote the incomplete Gamma function and the confluent hypergeometric function, respectively, which are, for instance, defined in [1, Equations 6.5.3 and 13.1.2]. (In particular, since $\beta = n+2$ is a positive integer here, we may assume ${}_1F_1$ to be the first standard solution of Kummer's equation; see again [1, Section 13] for details.) Observing that $z = (1+b)t$ in our case, substituting into Equation (C.3), simplifying, and rearranging, we find the expression in (34).

The proof in the case where $m = 1$ is similar: differentiating Equation (C.2) with respect to z' and evaluating the result at $z' = 0$ (which is vacuous in our case), we have

$$\frac{\partial}{\partial(z')}F(z',z,t,\varepsilon)\Big|_{z'=0} = \varepsilon\frac{a}{1-b(z-1)}\big\{1-\mathrm{e}^{-[1-b(z-1)]t}\big\} + \mathcal{O}(\varepsilon^2). \tag{C.5}$$

Noting that $\frac{\partial^n}{\partial z^n}[1-b(z-1)]^{-1}\big|_{z=0} = n!\frac{b^n}{(1+b)^{n+1}}$ for any $n \in \mathbb{N}_0$ and applying the Product Rule, as before, we find

$$\frac{\partial^n}{\partial z^n}\left\{\frac{1}{1-b(z-1)}\mathrm{e}^{-[1-b(z-1)]t}\right\}\Big|_{z=0} = b^n\sum_{k=0}^{n}\binom{n}{k}k!\frac{t^{n-k}}{(1+b)^{k+1}}\cdot\mathrm{e}^{-(1+b)t};$$

hence,

$$P_{1n}(t,\varepsilon) = \varepsilon\frac{ab^n}{(1+b)^{n+1}}\left[1-\sum_{k=0}^{n}\frac{1}{(n-k)!}(1+b)^{n-k}t^{n-k}\cdot\mathrm{e}^{-(1+b)t}\right] + \mathcal{O}(\varepsilon^2).$$

Finally, we make use of the identity $\sum_{k=0}^{n}\frac{1}{(n-k)!}z^{n-k} = \frac{\Gamma(n+1,z)}{n!}\mathrm{e}^z$, which we combine with (C.4) to obtain Equation (35), as claimed. (While that equation is valid for any $n \in \mathbb{N}_0$, we remark that (C.5) directly implies $P_{10}(t,\varepsilon) = \varepsilon\frac{a}{1+b}\big[1-\mathrm{e}^{-(1+b)t}\big] + \mathcal{O}(\varepsilon^2)$ for $n = 0$.) □

Proof of Proposition 4.2. We first discuss the case where $m = 0$, verifying Equation (38). Abusing notation, as above, we rewrite the expansion for F in Equation (30) in terms of z, and we evaluate the result for $m_0 = 0 = n_0$ and $z' = 0$ to find

$$\begin{aligned} F(0,z,\tau,\varepsilon) &= \left(1-\varepsilon\frac{a}{2}\left\{\frac{1}{[1-b(z-1)]^2}+\frac{1}{[1-b(z-1)\mathrm{e}^{-\tau}]^2}\right\}\right)\left[\frac{1-b(z-1)\mathrm{e}^{-\tau}}{1-b(z-1)}\right]^a + \mathcal{O}(\varepsilon^2) \\ &= F_0(z,\tau) + \varepsilon F_1(0,z,\tau) + \mathcal{O}(\varepsilon^2). \end{aligned} \tag{C.6}$$

Given the definition of $P_{0n}(\tau) = \frac{1}{n!}\frac{\partial^n}{\partial z^n}F(0,z,\tau,\varepsilon)\big|_{z=0}$, we hence need to determine the n-th derivative of (C.6) for arbitrary $n \in \mathbb{N}$. The derivation of the leading-order term $\frac{\partial^n}{\partial z^n}F_0$ can be found in [12, Supporting Information]; cf. also Equation (B.8). For the derivatives of the $\mathcal{O}(\varepsilon)$-correction F_1, we recall that $[1-b(z-1)]^{-2} = (1+b)^{-2}\big(1-\frac{b}{1+b}z\big)^{-2}$, which implies $\frac{\partial^k}{\partial z^k}[1-b(z-1)]^{-2}\big|_{z=0} = (1+b)^{-2}\Gamma(k+2)\big(\frac{b}{1+b}\big)^k$; see the proof of Proposition 4.1. Similarly, we may write $[1-b(z-1)\mathrm{e}^{-\tau}]^{-2} = (1+b\mathrm{e}^{-\tau})^{-2}\big(1-\frac{b}{\mathrm{e}^{\tau}+b}z\big)^{-2}$ to find $\frac{\partial^k}{\partial z^k}[1-b(z-1)\mathrm{e}^{-\tau}]^{-2}\big|_{z=0} = (1+b\mathrm{e}^{-\tau})^{-2}\Gamma(k+2)\big(\frac{b}{\mathrm{e}^{\tau}+b}\big)^k$. Applying the Product Rule and making again use of Equation (B.8), we then calculate

$$\begin{aligned} \frac{\partial^n}{\partial z^n}F_1(0,z,\tau)\Big|_{z=0} &= -\frac{\partial^n}{\partial z^n}\left(\frac{a}{2}\left\{\frac{1}{[1-b(z-1)]^2}+\frac{1}{[1-b(z-1)\mathrm{e}^{-\tau}]^2}\right\}\left[\frac{1-b(z-1)\mathrm{e}^{-\tau}}{1-b(z-1)}\right]^a\right)\Big|_{z=0} \\ &= -\frac{a}{2}\sum_{k=0}^{n}\binom{n}{k}\frac{\partial^k}{\partial z^k}\left\{\frac{1}{[1-b(z-1)]^2}+\frac{1}{[1-b(z-1)\mathrm{e}^{-\tau}]^2}\right\}\frac{\partial^{n-k}}{\partial z^{n-k}}\left[\frac{1-b(z-1)\mathrm{e}^{-\tau}}{1-b(z-1)}\right]^a\Big|_{z=0} \\ &= -\frac{a}{2}\sum_{k=0}^{n}\binom{n}{k}\Gamma(k+2)b^k\left[\frac{1}{(1+b)^{k+2}}+\frac{\mathrm{e}^{2\tau}}{(\mathrm{e}^{\tau}+b)^{k+2}}\right] \\ &\quad\times\frac{\Gamma(a+n-k)}{\Gamma(a)}\Big(\frac{b}{1+b}\Big)^{n-k}\Big(\frac{1+b\mathrm{e}^{-\tau}}{1+b}\Big)^a{}_2F_1\big(-n+k,-a;1-a-n+k;\tfrac{1+b}{\mathrm{e}^{\tau}+b}\big) \\ &= -n!\frac{a}{2}\frac{b^n}{(1+b)^{n+2}}\Big(\frac{1+b\mathrm{e}^{-\tau}}{1+b}\Big)^a\sum_{k=0}^{n}\frac{k+1}{(n-k)!}\frac{\Gamma(a+n-k)}{\Gamma(a)}\left[1+\Big(\frac{1+b}{\mathrm{e}^{\tau}+b}\Big)^{k+2}\mathrm{e}^{2\tau}\right] \\ &\quad\times{}_2F_1\big(-n+k,-a;1-a-n+k;\tfrac{1+b}{\mathrm{e}^{\tau}+b}\big), \end{aligned}$$

which concludes the verification of (38).

Next, we consider the case where $m=1$: since $\frac{\partial}{\partial z'}F(z',z,\tau,\varepsilon)\big|_{z'=0} = \varepsilon\frac{a}{1-b(z-1)}\big[\frac{1-b(z-1)\mathrm{e}^{-\tau}}{1-b(z-1)}\big]^a$, by Equation (30), and since we can show as above that

$$\begin{aligned}
&\frac{\partial^n}{\partial z^n}\left\{\frac{a}{1-b(z-1)}\left[\frac{1-b(z-1)\mathrm{e}^{-\tau}}{1-b(z-1)}\right]^a\right\}\Bigg|_{z=0} \\
&\quad = a\sum_{k=0}^n\binom{n}{k}\frac{\partial^k}{\partial z^k}\frac{1}{1-b(z-1)}\cdot\frac{\partial^{n-k}}{\partial z^{n-k}}\left[\frac{1-b(z-1)\mathrm{e}^{-\tau}}{1-b(z-1)}\right]^a\Bigg|_{z=0} \\
&\quad = n!a\frac{b^n}{(1+b)^{n+1}}\Big(\frac{1+b\mathrm{e}^{-\tau}}{1+b}\Big)^a\sum_{k=0}^n\frac{1}{(n-k)!}\frac{\Gamma(a+n-k)}{\Gamma(a)}{}_2F_1\big(-n+k,-a;1-a-n+k;\tfrac{1+b}{\mathrm{e}^\tau+b}\big),
\end{aligned}$$

we obtain Equation (39).

Finally, since $\frac{\partial^m}{\partial(z')^m}F\equiv 0$ to first order in ε whenever $m\geq 2$, again by Equation (30), it follows that $P_{mn}(\tau,\varepsilon)\equiv 0$ then, as claimed, which concludes the proof. □

Proof of Corollary 4.1. We first consider the case where $m=0$. The leading-order term in Equation (41) can then be found in [12, Equation (9)]; to determine the ε-dependent first-order correction, we take the limit as $\tau\to\infty$ in (38), noting that ${}_2F_1(-k,-a;1-a-k;\frac{1+b}{\mathrm{e}^\tau+b})\to 1$ in that limit. Making use of the identity

$$\sum_{k=0}^n\frac{k+1}{(n-k)!}\Gamma(a+n-k)=\frac{(a+n+1)(a+n)}{(a+1)a}\frac{\Gamma(a+n)}{\Gamma(n+1)}$$

(which can be verified directly), as well as of the fact that

$$\lim_{\tau\to\infty}\Big(\frac{1+b}{\mathrm{e}^\tau+b}\Big)^{k+2}\mathrm{e}^{2\tau}=(1+b)^2\delta_{k0}\qquad\text{for } k=0,\dots,n,$$

where δ_{jk} denotes the Kronecker delta, as before, we obtain Equation (41).

Similarly, for $m=1$, we note that $\sum_{k=0}^n\frac{\Gamma(a+n-k)}{(n-k)!}=\frac{a+n}{a}\frac{\Gamma(a+n)}{\Gamma(n+1)}$ in (39), which yields Equation (42), as claimed. □

Proof of Proposition 4.3. We recall the uniform expansion for the generating function F in Equation (31), as well as the fact that only contributions from $m=0$ and $m=1$ have to be taken into account to the order considered here. As $P_n(\tau,t,\varepsilon)$ is obtained by repeated differentiation of (31) with respect to v, and as the contribution from $\frac{\partial^n}{\partial z^n}\big[F_0(z,\tau)+\varepsilon F_1(z',z,\tau)\big]\big|_{(z',z)=(1,0)}$ therein yields precisely $P_n(\tau,\varepsilon)$, cf. Equation (40), it only remains to determine $\frac{\partial^n}{\partial z^n}\mathcal{F}_1'(z',z,t)\big|_{(z',z)=(1,0)}$. (Here, we have again abused notation, replacing (u,v) with (z',z).) To that end, we note that

$$\begin{aligned}
\frac{\partial^n}{\partial z^n}\mathcal{F}_1'(1,z,t) &= a\frac{\partial^n}{\partial z^n}\left\{\frac{b(z-1)}{[1-b(z-1)]^2}\mathrm{e}^{-[1-b(z-1)]t}\right\}\Bigg|_{z=0} \\
&= a\sum_{k=0}^n\binom{n}{k}\frac{\partial^k}{\partial z^k}\frac{b(z-1)}{[1-b(z-1)]^2}\frac{\partial^{n-k}}{\partial z^{n-k}}\mathrm{e}^{-[1-b(z-1)]t}\Bigg|_{z=0} \\
&= -n!a\frac{b^n}{(1+b)^{n+2}}\sum_{k=0}^n\frac{b-k}{(n-k)!}(1+b)^{n-k}t^{n-k}\cdot\mathrm{e}^{-(1+b)t},
\end{aligned}$$

where we have made use of the relations $\frac{\partial^k}{\partial z^k}\frac{b(z-1)}{[1-b(z-1)]^2}\big|_{z=0}=-k!\frac{b^k(b-k)}{(1+b)^{k+2}}$ and $\frac{\partial^k}{\partial z^k}\mathrm{e}^{-[1-b(z-1)]t}\big|_{z=0}=b^kt^k\mathrm{e}^{-(1+b)t}$, with $k\in\mathbb{N}$; recall the proof of Proposition 4.1. Finally, we may verify directly that

$$\sum_{k=0}^{n}\frac{b-k}{(n-k)!}z^{n-k}=\frac{1}{n!}\big[(b-n+z)\Gamma(n+1,z)\mathrm{e}^z-z^{n+1}\big].$$

Combining the above identity with Equation (C.4), we obtain (44), as claimed. □

C.3. **Proofs for Section B.**

Proof of Proposition B.1. Rewriting Equation (B.1) in terms of $z'=1+u$ and $z=1+v$, we obtain (with an abuse of notation)

$$\mathcal{F}_0(z',z,t)=\left\{\frac{1}{1-b(z-1)}+\left[z'-\frac{1}{1-b(z-1)}\right]\mathrm{e}^{-[1-b(z-1)]t}\right\}^{m_0}z^{n_0};\tag{C.7}$$

see also [3, Equation (21)]. Given Equation (C.7), the relation in (32) then immediately implies $P_{mn|m_0n_0}(t,0)\equiv 0$ for any $m>m_0\geq 0$ and arbitrary $n_0\in\mathbb{N}_0$; hence, $P^\infty_{mn|m_0n_0}(0)\equiv 0$ in that case, as well. For $m_0\geq m\geq 1$, on the other hand, we exploit the fact that

$$\frac{\partial^m}{\partial(z')^m}\mathcal{F}_0(z',z,t)=m!\left\{\frac{1}{1-b(z-1)}+\left[z'-\frac{1}{1-b(z-1)}\right]\mathrm{e}^{-[1-b(z-1)]t}\right\}^{m_0-m}z^{n_0}\mathrm{e}^{-m[1-b(z-1)]t},$$

i.e., that each differentiation with respect to z' yields an additional factor of $\mathrm{e}^{-[1-b(z-1)]t}$, irrespective of $n_0\in\mathbb{N}_0$. Thus, we conclude that $P_{mn|m_0n_0}(t,0)$ then decays to zero exponentially as $t\to\infty$, which shows (i).

To prove (ii), we note that (C.7) reduces to $\mathcal{F}_0(z)\equiv z^{n_0}$ when $m_0=0$; hence, it follows trivially that $P_{0n|00}(t,0)\equiv 0$, while the statement for $n_0\in\mathbb{N}$ is obtained from the identity $\frac{d^n}{dz^n}z^{n_0}\big|_{z=0}=\delta_{nn_0}n_0!$.

Finally, it remains to derive Equation (B.3). For $n<n_0$, Equation (C.7), in combination with $P_{0n|m_0n_0}(t,0)=\frac{1}{n!}\frac{\partial^n}{\partial z^n}\mathcal{F}_0(0,z,t)\big|_{z=0}$, implies that $P_{0n|m_0n_0}(t,0)\equiv 0$; hence, in particular, $P^\infty_{0n|m_0n_0}(0)\equiv 0$. To derive the expression for $n\geq n_0$, we note that

$$\begin{aligned}
P_{0n|m_0n_0}(t,0)&=\frac{1}{n!}\sum_{k=0}^{n}\binom{n}{k}\frac{\partial^k}{\partial z^k}\left(\frac{1}{1-b(z-1)}\big\{1-\mathrm{e}^{-[1-b(z-1)]t}\big\}\right)^{m_0}\frac{\partial^{n-k}}{\partial z^{n-k}}z^{n_0}\Bigg|_{z=0}\\
&=\frac{1}{(n-n_0)!}\frac{\partial^{n-n_0}}{\partial z^{n-n_0}}\left(\frac{1}{1-b(z-1)}\big\{1-\mathrm{e}^{-[1-b(z-1)]t}\big\}\right)^{m_0}\Bigg|_{z=0}\\
&=\frac{1}{(n-n_0)!}\sum_{j=0}^{n-n_0}\binom{n-n_0}{j}\frac{\partial^j}{\partial z^j}\frac{1}{[1-b(z-1)]^{m_0}}\frac{\partial^{n-n_0-j}}{\partial z^{n-n_0-j}}\big\{1-\mathrm{e}^{-[1-b(z-1)]t}\big\}^{m_0}\Bigg|_{z=0}\\
&=\sum_{j=0}^{n-n_0}\binom{m_0+j-1}{m_0-1}\frac{b^j}{(1+b)^{m_0+j}}\frac{1}{(n-n_0-j)!}\frac{\partial^{n-n_0-j}}{\partial z^{n-n_0-j}}\big\{1-\mathrm{e}^{-[1-b(z-1)]t}\big\}^{m_0}\Bigg|_{z=0},
\end{aligned}\tag{C.8}$$

where we have again used the fact that $\frac{d^{n-k}}{dz^{n-k}}z^{n_0}\big|_{z=0}=\delta_{n-k,n_0}n_0!$, as well as the relation

$$\frac{\partial^j}{\partial z^j}[1-b(z-1)]^{-m_0}\Big|_{z=0}=(1+b)^{-m_0}\frac{\partial^j}{\partial z^j}\Big(1-\frac{b}{1+b}z\Big)^{-m_0}\Big|_{z=0}=\frac{(m_0+j-1)!}{(m_0-1)!}\frac{b^j}{(1+b)^{m_0+j}};$$

here, the last equality follows from $\frac{\partial^j}{\partial z^j}(1-qz)^{-a}\big|_{z=0}=\frac{\Gamma(a+j)}{\Gamma(a)}q^j$, where Γ stands for the Gamma function [1, Section 6]; see [12, Supporting Information, Equation (37)]. Noting that only $j=n-n_0$ in (C.8) gives a contribution in the limit as $t\to\infty$ and evaluating the resulting expression at $z=0$, we find $P^\infty_{0n|m_0n_0}(0)$, as stated, which completes the proof of (iii). □

Proof of Proposition B.2. We begin by recalling the leading-order asymptotics of F from (B.4), rewritten in terms of $z = 1 + v$:

$$F_0(z,\tau) = \frac{[1+(z-1)\mathrm{e}^{-\tau}]^{n_0}}{[1-b(z-1)\mathrm{e}^{-\tau}]^{m_0}}\left[\frac{1-b(z-1)\mathrm{e}^{-\tau}}{1-b(z-1)}\right]^a; \tag{C.9}$$

consequently,

$$P_{0n|m_0n_0}(\tau,0) = \frac{1}{n!}\sum_{k=0}^{n}\binom{n}{k}\frac{\partial^k}{\partial z^k}\frac{[1+(z-1)\mathrm{e}^{-\tau}]^{n_0}}{[1-b(z-1)\mathrm{e}^{-\tau}]^{m_0}}\frac{\partial^{n-k}}{\partial z^{n-k}}\left[\frac{1-b(z-1)\mathrm{e}^{-\tau}}{1-b(z-1)}\right]^a\bigg|_{z=0} \tag{C.10}$$

to lowest order in ε, by Equation (37).

Next, we note that $1+(z-1)\mathrm{e}^{-\tau} = \big(1-\frac{1}{1-\mathrm{e}^{\tau}}z\big)(1-\mathrm{e}^{-\tau})$ and $1-b(z-1)\mathrm{e}^{-\tau} = \big(1-\frac{b}{\mathrm{e}^{\tau}+b}z\big)(1+b\mathrm{e}^{-\tau})$; hence,

$$\frac{[1+(z-1)\mathrm{e}^{-\tau}]^{n_0}}{[1-b(z-1)\mathrm{e}^{-\tau}]^{m_0}} = \frac{(1-\mathrm{e}^{-\tau})^{n_0}}{(1+b\mathrm{e}^{-\tau})^{m_0}}\frac{\big(1-\frac{b}{\mathrm{e}^{\tau}+b}z\big)^{-m_0}}{\big(1-\frac{1}{1-\mathrm{e}^{\tau}}z\big)^{-n_0}}. \tag{C.11}$$

Making again use of the relations $\frac{\partial^k}{\partial z^k}(1-qz)^{-a}\big|_{z=0} = \frac{\Gamma(a+k)}{\Gamma(a)}q^k$ and

$$\frac{\partial^k}{\partial z^k}\frac{f(z)}{g(z)} = k!\sum_{j=0}^{k}\frac{\partial^{k-j}}{\partial z^{k-j}}f(z)\sum_{i=0}^{j}\frac{(-1)^i(j+1)g(z)^{-(i+1)}}{(i+1)!(k-j)!(j-i)!}\frac{\partial^j}{\partial z^j}g(z)^i,$$

cf. [12, Supporting Information, Equations (37) and (38)], we then calculate

$$\frac{\partial^k}{\partial z^k}\frac{\big(1-\frac{b}{\mathrm{e}^{\tau}+b}z\big)^{-m_0}}{\big(1-\frac{1}{1-\mathrm{e}^{\tau}}z\big)^{-n_0}}\bigg|_{z=0} = k!\sum_{j=0}^{k}\frac{\Gamma(m_0+k-j)}{\Gamma(m_0)}\Big(\frac{b}{\mathrm{e}^{\tau}+b}\Big)^{k-j}$$
$$\times\sum_{i=0}^{j}\frac{(-1)^i(j+1)}{(i+1)!(k-j)!(j-i)!}\frac{\Gamma(in_0+j)}{\Gamma(in_0)}\frac{1}{(1-\mathrm{e}^{\tau})^j}.$$

Noting that the reciprocal Gamma function $\frac{1}{\Gamma}$ is zero for $in_0 = 0$, as well as that

$$\sum_{i=1}^{j}\frac{(-1)^i\Gamma(in_0+j)}{\Gamma(in_0)(i+1)!(j-i)!} = \frac{(-1)^j\Gamma(n_0+1)}{\Gamma(n_0-j+1)(j+1)!},$$

by [12, Supporting Information, Equation (40)], we may apply the identity [4, Equation 15.2.4]

$${}_2F_1(-k,\alpha_2;\beta;z) = \sum_{j=0}^{k}\frac{(-1)^j}{j!}z^j\frac{\Gamma(k+1)}{\Gamma(k-j+1)}\frac{(\alpha_2)_j}{(\beta)_j} \tag{C.12}$$

to obtain

(C.13)

$$\frac{\partial^k}{\partial z^k}\frac{\big(1-\frac{b}{\mathrm{e}^{\tau}+b}z\big)^{-m_0}}{\big(1-\frac{1}{1-\mathrm{e}^{\tau}}z\big)^{-n_0}}\bigg|_{z=0} = \Big(\frac{b}{\mathrm{e}^{\tau}+b}\Big)^k\sum_{j=0}^{k}\frac{(-1)^j}{j!}\left[\frac{\mathrm{e}^{\tau}+b}{b(1-\mathrm{e}^{\tau})}\right]^j\frac{k!}{(k-j)!}\frac{\Gamma(n_0+1)}{\Gamma(n_0-j+1)}\frac{\Gamma(m_0+k-j)}{\Gamma(m_0)}$$
$$= \frac{\Gamma(m_0+k)}{\Gamma(m_0)}\Big(\frac{b}{\mathrm{e}^{\tau}+b}\Big)^k{}_2F_1\big(-k,-n_0;1-m_0-k;\tfrac{\mathrm{e}^{\tau}+b}{b(1-\mathrm{e}^{\tau})}\big).$$

(Here, we have made use of the identities $\Gamma(m_0+k-j) = \frac{\Gamma(m_0+k)}{(-1)^j(1-m_0-k)_j}$ and $\Gamma(n_0-j+1) = \frac{\Gamma(n_0+1)}{(-1)^j(-n_0)_j}$, where $(z)_j = \frac{\Gamma(z+j)}{\Gamma(z)}$ are Pochhammer symbols [1, Equation 6.1.22], keeping in mind that $\frac{1}{\Gamma(n_0-j+1)}=0$ when n_0-j+1 is a negative integer; moreover, we remark that, since $1-m_0-k=-k+l$, with $l\in\mathbb{N}_0$, we need to assume a generalised definition of ${}_2F_1$ via

$$ {}_2F_1(\alpha_1,\alpha_2;\beta;z)=\lim_{\beta\to 1-m_0-k}\Big[\lim_{\alpha_1\to -k}{}_2F_1(\alpha_1,-n_0;\beta;z)\Big]; $$

see [12, Supporting Information, Equation (43)] and [4, Equation 15.2.5], respectively.) Combining Equations (C.10), (C.11), and (C.13) with the expression for P_n given in Equation (B.8) and noting that, by the definition of P_n, the latter equals $n!\frac{\partial^n}{\partial z^n}\big[\frac{1-b(z-1)\mathrm{e}^{-\tau}}{1-b(z-1)}\big]^a\big|_{z=0}$, we find (B.5), as claimed.

Finally, we emphasise that the validity of Equation (B.5) is restricted to $m_0\geq 2$, as the identity in (C.13) no longer holds as stated when $m_0=0$ or $m_0=1$. However, a slight adaptation of the above argument yields the corresponding Equations (B.6) and (B.7) in these cases, where we again follow the convention that the function $\frac{1}{\Gamma}$ vanishes whenever its argument is a negative integer. □

Proof of Proposition B.3. The proof is based on an adaptation of an argument that can be found in [12, Supporting Information]; see their Equations (45) through (47). However, while they derive propagators for $m_0=0$ only, we extend their result to arbitrary (positive) values of both m_0 and n_0.

Recalling that $\sum_{n=0}^{\infty}P_n(\tau,0)z^n=\big[\frac{1-b(z-1)\mathrm{e}^{-\tau}}{1-b(z-1)}\big]^a$ and following [12], we have

$$ F(z,\tau)=\frac{[1+(z-1)\mathrm{e}^{-\tau}]^{n_0}}{[1-b(z-1)\mathrm{e}^{-\tau}]^{m_0}}\sum_{n=0}^{\infty}P_n(\tau,0)z^n=\sum_{n=0}^{\infty}P_{0n|m_0n_0}(\tau,0)z^n; \tag{C.14} $$

see also Section 2.3 and, in particular, Equation (2). By the Binomial Theorem, we can write $[1+(z-1)\mathrm{e}^{-\tau}]^{n_0}=\sum_{r=0}^{n_0}\binom{n_0}{r}(1-\mathrm{e}^{-\tau})^{n_0-r}(z\mathrm{e}^{-\tau})^r$; moreover, since $|z|\leq 1$ and, hence, $\big|\frac{b}{\mathrm{e}^{\tau}+b}z\big|<1$, we may apply a version of Newton's generalised Binomial Theorem [9] to expand

$$ \begin{aligned} \frac{1}{[1-b(z-1)\mathrm{e}^{-\tau}]^{m_0}}&=\frac{1}{(1+b\mathrm{e}^{-\tau})^{m_0}}\frac{1}{(1-\frac{b}{\mathrm{e}^{\tau}+b}z)^{m_0}}=\frac{1}{(1+b\mathrm{e}^{-\tau})^{m_0}}\sum_{s=0}^{\infty}\binom{m_0+s-1}{m_0-1}\Big(\frac{b}{\mathrm{e}^{\tau}+b}\Big)^s z^s\\ &=\frac{1}{(1+b\mathrm{e}^{-\tau})^{m_0}}\sum_{s=0}^{\infty}\binom{m_0+s-1}{m_0-1}\Big(\frac{b}{1+b\mathrm{e}^{-\tau}}\Big)^s(z\mathrm{e}^{-\tau})^s. \end{aligned} $$

Substituting into (C.14), changing summation indices, and noting that $P_n(\tau)\equiv 0$ if $n<0$, we obtain (B.9), which completes the proof. (In particular, the validity of our argument for $m_0=0$ follows from a generalised definition of the binomial coefficient that can be found in [9].) □

Proof of Proposition B.4. We rewrite Equation (C.9) as

$$ F(z,\tau)=\frac{[1+(z-1)\mathrm{e}^{-\tau}]^{n_0}}{[1-b(z-1)]^{m_0}}\Big[\frac{1-b(z-1)\mathrm{e}^{-\tau}}{1-b(z-1)}\Big]^{a-m_0}=\frac{[1+(z-1)\mathrm{e}^{-\tau}]^{n_0}}{[1-b(z-1)]^{m_0}}\sum_{n=0}^{\infty}\widetilde{P}_n(\tau,0)z^n; $$

cf. (C.14). (In other words, the generating function F, as well as the resulting distribution P_n, are now interpreted as being dependent on $\tilde{a}$, instead of on a.) Applying the generalised Binomial Theorem to expand $[1-b(z-1)]^{-m_0}=(1+b)^{-m_0}\big(1-\frac{b}{1+b}z\big)^{-m_0}$ in the above expression, as in the proof of Proposition B.3, we obtain Equation (B.10), as stated. □

D. Table of probability distributions

Finally, in this section, we list the first-order asymptotic formulae for the marginal probability distribution of protein whose validity is investigated in detail in Section 5 of the main text. (For the reader's convenience, the list is given in tabular form below.)

Fast asymptotics (Equation (36)):
$$P_n(t,\varepsilon) \sim \begin{cases} 1-\varepsilon\frac{ab}{1+b}\Big\{t-\frac{1}{1+b}\big[1-\mathrm{e}^{-(1+b)t}\big]\Big\} & \text{for } n=0, \\ \frac{\varepsilon}{(n+1)!}ab^n t^{n+1}\Big\{(t+1)\,{}_1F_1\big(n+1;n+2;-(1+b)t\big) & \\ \quad -\frac{n+1}{1+b}\big[{}_1F_1\big(n+1;n+2;-(1+b)t\big)-\mathrm{e}^{-(1+b)t}\big]\Big\} & \text{for } n\in\mathbb{N} \end{cases}$$
Slow asymptotics (Equation (40)):
$$P_n(\tau,\varepsilon) \sim \frac{\Gamma(a+n)}{\Gamma(n+1)\Gamma(a)}\Big(\frac{b}{1+b}\Big)^n\Big(\frac{1+b\mathrm{e}^{-\tau}}{1+b}\Big)^a\Bigg({}_2F_1\big(-n,-a;1-a-n;\tfrac{1+b}{\mathrm{e}^{\tau}+b}\big)+\frac{\varepsilon}{2}\frac{a}{(1+b)^2} \times\sum_{k=0}^{n}\frac{\Gamma(n+1)}{\Gamma(n-k+1)}\frac{\Gamma(a+n-k)}{\Gamma(a+n)}\Bigg\{2(1+b)-(k+1)\Bigg[1+\Big(\frac{1+b}{\mathrm{e}^{\tau}+b}\Big)^{k+2}\mathrm{e}^{2\tau}\Bigg]\Bigg\} \times{}_2F_1\big(-n+k,-a;1-a-n+k;\tfrac{1+b}{\mathrm{e}^{\tau}+b}\big)\Bigg)$$
Stationary limit (Equation (43)):
$$P_n^{\infty}(\varepsilon) \sim \frac{\Gamma(a+n)}{\Gamma(n+1)\Gamma(a)}\Big(\frac{b}{1+b}\Big)^n\Big(1-\frac{b}{1+b}\Big)^a\Bigg[1-\varepsilon\frac{(a+1)ab^2-2(a+1)bn+n(n-1)}{2(a+1)(1+b)^2}\Bigg]$$
Uniform asymptotics (Equation (44)):
$$P_n(\tau,t,\varepsilon) \sim P_n(\tau,\varepsilon)+\varepsilon a\frac{b^n}{(1+b)^{n+2}}\big[n-b-(1+b)t\big]+\frac{\varepsilon}{(n+1)!}ab^n t^{n+1} \times\Bigg\{{}_1F_1\big(n+1;n+2;-(1+b)t\big)t-\frac{1}{1+b} \times\big[(n-b)\,{}_1F_1\big(n+1;n+2;-(1+b)t\big)-(n+1)\mathrm{e}^{-(1+b)t}\big]\Bigg\}$$

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