

Supplementary Material

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1. INTRODUCTION

A. Growth Laws

B. Scalable Reaction Networks

The biomass of a

In our model, the reaction network can be formulated as the following system of (nonlinear) ODEs of the absolute biomass X_i :

$$\begin{aligned}\frac{dX_1}{dt} &= bX_3 - \frac{a_1 X_1 X_4}{k_1 N + X_1}, \\ \frac{dX_2}{dt} &= \frac{a_1 X_1 X_4}{k_1 N + X_1} - \frac{a_1 X_2 X_5}{k_2 + X_2}, \\ \frac{dX_3}{dt} &= \theta_1 \frac{a_1 X_2 X_5}{k_2 N + X_2}, \\ \frac{dX_4}{dt} &= \theta_2 \frac{a_1 X_2 X_5}{k_2 N + X_2}, \\ \frac{dX_5}{dt} &= \theta_3 \frac{a_1 X_2 X_5}{k_2 N + X_2},\end{aligned}\tag{S1}$$

where $N = X_1 + X_2 + X_3 + X_4 + X_5$ is the total biomass. In the $X \rightarrow \infty$ limit, $X_i \sim e^{\lambda t}$ should exhibit exponential growth, where λ is the growth rate. A cell is made up of small molecules (metabolites, amino acids, and peptides) and large molecules (proteins). The total biomass N is the sum of the absolute biomass of all components in the cell. The **biomass fraction** of the i -th component is defined as $Y_i = X_i/N$, so that $\sum_i Y_i = 1$.

Assuming the system has an exponential growth in the long time limit, we have $N(t) \sim e^{\lambda t}$, where λ is the growth rate. Therefore the **growth rate** is appropriately defined as

$$\lambda = \frac{d \log N}{dt} = \frac{1}{N} \frac{dN}{dt}.\tag{S2}$$

In the limit $t \rightarrow \infty$, we should expect the protein fractions Y_i to approach a steady state, i.e. a fix point of the ODE system. We do a change of variables from biomass space with coordinate (X_i, N) to the biomass fraction space with coordinate Y_i , a simplex space. Then

$$\frac{dY_i}{dt} = \frac{1}{N} \frac{dX_i}{dt} - \frac{X_i}{N^2} \frac{dN}{dt} = \frac{1}{N} \frac{dX_i}{dt} - \lambda Y_i.\tag{S3}$$

If the biomass ODE system is given by $\frac{d\mathbf{X}}{dt} = \mathbf{F}(X)$, then the biomass fraction ODE system is conveniently expressed as

$$\frac{d\mathbf{Y}}{dt} = \frac{1}{N} \mathbf{F}(N\mathbf{Y}) - \lambda \mathbf{Y}.\tag{S4}$$

A Scalable Reaction Network (SRN) is defined as a reaction network such that $\mathbf{F}(N\mathbf{Y}) = N\mathbf{G}(\mathbf{Y})$, i.e. the reaction fluxes scale linearly with the total biomass N . Most biological reaction networks are expected to be SRNs, since it has been observed that

C. ODE

The system of ODEs describing for our cell model is

$$\frac{dY_1}{dt} = bY_3 - \frac{a_1 Y_1 Y_4}{k_1 + Y_1} - bY_3 Y_1,\tag{S5a}$$

$$\frac{dY_2}{dt} = \frac{a_1 Y_1 Y_4}{k_1 + Y_1} - \frac{a_1 Y_2 Y_5}{k_2 + Y_2} - bY_3 Y_2,\tag{S5b}$$

$$\frac{dY_k}{dt} = \theta_k \frac{a_1 Y_2 Y_5}{k_2 + Y_2} \quad (k = 1, 2, 3).\tag{S5c}$$

Here Y_j is the biomass fraction of the j -th node in the system, while Y_3, Y_4, Y_5 are protein sectors that make up the (three-sector) proteome partition.

2. THEORY

A. Solution of the Three-Sector Partition Model

As time tends to infinity, the biomass fractions for this system tend to a steady limit, i.e. no oscillation is observed. So we have the steady-state approximation $dY/dt \rightarrow 0$ when $t > T$, and $Y(t) \approx Y^*$ is the steady-state, which for simplicity we denote by Y . Then equations (S5) become

$$bY_3 - \frac{a_1 Y_1 Y_4}{k_1 + Y_1} - bY_3 Y_1 = 0, \quad (\text{S6a})$$

$$\frac{a_1 Y_1 Y_4}{k_1 + Y_1} - \frac{a_2 Y_2 Y_5}{k_2 + Y_2^*} - bY_3 Y_2 = 0, \quad (\text{S6b})$$

$$\theta_1 \left(\frac{a_2 Y_2 Y_5}{k_1 + Y_2} \right) - b(Y_3)^2 = 0, \quad (\text{S6c})$$

$$\theta_2 \left(\frac{a_2 Y_2 Y_5}{k_1 + Y_2} \right) - bY_3 Y_4 = 0, \quad (\text{S6d})$$

$$\theta_3 \left(\frac{a_2 Y_2 Y_5}{k_1 + Y_2} \right) - bY_3 Y_5 = 0. \quad (\text{S6e})$$

(S6f)

Since $Y_3, Y_4, Y_5 \neq 0$, the equations (S6c), (S6d), and (S6e) show that

$$Y_3 : Y_4 : Y_5 = \theta_1 : \theta_2 : \theta_3.$$

Work with Y_3 , so $Y_4 = (\theta_2/\theta_1)Y_3$ and $Y_5 = (\theta_3/\theta_1)Y_3$. Then the first two equations become

$$(Y_1)^2 + \left(\frac{a_1 \theta_2}{b \theta_1} + k_1 - 1 \right) Y_1 - k_1 = 0, \quad (\text{S7a})$$

$$(Y_2)^2 + \left(\frac{a_1 \theta_2}{b \theta_1} + k_1 - (1 - Y_1) \right) Y_2 - (1 - Y_1)k_2 = 0. \quad (\text{S7b})$$

(S7c)

Equation (S6e) gives

$$Y_3 = \left(\frac{a_2 \theta_3}{b} \right) \left(\frac{Y_2}{k_2 + Y_2} \right). \quad (\text{S8})$$

That is, given $(\theta_1, \theta_2, \theta_3)$, we have an analytic solution of the steady state $Y = Y[\theta_1, \theta_2, \theta_3]$, given by equation (S9):

$$1 - Y_1 = \frac{1}{2} \left[-\sqrt{\left(\frac{a_1 \theta_2}{b \theta_1} + k_1 - 1 \right)^2 + 4k_1} + \left(\frac{a_1 \theta_2}{b \theta_1} + k_1 + 1 \right) \right].$$

$$Y_1 = \frac{1}{2} \left[\sqrt{\left(\frac{a_1\theta_2}{b\theta_1} + k_1 - 1 \right)^2 + 4k_1} - \left(\frac{a_1\theta_2}{b\theta_1} + k_1 - 1 \right) \right], \quad (\text{S9a})$$

$$\begin{aligned} Y_2 &= \frac{1}{2} \left[\sqrt{\left(\frac{a_2\theta_3}{b\theta_1} + k_2 - (1 - Y_1) \right)^2 + 4(1 - Y_1)k_2} - \left(\frac{a_2\theta_3}{b\theta_1} + k_2 - (1 - Y_1) \right) \right] \\ &= \frac{1}{2} \sqrt{4k_1 \left\{ \frac{1}{2} \left[-\sqrt{\left(\frac{a_1\theta_2}{b\theta_1} + k_1 - 1 \right)^2 + 4k_1} + \left(\frac{a_1\theta_2}{b\theta_1} + k_1 + 1 \right) \right] \right\}^2 + } \\ &\quad - \frac{1}{2} \left\{ \frac{a_2\theta_3}{b\theta_1} + k_2 - \frac{1}{2} \left[-\sqrt{\left(\frac{a_1\theta_2}{b\theta_1} + k_1 - 1 \right)^2 + 4k_1} + \left(\frac{a_1\theta_2}{b\theta_1} + k_1 + 1 \right) \right] \right\}, \end{aligned} \quad (\text{S9b})$$

$$Y_3 = \left(\frac{a_2\theta_3}{b} \right) \left(\frac{Y_2}{k_2 + Y_2} \right), \quad (\text{S9c})$$

$$Y_4 = \left(\frac{a_2\theta_2\theta_3}{b\theta_1} \right) \left(\frac{Y_2}{k_2 + Y_2} \right), \quad (\text{S9d})$$

$$Y_5 = \left(\frac{a_2\theta_3^2}{b\theta_1} \right) \left(\frac{Y_2}{k_2 + Y_2} \right). \quad (\text{S9e})$$

This is an expression of $Y = Y(\theta_1, \theta_2, \theta_3)$, where θ is undetermined. The main result expresses θ in terms of system parameters a_1, a_2, b, k_1, k_2 , and hence Y in terms of a_1, a_2, b, k_1, k_2 . In the above solution, the minus sign solution of the quadratic equations

$$Y_1^2 + \left(\frac{a_1\theta_2}{b\theta_1} + k_1 - 1 \right) Y_1 - k_1 = 0, \quad (\text{S10})$$

$$Y_2^2 + \left[\frac{a_2\theta_3}{b\theta_1} + k_2 - (1 - Y_1) \right] Y_2 - k_2 (1 - Y_1) = 0 \quad (\text{S11})$$

is discarded, since biomass fraction must be positive.

B. Derivation of the Partition Strength in the Low Nutrient Limit

The partition strength is given here up to order $O(b^2)$:

$$\theta_1 = 1 - A\sqrt{b} - \frac{1}{2}A \left(2C - 3A^2 + 4D \right) b^{3/2} + O(b^2), \quad (\text{S12})$$

$$\theta_2 = \sqrt{\frac{k_1}{a_1}} \left[\sqrt{b} - \frac{1}{2}A^2 b^{3/2} - \left(AC - A^3 + 2AD \right) b^2 \right] + O(b^{5/2}), \quad (\text{S13})$$

$$\theta_3 = \sqrt{\frac{k_2}{a_2}} \left[\sqrt{b} - \frac{1}{2}A^2 b^{3/2} - \left(AC - A^3 + 2AD \right) b^2 \right] + O(b^{5/2}), \quad (\text{S14})$$

where

$$A = \sqrt{\frac{k_1}{a_1}} + \sqrt{\frac{k_2}{a_2}}, \quad B = \frac{k_1}{a_1} + \frac{k_2}{a_2}, \quad C = \frac{a_1}{k_1} + \frac{a_2}{k_2}, \quad D = \sqrt{\frac{k_1 k_2}{a_1 a_2}}, \quad E = \frac{1}{a_1} + \frac{1}{a_2}. \quad (\text{S15})$$

are symmetric in $(k_1, a_1), (k_2, a_2)$. To derive this, consider the series expansion of Y_1, Y_2, Y_3 in the limit $b \rightarrow 0$.

$$Y_1 = \left(\frac{k_1 \theta_1}{a_1 \theta_2} \right) b + \left[\frac{k_1 \theta_1^2 (1 - k_1)}{a_1^2 \theta_2^2} \right] b^2 + O(b^3), \quad (\text{S16})$$

$$Y_2 = \left(\frac{k_2 \theta_1}{a_2 \theta_3} \right) b - \left[\frac{k_2 \theta_1^2 (k_1 a_2 \theta_3 + k_2 a_1 \theta_2 - a_1 \theta_2)}{a_1 a_2^2 \theta_2 \theta_3^2} \right] b^2 + O(b^3), \quad (\text{S17})$$

$$Y_3 = \theta_1 - b \theta_1^2 \left(\frac{k_1}{a_1 \theta_2} + \frac{k_2}{a_2 \theta_3} \right) + b^2 \theta_1^3 \left[\frac{k_1 k_2}{a_1 a_2 \theta_2 \theta_3} - \frac{k_1 (1 - k_1)}{a_1^2 \theta_2^2} - \frac{k_2 (1 - k_2)}{a_2^2 \theta_3^2} \right]. \quad (\text{S18})$$

Therefore

$$\lambda = b \theta_1 - b^2 \theta_1^2 \left(\frac{k_1}{a_1 \theta_2} + \frac{k_2}{a_2 \theta_3} \right) + b^3 \theta_1^3 \left[\frac{k_1 k_2}{a_1 a_2 \theta_2 \theta_3} - \frac{k_1 (1 - k_1)}{a_1^2 \theta_2^2} - \frac{k_2 (1 - k_2)}{a_2^2 \theta_3^2} \right]. \quad (\text{S19})$$

By the method of Lagrange multipliers, set the Lagrangian to $L(\theta) = \lambda(\theta) - \mu (\theta_1 + \theta_2 + \theta_3 - 1)$ with Lagrange multiplier μ . Then

$$\frac{\partial L}{\partial \theta_1} = b - 2b^2 \theta_1 \left(\frac{k_1}{a_1 \theta_2} + \frac{k_2}{a_2 \theta_3} \right) + 3b^3 \theta_1^2 \left[\frac{k_1 k_2}{a_1 a_2 \theta_2 \theta_3} - \frac{k_1 (1 - k_1)}{a_1^2 \theta_2^2} - \frac{k_2 (1 - k_2)}{a_2^2 \theta_3^2} \right] - \mu, \quad (\text{S20})$$

$$\frac{\partial L}{\partial \theta_2} = \left(\frac{k_1 \theta_1^2}{a_1 \theta_2^2} \right) b^2 - \theta_1^3 \left[\frac{k_1 k_2}{a_1 a_2 \theta_2 \theta_3} - \frac{2k_1 (1 - k_1)}{a_1^2 \theta_2^3} \right] b^3 - \mu, \quad (\text{S21})$$

$$\frac{\partial L}{\partial \theta_3} = \left(\frac{k_2 \theta_1^2}{a_2 \theta_3^2} \right) b^2 - \theta_1^3 \left[\frac{k_1 k_2}{a_1 a_2 \theta_2 \theta_3} - \frac{2k_2 (1 - k_2)}{a_2^2 \theta_3^3} \right] b^3 - \mu. \quad (\text{S22})$$

(S23)

Keep only terms of order up to $O(b^2)$ and solve equations (S21, S22), we get an important relationship that generalizes to the n -sector model,

$$\frac{\theta_2}{\theta_3} = \sqrt{\frac{k_1 a_2}{k_2 a_1}}. \quad (\text{S24})$$

Then equation (S20) becomes a quadratic in θ_1/θ_2 :

$$\left(\frac{b k_1}{a_1} \right) \left(\frac{\theta_1}{\theta_2} \right)^2 + 2b \sqrt{\frac{k_1}{a_1}} A \left(\frac{\theta_1}{\theta_2} \right) - 1 = 0, \quad (\text{S25})$$

where $A = \sqrt{\frac{k_1}{a_1}} + \sqrt{\frac{k_2}{a_2}}$. The solution admits an asymptotic expansion in the form of a Puiseux series:

$$r \equiv \frac{\theta_1}{\theta_2} = \sqrt{\frac{a_1}{k_1}} \left(\frac{1}{\sqrt{b}} - A + \frac{1}{2} A^2 \sqrt{b} \right) + O(b), \quad (\text{S26})$$

and

$$s \equiv \frac{\theta_1}{\theta_3} = \sqrt{\frac{a_2}{k_3}} \left(\frac{1}{\sqrt{b}} - A + \frac{1}{2} A^2 \sqrt{b} \right) + O(b). \quad (\text{S27})$$

The symmetry in the equations hints that we should solve for θ_1 first, then find $\theta_2 = \theta_1/r, \theta_3 = \theta_1/s$. We expand up to order $O(b^{3/2})$ and solve for θ_1 .

$$\theta_1 = (1 + 1/r + 1/s)^{-1}, \quad (\text{S28})$$

then

$$\theta_1 = 1 - A \sqrt{b} - \frac{1}{2} A^3 b^{3/2} + O(b^2), \quad (\text{S29a})$$

$$\theta_2 = \sqrt{\frac{k_1}{a_1}} \left(\sqrt{b} - \frac{1}{2} A^2 b^{3/2} \right) + O(b^2), \quad (\text{S29b})$$

$$\theta_3 = \sqrt{\frac{k_2}{a_2}} \left(\sqrt{b} - \frac{1}{2} A^2 b^{3/2} \right) + O(b^2). \quad (\text{S29c})$$

C. Derivation of Protein Fraction and Growth Rate During Starvation

C.1. Trajectories and Growth Rate

The growth rate λ is given as a perturbative series in \sqrt{b} :

$$\lambda = b - 2Ab^{3/2} + \left[2A^2 + B + D - E \right] b^2, \quad (\text{S30})$$

which is easily derived by plugging in equations for θ . This formula makes intuitively sense, since it is invariant under exchange of indices (i.e. $(a_1, k_1) \rightarrow (a_2, k_2)$), as will be observed for many quantities below.

Substitute in expressions for θ to get

$$Y_1 = \sqrt{\frac{k_1}{a_1}} \sqrt{b} + \left(\frac{1}{a_1} (1 - k_1) - A \sqrt{\frac{k_1}{a_1}} \right) b + \sqrt{\frac{k_1}{a_1}} A^2 b^{3/2} + O(b^2), \quad (\text{S31})$$

$$Y_2 = \sqrt{\frac{k_2}{a_2}} \sqrt{b} + \left(\sqrt{\frac{k_2}{a_2}} A + D - \frac{(1 - k_2)}{a_2} \right) b + \left[\frac{1}{2} \sqrt{\frac{k_2}{a_2}} A^2 + 2AD - 2A \frac{(1 - k_2)}{a_2} \right] b^{3/2} + O(b^2), \quad (\text{S32})$$

$$Y_3 = 1 - 2A\sqrt{b} + \left[2A^2 + B + D - E \right] b + O(b^{3/2}), \quad (\text{S33})$$

$$Y_4 = \sqrt{\frac{k_1}{a_1}} \left[\sqrt{b} - Ab + \left(\frac{1}{2} A^2 + B + D - E \right) b^{3/2} \right] + O(b^2), \quad (\text{S34})$$

$$Y_5 = \sqrt{\frac{k_2}{a_2}} \left[\sqrt{b} - Ab + \left(\frac{1}{2} A^2 + B + D - E \right) b^{3/2} \right] + O(b^2). \quad (\text{S35})$$

We also have the fraction of small molecules (intermediate metabolites, amino acids, and peptides) and of large molecules (transport/metabolic/ribosomal and translational proteins), denoted Small and Large respectively.

$$\text{Small} = A\sqrt{b} - \left(A^2 + B + D - E \right) b + O(b^{3/2}), \quad (\text{S36})$$

$$\text{Large} = 1 - \text{Small} = 1 - A\sqrt{b} + \left(A^2 + B + D - E \right) b + O(b^{3/2}). \quad (\text{S37})$$

These are also invariant under the exchange of indices, so the rate of nutrient processing does not affect the overall fraction of products.

C.2. Growth Rate and Ribosomal Protein Fraction

Equations (S30) and (S35) express λ and Y_5 in terms of nutrient level b . Recall the theory of **series reversion**: Suppose $y = f(x) = a_1x + a_2x^2 + a_3x^3 + a_4x^4 + a_5x^5 + \dots$. Then the inverse series $x = f^{-1}(y)$ up to the 5th order is:

$$\begin{aligned} x &= \frac{1}{a_1}y - \frac{a_2}{a_1^2}y^2 + \frac{2a_2^2 - a_1a_3}{a_1^5}y^3 \\ &\quad + \frac{5a_1a_2a_3 - 5a_2^3 - a_1^2a_4}{a_1^7}y^4 \\ &\quad + \frac{-6a_2^4 + 9a_1a_2^2a_3 - 3a_1^2a_3^2 - 4a_1^2a_2a_4 + a_1^3a_5}{a_1^9}y^5 + \dots \end{aligned}$$

We have

$$\sqrt{b} = \sqrt{\frac{a_2}{k_2}} R + A \left(\sqrt{\frac{a_2}{k_2}} R \right)^2 + \left(\frac{3A^2 - 2B - 2D + 2E}{2} \right) \left(\sqrt{\frac{a_2}{k_2}} R \right)^3 + O(R^4). \quad (\text{S38})$$

Then the growth rate can be written in terms of ribosomal protein fraction R if we plug in \sqrt{b} :

$$\lambda = \frac{a_2}{k_2} R^2 - \left(\frac{a_2}{k_2} \right)^2 (B + D - E) R^4 + \left(\frac{a_2}{k_2} \right)^{5/2} 8A(B + D - E) R^5 + O(R^6). \quad (\text{S39})$$

D. Discussion of the General System

D.1. Solution

The n -sector partition model has $2n - 1$ nodes and fluxes, and obeys the following system of $2n - 1$ ODEs:

$$\frac{dY_1}{dt} = bY_n - \frac{a_1 Y_1 Y_{n+1}}{k_1 + Y_1} - bY_n Y_1, \quad (\text{S40a})$$

$$\frac{dY_2}{dt} = \frac{a_1 Y_1 Y_{n+1}}{k_1 + Y_1} - \frac{a_1 Y_2 Y_{n+2}}{k_2 + Y_2} - bY_n Y_2, \quad (\text{S40b})$$

⋮

$$\frac{dY_{n-1}}{dt} = \frac{a_{n-2} Y_{n-2} Y_{2n-2}}{k_{n-2} + Y_{n-2}} - \frac{a_{n-1} Y_{n-1} Y_{2n-1}}{k_{n-1} + Y_{n-1}} - bY_n Y_{n-1}, \quad (\text{S40c})$$

$$\frac{dY_n}{dt} = \theta_1 \left(\frac{a_{n-1} Y_{n-1} Y_{2n-1}}{k_{n-1} + Y_{n-1}} \right) - bY_n^2 = 0, \quad (\text{S40d})$$

⋮

$$\frac{dY_{2n-1}}{dt} = \theta_n \left(\frac{a_{n-1} Y_{n-1} Y_{2n-1}}{k_{n-1} + Y_{n-1}} \right) - bY_n Y_{2n-1} = 0. \quad (\text{S40e})$$

Following the same algebraic method as before, the solution is given by equations (S41a), (S41b), and (S41c).

$$Y_1 = \frac{1}{2} \left[\sqrt{\left(\frac{a_1 \theta_2}{b \theta_1} + k_1 - 1 \right)^2 + 4k_1} - \left(\frac{a_1 \theta_2}{b \theta_1} + k_1 - 1 \right) \right], \quad (\text{S41a})$$

$$Y_j = \frac{1}{2} \left[\sqrt{\left(\frac{a_j \theta_{j+1}}{b \theta_1} + k_1 - \left(1 - \sum_{r=1}^{j-1} Y_r \right) \right)^2 + 4k_j} - \left(\frac{a_j \theta_{j+1}}{b \theta_1} + k_j - \left(1 - \sum_{r=1}^{j-1} Y_r \right) \right) \right] \quad (2 \leq j \leq n-1), \quad (\text{S41b})$$

$$Y_j = \theta_{j-n+1} \left(\frac{a_{n-1} \theta_n}{b \theta_1} \right) \frac{Y_{n-1}}{k_{n-1} + Y_{n-1}} \quad (n \leq j \leq 2n-1). \quad (\text{S41c})$$

$$(\text{S41d})$$

Looking at the solution, it is true that

$$\sqrt{\left(\frac{a_j \theta_{j+1}}{b \theta_1} + k_1 - \left(1 - \sum_{r=1}^{j-1} Y_r \right) \right)^2 + 4k_j} \geq \left| \frac{a_j \theta_{j+1}}{b \theta_1} + k_1 - \left(1 - \sum_{r=1}^{j-1} Y_r \right) \right|, \quad (\text{S42})$$

so the solution with $-$ sign is always negative and hence not physical. By the same reasoning, all Y_j for $1 \leq j \leq n-1$ are positive, hence all Y_j for $1 \leq j \leq 2n-1$ are positive. This makes sure there is a unique global steady state, and such a state always exists.

D.2. Example Calculation for $n = 4$

The solution to the general case has been discussed above, so here we elaborate on details of the generalization with the case $n = 4$. For sake of brevity, higher partitions will be omitted, but the techniques and notation introduced in this example can easily generalize by means of mathematical induction.

Using the general solution for n -sector partition equations (S41), the solution for four-sector partition is

$$Y_1 = \frac{1}{2} \left[\sqrt{\left(\frac{a_1\theta_2}{b\theta_1} + k_1 - 1 \right)^2 + 4k_1} - \left(\frac{a_1\theta_2}{b\theta_1} + k_1 - 1 \right) \right], \quad (\text{S43a})$$

$$Y_2 = \frac{1}{2} \left\{ \sqrt{\left[\frac{a_2\theta_3}{b\theta_1} + k_2 - (1 - Y_1) \right]^2 + 4k_2(1 - Y_1)} - \left[\frac{a_2\theta_3}{b\theta_1} + k_2 - (1 - Y_1) \right] \right\}, \quad (\text{S43b})$$

$$Y_3 = \frac{1}{2} \left\{ \sqrt{\left[\frac{a_3\theta_4}{b\theta_1} + k_3 - (1 - Y_1 - Y_2) \right]^2 + 4k_3(1 - Y_1 - Y_2)} - \left[\frac{a_3\theta_4}{b\theta_1} + k_3 - (1 - Y_1 - Y_2) \right] \right\}, \quad (\text{S43c})$$

$$Y_4 = \left(\frac{a_3\theta_4}{b} \right) \frac{Y_3}{k_3 + Y_3}, \quad (\text{S43d})$$

$$Y_5 = \frac{\theta_2}{\theta_1} Y_4, \quad Y_6 = \frac{\theta_3}{\theta_1} Y_4, \quad Y_7 = \frac{\theta_4}{\theta_1} Y_4. \quad (\text{S43e})$$

Expand in the limit of small b , then the transport and metabolic molecules have fractions

$$Y_1 = \frac{bk_1\theta_1}{a_1\theta_2} \left[1 + (1 - k_1) \frac{b\theta_1}{a_1\theta_2} \right] + O(b^3), \quad (\text{S44a})$$

$$Y_2 = \frac{bk_2\theta_1}{a_2\theta_3} \left[1 + b\theta_1 \left(\frac{1 - k_2}{a_2\theta_3} - \frac{k_1}{a_1\theta_2} \right) \right] + O(b^3), \quad (\text{S44b})$$

$$Y_3 = \theta_1 \left[1 - b\theta_1 \left(\frac{k_1}{a_1\theta_2} + \frac{k_2}{a_2\theta_3} + \frac{k_3}{a_3\theta_4} \right) \right] + O(b^2). \quad (\text{S44c})$$

The form of the growth rate

$$\lambda = b\theta_1 \left[1 - b\theta_1 \left(\frac{k_1}{a_1\theta_2} + \frac{k_2}{a_2\theta_3} + \frac{k_3}{a_3\theta_4} \right) \right] + O(b^3) \quad (\text{S45})$$

is similar to that of the three-sector case. Let $A_4 = \sqrt{\frac{k_1}{a_1}} + \sqrt{\frac{k_2}{a_2}} + \sqrt{\frac{k_3}{a_3}}$. Carrying out the same computations of Lagrange multipliers, we find

$$\theta_2 : \theta_3 : \theta_4 = \sqrt{\frac{k_1}{a_1}} : \sqrt{\frac{k_2}{a_2}} : \sqrt{\frac{k_3}{a_3}}, \quad (\text{S46})$$

and

$$\frac{\theta_1}{\theta_2} = \sqrt{\frac{a_1}{k_1}} \left(\frac{1}{\sqrt{b}} - A_4 + \frac{1}{2} A_4^2 \sqrt{b} \right) + O(b), \quad (\text{S47a})$$

$$\frac{\theta_1}{\theta_3} = \sqrt{\frac{a_2}{k_2}} \left(\frac{1}{\sqrt{b}} - A_4 + \frac{1}{2} A_4^2 \sqrt{b} \right) + O(b), \quad (\text{S47b})$$

$$\frac{\theta_1}{\theta_3} = \sqrt{\frac{a_3}{k_3}} \left(\frac{1}{\sqrt{b}} - A_4 + \frac{1}{2} A_4^2 \sqrt{b} \right) + O(b). \quad (\text{S47c})$$

Solve for θ_1 by normalization, then solve for $\theta_{j=2,3,4}$. Generalize the index-invariant variables

Then

$$\theta_1 = \left(1 + \frac{\theta_2}{\theta_1} + \frac{\theta_3}{\theta_1} + \frac{\theta_4}{\theta_1} \right)^{-1} = 1 - A_4 \sqrt{b} - \frac{1}{2} A_4 \left(2C_4 - 3A_4^2 + 4D_4 \right) b^{3/2} + O(b^2), \quad (\text{S48a})$$

$$\theta_2 = \sqrt{\frac{k_1}{a_1}} \left[\sqrt{b} - \frac{1}{2} A_4^2 b^{3/2} - \left(A_4 C_4 - A_4^3 + 2A_4 D_4 \right) b^2 \right] + O(b^{5/2}), \quad (\text{S48b})$$

$$\theta_3 = \sqrt{\frac{k_2}{a_2}} \left[\sqrt{b} - \frac{1}{2} A_4^2 b^{3/2} - \left(A_4 C_4 - A_4^3 + 2A_4 D_4 \right) b^2 \right] + O(b^{5/2}), \quad (\text{S48c})$$

$$\theta_4 = \sqrt{\frac{k_3}{a_3}} \left[\sqrt{b} - \frac{1}{2} A_4^2 b^{3/2} - \left(A_4 C_4 - A_4^3 + 2A_4 D_4 \right) b^2 \right] + O(b^{5/2}). \quad (\text{S48d})$$

With the new expressions for θ , substitution followed by expansion up to leading orders gives similar formulae as in the three-sector case for other physical quantities, but with the variables A, B, C, D, E replaced by their respective generalizations A_4, B_4, C_4, D_4, E_4 and the addition of a fourth component θ_4 .

In particular, we have

$$\lambda = b - 2A_4b^{3/2} + \left(2A_4^2 + B_4 + D_4 - E_4\right)b^2 + O(b^{5/2}), \quad (\text{S49})$$

which is invariant under permutation of indices $1 \leftrightarrow 2 \leftrightarrow 3$.

E. Derivation of Protein Fraction and Growth Rate in High Nutrient Environment

E.1. Trajectories and Growth Rate

Large supply or demand limits yield corner solutions. In optimal resource allocation (e.g. flux-balance analysis), an unconstrained input leads to one pathway dominating flux. in a high- b regime the metabolic sector Y_4 can hardly operate, while the ribosomal/translational sector dominates. Biologically, this implies nearly all proteome is allocated for ribosomes and translational molecules, shutting down metabolic enzyme production.

The partition strength is given here up to order $O(b^{-3})$:

$$\theta_1 = \frac{1}{(2\alpha + \beta\alpha^2)b} + \frac{1}{(2\alpha + \beta\alpha^2)^2b^2} + O(b^{-3}), \quad (\text{S50a})$$

$$\theta_2 = \frac{\alpha}{2\alpha + \beta\alpha^2} - \frac{\alpha}{(2\alpha + \beta\alpha^2)^2b} + \frac{\alpha}{(2\alpha + \beta\alpha^2)^3b^2} + O(b^{-3}), \quad (\text{S50b})$$

$$\theta_3 = \frac{\alpha + \beta\alpha^2}{2\alpha + \beta\alpha^2} - \frac{\alpha + \beta\alpha^2}{(2\alpha + \beta\alpha^2)^2b} + \frac{\alpha + \beta\alpha^2}{(2\alpha + \beta\alpha^2)^3b^2} + O(b^{-3}), \quad (\text{S50c})$$

$$\alpha = \frac{k_2^2(1+k_1)^4a_2}{(1+k_1+k_1k_2)^2a_1^2 - k_2(1+k_1)^2a_1a_2 + (1+k_1)^4(1+k_2)a_2^2}, \quad (\text{S50d})$$

$$\beta = \frac{(1+k_1+k_1k_2)a_1 + (1+k_1)^2a_2}{(1+k_1)^2k_2}. \quad (\text{S50e})$$

Note that $\theta_1 + \theta_2 + \theta_3 = 1$ up to order $O(b^{-2})$. To derive this, consider the asymptotic expansion of Y_1, Y_2, Y_3 in the limit $b \rightarrow \infty$.

$$Y_1 = 1 - \frac{1}{1+k_1} \left(\frac{a_1\theta_2}{b\theta_1} \right) + \frac{k_1}{(1+k_1)^3} \left(\frac{a_1\theta_2}{b\theta_1} \right)^2, \quad (\text{S51a})$$

$$Y_2 = \frac{1}{1+k_1} \left(\frac{a_1\theta_2}{b\theta_1} \right) - \frac{1}{(1+k_1)^3} \left[k_1 + \frac{(1+k_1)^2a_2\theta_3}{k_2a_1\theta_2} \right] \left(\frac{a_1\theta_2}{b\theta_1} \right)^2, \quad (\text{S51b})$$

$$Y_3 = \frac{a_1a_2}{(1+k_1)k_2b^2} \left(\frac{\theta_2\theta_3}{\theta_1} \right) - \frac{a_1a_2}{(1+k_1)^3k_2^2} \left(\frac{\theta_2\theta_3}{\theta_1^2} \right) \left[(1+k_1)^2a_2\theta_3 + (1+k_1+k_1k_2)a_1\theta_2 \right] \frac{1}{b^3}. \quad (\text{S51c})$$

The growth rate is

$$\lambda = \frac{a_1a_2}{(1+k_1)k_2b} \left(\frac{\theta_2\theta_3}{\theta_1} \right) - \frac{a_1a_2}{(1+k_1)^3k_2^2b^2} \left(\frac{\theta_2\theta_3}{\theta_1^2} \right) \left[(1+k_1)^2a_2\theta_3 + (1+k_1+k_1k_2)a_1\theta_2 \right]. \quad (\text{S52})$$

Again by the method of Lagrange multipliers, set the Lagrangian to $L(\theta) = \lambda(\theta) - \mu(\theta_1 + \theta_2 + \theta_3 - 1)$ with Lagrange multiplier μ . Then

$$\frac{\partial L}{\partial \theta_1} = -\frac{a_1a_2\theta_2\theta_3}{(1+k_1)k_2\theta_1^2b} + \frac{2a_1a_2\theta_2\theta_3[(1+k_1+k_1k_2)a_1\theta_2 + (1+k_1)^2a_2\theta_3]}{(1+k_1)^3k_2^2\theta_1^3b^2} - \mu, \quad (\text{S53a})$$

$$\frac{\partial L}{\partial \theta_2} = \frac{a_1a_2\theta_3}{(1+k_1)k_2\theta_1b} - \frac{a_1a_2\theta_3[2(1+k_1+k_1k_2)a_1\theta_2 + (1+k_1)^2a_2\theta_3]}{(1+k_1)^3k_2^2\theta_1^2b^2} - \mu, \quad (\text{S53b})$$

$$\frac{\partial L}{\partial \theta_3} = \frac{a_1a_2\theta_3}{(1+k_1)k_2\theta_1b} - \frac{a_1a_2\theta_2[(1+k_1+k_1k_2)a_1\theta_2 + 2(1+k_1)^2a_2\theta_3]}{(1+k_1)^3k_2^2\theta_1^2b^2} - \mu. \quad (\text{S53c})$$

Let $p = \theta_3/\theta_1$, $q = \theta_2/\theta_1$, $P \equiv r/b$, $Q = q/b$. From equations (S53b) and (S53c), up to order $O(b^{-2})$ we have

$$\frac{a_1 a_2^2}{(1+k_1)k_2^2} P^2 + \left[\frac{a_1 a_2}{(1+k_1)k_2} - \frac{2a_1 a_2 ((1+k_1+k_1 k_2)a_1 + (1+k_1)^2 a_2)}{(1+k_1)^3 k_2^2} Q \right] P \quad (\text{S54})$$

$$+ \left[\frac{a_1^2 a_2 (1+k_1+k_1 k_2)}{(1+k_1)^3 k_2^2} Q^2 - \frac{a_1 a_2}{(1+k_1)k_2} Q \right] = 0. \quad (\text{S55})$$

Solve for P and keep terms up to $O(b^{-2})$, i.e. Q^2 .

$$\begin{aligned} P &= Q + \frac{(1+k_1+k_1 k_2)a_1 + (1+k_1)^2 a_2}{(1+k_1)^2 k_2} Q^2 + O(Q^3) \\ &\equiv Q + \beta Q^2 + O(Q^3). \end{aligned} \quad (\text{S56})$$

Notice that when Q is small, this reduces to the previous (unphysical) result. However, the coefficient of Q^2 is approximately ~ 40000 for $a_1 = 23.8$, $k_1 = 0.1$, $a_2 = 1.42$, $k_2 = 0.003$, while $Q \sim 0.01/b$, so the expression is reasonable. Plug equation (S56) into equation (S53a) and use equation (S53b), we have

$$\left[\frac{a_1 a_2}{(1+k_1)k_2} - \frac{2a_1^2 a_2 (1+k_1+k_1 k_2)}{(1+k_1+k_1 k_2)^3 k_2^2} - \frac{a_1 a_2^2}{(1+k_1)k_2} \right] \left[Q + \frac{(1+k_1+k_1 k_2)a_1 + (1+k_1)^2 a_2}{(1+k_1)^2 k_2} Q^2 \right] \quad (\text{S57})$$

$$= \frac{a_1 a_2}{(1+k_1)k_2} Q - \frac{a_1^2 a_2 (1+k_1+k_1 k_2)}{(1+k_1)^3 k_2} Q^2 - \frac{2a_1 a_2^2}{(1+k_1)k_2} Q \left[Q + \frac{(1+k_1+k_1 k_2)a_1 + (1+k_1)^2 a_2}{(1+k_1)^2 k_2} Q^2 \right]. \quad (\text{S58})$$

Leading factor $O(Q)$ cancels out, and dividing by Q gives

$$Q = \frac{k_2^2 (1+k_1)^4 a_2}{(1+k_1+k_1 k_2)^2 a_1^2 - k_2 (1+k_1)^2 a_1 a_2 + (1+k_1)^4 (1+k_2) a_2^2} \equiv \alpha. \quad (\text{S59})$$

By equation (S56),

$$P = \alpha + \beta \alpha^2 = O(1), \quad (\text{S60})$$

so both θ_2/θ_1 and θ_3/θ_1 are $O(b)$. To determine the specific dependencies, solve for θ_1 with

$$\theta_1 = \left(1 + \frac{\theta_2}{\theta_1} + \frac{\theta_3}{\theta_1} \right)^{-1} = \frac{1}{(2\alpha + \beta \alpha^2)b} - \frac{1}{(2\alpha + \beta \alpha^2)^2 b^2} + O(b^{-3}). \quad (\text{S61})$$

up to leading order. Then θ_2 and θ_3 can be derived from equations (S60) and (S59).

F. Derivation of Partition Strengths in the Bottleneck Limit

In a metabolic chain of m intermediate reactions, let m denote the single **bottleneck reaction**, while all other a_i 's are of similar magnitude. Consider as a simple example the case of $n = 3$ and $m = 1$, with the transport (b) and last reaction (a_2) being fast and the middle reaction (a_1) being slow.

We begin with the three-sector model, where their analytic solution has been worked out.

F.1. First Metabolic Step Limited

If the first metabolic step is a bottleneck reaction, following the same procedure as before, we can expand in the limit of small a_1 .

The third-order expansions are

$$\begin{aligned}
Y_1 &= 1 + \left(-\frac{\theta_2}{b\theta_1(k_1+1)} \right) a_1 + \frac{k_1\theta_2^2}{b^2\theta_1^2(k_1+1)^3} a_1^2, \\
Y_2 &= \frac{k_2\theta_2}{(a_2\theta_3+bk_2\theta_1)(k_1+1)} a_1 \\
&\quad + \left(-\frac{k_2\theta_2^2 (a_2^2 k_1 \theta_3^2 - a_2 b \theta_1 \theta_3 + b^2 k_1 k_2^2 \theta_1^2 - a_2 b k_1 \theta_1 \theta_3 + 2 a_2 b k_1 k_2 \theta_1 \theta_3)}{b\theta_1 (a_2 \theta_3 + b k_2 \theta_1)^3 (k_1 + 1)^3} \right) a_1^2, \\
Y_3 &= \frac{a_2 \theta_2 \theta_3}{b^2 \theta_1 (a_2 \theta_3 + b k_2 \theta_1)^3 (k_1 + 1)^3} \left(a_2^2 b k_1^2 \theta_1 \theta_3^2 + 2 a_2^2 b k_1 \theta_1 \theta_3^2 + a_2^2 b \theta_1 \theta_3^2 + b^3 k_2^2 \theta_1^3 \right. \\
&\quad \left. + 2 a_2 b^2 k_1^2 k_2 \theta_1^2 \theta_3 + 4 a_2 b^2 k_1 k_2 \theta_1^2 \theta_3 + 2 a_2 b^2 k_2 \theta_1^2 \theta_3 + b^3 k_1^2 k_2^2 \theta_1^3 + 2 b^3 k_1 k_2^2 \theta_1^3 \right) a_1 \\
&\quad + \left(-\frac{a_2 \theta_2 \theta_3 (a_2^2 k_1 \theta_2 \theta_3^2 + b^2 k_2 \theta_1^2 \theta_2 + b^2 k_1 k_2 \theta_1^2 \theta_2 + b^2 k_1 k_2^2 \theta_1^2 \theta_2 + 2 a_2 b k_1 k_2 \theta_1 \theta_2 \theta_3)}{b^2 \theta_1 (a_2 \theta_3 + b k_2 \theta_1)^3 (k_1 + 1)^3} \right) a_1^2.
\end{aligned} \tag{S62}$$

Hence the growth rate function is

$$\begin{aligned}
\bar{\lambda}(\theta_1, \theta_2, \theta_3) &= \frac{a_2 \theta_2 \theta_3}{b^2 \theta_1 (a_2 \theta_3 + b k_2 \theta_1)^3 (k_1 + 1)^3} \\
&\quad \times \left(a_2^2 b k_1^2 \theta_1 \theta_3^2 + 2 a_2^2 b k_1 \theta_1 \theta_3^2 + a_2^2 b \theta_1 \theta_3^2 + 2 a_2 b^2 k_1^2 k_2 \theta_1^2 \theta_3 + 4 a_2 b^2 k_1 k_2 \theta_1^2 \theta_3 \right. \\
&\quad \left. + 2 a_2 b^2 k_2 \theta_1^2 \theta_3 + b^3 k_1^2 k_2^2 \theta_1^3 + 2 b^3 k_1 k_2^2 \theta_1^3 + b^3 k_2^2 \theta_1^3 \right) a_1 \\
&\quad + \left(-\frac{a_2 \theta_2 \theta_3 (a_2^2 k_1 \theta_2 \theta_3^2 + b^2 k_2 \theta_1^2 \theta_2 + b^2 k_1 k_2 \theta_1^2 \theta_2 + b^2 k_1 k_2^2 \theta_1^2 \theta_2 + 2 a_2 b k_1 k_2 \theta_1 \theta_2 \theta_3)}{b^2 \theta_1 (a_2 \theta_3 + b k_2 \theta_1)^3 (k_1 + 1)^3} \right) a_1^2.
\end{aligned} \tag{S63}$$

By the method of Lagrange multipliers, set $L(\theta) = \lambda(\theta) - \mu(\theta_1 + \theta_2 + \theta_3)$, where μ is the Lagrange

multiplier. The optimality conditions are given by

$$\frac{\partial L}{\partial \theta_1} = -\frac{a_2 \theta_2 \theta_3}{b \theta_1^2 (a_2 \theta_3 + b k_2 \theta_1)^4 (k_1 + 1)^3} \left(b^4 k_2^3 \theta_1^4 + 2 a_2^2 b^2 k_1 k_2 \theta_1^2 \theta_3^2 + a_2^2 b^2 k_2 \theta_1^2 \theta_3^2 \right. \quad (\text{S64a})$$

$$\left. + 2 a_2 b^3 k_1^2 k_2^2 \theta_1^3 \theta_3 + 4 a_2 b^3 k_1 k_2^2 \theta_1^3 \theta_3 + 2 a_2 b^3 k_2^2 \theta_1^3 \theta_3 + b^4 k_1^2 k_2^3 \theta_1^4 + 2 b^4 k_1 k_2^3 \theta_1^4 \right) \quad (\text{S64b})$$

$$+ a_2^2 b^2 k_1^2 k_2 \theta_1^2 \theta_3^2 \Big) a_1 \quad (\text{S64c})$$

$$+ \frac{a_2 \theta_2 \theta_3}{b \theta_1^2 (a_2 \theta_3 + b k_2 \theta_1)^4 (k_1 + 1)^3} \left(2 b^3 k_2^2 \theta_1^3 \theta_2 + a_2^3 k_1 \theta_2 \theta_3^3 \right. \quad (\text{S64d})$$

$$\left. + 2 b^3 k_1 k_2^2 \theta_1^3 \theta_2 + 2 b^3 k_1 k_2^3 \theta_1^3 \theta_2 - a_2 b^2 k_2 \theta_1^2 \theta_2 \theta_3 - a_2 b^2 k_1 k_2 \theta_1^2 \theta_2 \theta_3 \right) \quad (\text{S64e})$$

$$+ 4 a_2^2 b k_1 k_2 \theta_1 \theta_2 \theta_3^2 + 5 a_2 b^2 k_1 k_2^2 \theta_1^2 \theta_2 \theta_3 \Big) a_1^2 - \mu = 0, \quad (\text{S64f})$$

$$\frac{\partial L}{\partial \theta_2} = \frac{a_2 \theta_3 \left(a_2^2 b k_1^2 \theta_1 \theta_3^2 + 2 a_2^2 b k_1 \theta_1 \theta_3^2 + a_2^2 b \theta_1 \theta_3^2 + 2 a_2 b^2 k_1^2 k_2 \theta_1^2 \theta_3 + 4 a_2 b^2 k_1 k_2 \theta_1^2 \theta_3 + 2 a_2 b^2 k_2 \theta_1^2 \theta_3 + b^3 k_1^2 k_2^2 \theta_1^3 \right)}{b \theta_1 (a_2 \theta_3 + b k_2 \theta_1)^3 (k_1 + 1)^3} \quad (\text{S64g})$$

$$- \frac{a_2 \theta_3 \left(2 a_2^2 k_1 \theta_2 \theta_3^2 + 2 b^2 k_2 \theta_1^2 \theta_2 + 2 b^2 k_1 k_2 \theta_1^2 \theta_2 + 2 b^2 k_1 k_2^2 \theta_1^2 \theta_2 + 4 a_2 b k_1 k_2 \theta_1 \theta_2 \theta_3 \right)}{b \theta_1 (a_2 \theta_3 + b k_2 \theta_1)^3 (k_1 + 1)^3} a_1^2 \quad (\text{S64h})$$

$$\frac{\partial L}{\partial \theta_3} = \frac{a_2 k_2 \theta_2 \left(a_2^2 b k_1^2 \theta_1 \theta_3^2 + 2 a_2^2 b k_1 \theta_1 \theta_3^2 + a_2^2 b \theta_1 \theta_3^2 + 2 a_2 b^2 k_1^2 k_2 \theta_1^2 \theta_3 + 4 a_2 b^2 k_1 k_2 \theta_1^2 \theta_3 + 2 a_2 b^2 k_2 \theta_1^2 \theta_3 + b^3 k_1^2 k_2^2 \theta_1^3 \right)}{(a_2 \theta_3 + b k_2 \theta_1)^4 (k_1 + 1)^3} \quad (\text{S64i})$$

$$- \frac{a_2 k_2 \theta_2 \left(a_2^2 k_1 \theta_2 \theta_3^2 + b^2 k_2 \theta_1^2 \theta_2 + b^2 k_1 k_2 \theta_1^2 \theta_2 - 2 a_2 b \theta_1 \theta_2 \theta_3 + b^2 k_1 k_2^2 \theta_1^2 \theta_2 - 2 a_2 b k_1 \theta_1 \theta_2 \theta_3 + 2 a_2 b k_1 k_2 \theta_1 \theta_2 \theta_3 \right)}{(a_2 \theta_3 + b k_2 \theta_1)^4 (k_1 + 1)^3} a_1^2 \quad (\text{S64j})$$

F.2. General Discussion

It may be expected that various bottleneck reactions in a long metabolic chain can be treated similarly, i.e. the steady-state protein fraction distribution given a_i is the single bottleneck reaction constant should be similar. However, the mathematical treatment returns vastly different forms analytically.

For simplicity, we will discuss the starvation and overabundance limits with a single bottleneck reaction, leading to more analytic details. The general case with multiple bottlenecks has been treated above with extensive approximation, so much physics has been masked.

3. THEORY FOR MASS-ACTION KINETICS

A. Solution of the Three-Sector Partition Model

The three-sector model with mass-action kinetics, unlike the more general Michaelis-Menten kinetics discussed above, can be solved analytically. The system is described by the system of ODEs:

$$\frac{dY_1}{dt} = b Y_3 - r_1 Y_1 Y_4 - b Y_1 Y_3, \quad (\text{S65a})$$

$$\frac{dY_2}{dt} = r_1 Y_1 Y_4 - r_2 Y_2 Y_5 - b Y_2 Y_3, \quad (\text{S65b})$$

$$\frac{dY_3}{dt} = \theta_1 r_2 Y_2 Y_5 - b Y_3^2, \quad (\text{S65c})$$

$$\frac{dY_4}{dt} = \theta_2 r_2 Y_2 Y_5 - b Y_3 Y_4, \quad (\text{S65d})$$

$$\frac{dY_5}{dt} = \theta_3 r_2 Y_2 Y_5 - b Y_3 Y_5. \quad (\text{S65e})$$

The steady-state solutions are obtained by setting $dY/dt \rightarrow 0$, and suppress the * for optimized values.

$$bY_3 = r_1 Y_1 Y_4 + b Y_1 Y_3, \quad (\text{S66a})$$

$$r_1 Y_1 Y_4 = r_2 Y_2 Y_5 + b Y_2 Y_3, \quad (\text{S66b})$$

$$\theta_1 r_2 Y_2 Y_5 = b Y_3^2, \quad (\text{S66c})$$

$$\theta_2 r_2 Y_2 Y_5 = b Y_3 Y_4, \quad (\text{S66d})$$

$$\theta_3 r_2 Y_2 Y_5 = b Y_3 Y_5. \quad (\text{S66e})$$

Solving them, again with $Y_3 : Y_4 : Y_5 = \theta_1 : \theta_2 : \theta_3$, gives

$$Y_1 = \left(1 + \frac{r_1 \theta_2}{b \theta_1} \right)^{-1}, \quad (\text{S67a})$$

$$Y_2 = \left(\frac{r_1 \theta_2}{b \theta_1} \right) \left[\left(1 + \frac{r_2 \theta_3}{b \theta_1} \right) \left(1 + \frac{r_1 \theta_2}{b \theta_1} \right) \right]^{-1}, \quad (\text{S67b})$$

$$Y_3 = \left(\frac{r_2 \theta_3}{b} Y_2 \right), \quad Y_4 = \left(\frac{r_2 \theta_2 \theta_3}{b \theta_1} \right) Y_2, \quad Y_5 = \left(\frac{r_2 \theta_3^2}{b \theta_1} \right) Y_2. \quad (\text{S67c})$$

$$(\text{S67d})$$

Interestingly, in this limit, the partition strength θ has an analytic solution in the form of a root to a sixth-degree polynomial. The partition strength corresponding to ribosome fraction θ_3 is a root of the polynomial

$$\begin{aligned} & \left(r_1^2 + 2r_1 r_2 + r_2^2 - 5r_1^2 r_2 - 2r_1 r_2^2 - r_2^3 - r_2^4 + 4r_1^3 r_2^2 + 4r_1^2 r_2^3 + 3r_1 r_2^4 - 4r_1^3 r_2^3 - 3r_1^2 r_2^4 + r_1^3 r_2^4 \right) x^6 \\ & - \left(5r_1^2 + 2r_1 r_2 + r_2^2 - 8r_1^2 r_2 + r_1 r_2^2 + 3r_2^3 - 4r_1^3 r_2 - 11r_1^2 r_2^2 - 7r_1 r_2^3 + 14r_1^3 r_2^2 + 10r_1^2 r_2^3 - 6r_1^3 r_2^3 \right) x^5 \\ & + \left(8r_1^2 - r_1 r_2 - 2r_2^2 + r_1^3 + 7r_1^2 r_2 + 6r_1 r_2^2 - 14r_1^3 r_2 - 22r_1^2 r_2^2 - 2r_1 r_2^3 + 17r_1^3 r_2^2 + 4r_1^2 r_2^3 - 2r_1^3 r_2^3 \right) x^4 \\ & - r_1 \left(2r_1 - r_2 + 4r_1^2 + 22r_1 r_2 + 3r_2^2 - 18r_1^2 r_2 - 13r_1 r_2^2 + 8r_1^2 r_2^2 \right) x^3 \\ & + r_1 \left(-7r_1 - r_2 + 6r_1^2 + 16r_1 r_2 + r_2^2 - 10r_1^2 r_2 - 2r_1 r_2^2 + r_1^2 r_2^2 \right) x^2 \\ & + r_1 \left(7r_1 + r_2 - 4r_1^2 - 4r_2 r_1 + 2r_2 r_1^2 \right) x + r_1^2 (r_1 - 2), \end{aligned} \quad (\text{S68})$$

where we have set $b = 1$ by a change of time unit. The other two partition strengths are fifth-degree polynomials in θ_3 . Checking with MATLAB factor() returns no further factorization.

To get a better understanding of the behavior of the partition strengths, we consider various limits of the system, including **starvation**, **overabundance of nutrient**, and the presence of a **single bottleneck reaction**. Later, we will extend the analysis to m bottleneck reactions in a general metabolic chain with N partitions.

For each limit, we define the growth rate objective function $L(\theta, \mu) = bY_3(\theta) - \mu(\theta_1 + \theta_2 + \theta_3 - 1)$.

B. Derivation of Partition Strengths in the Starvation Limit

Again we expand the protein fractions as a series in b .

$$Y_1 = \frac{\theta_1}{r_1 \theta_2} b - \frac{\theta_1^2}{r_1^2 \theta_2^2} b^2 + O(b^3), \quad (\text{S69a})$$

$$Y_2 = \frac{\theta_1}{r_2 \theta_3} b - \frac{\theta_1 (r_1 \theta_1 \theta_2 + r_2 \theta_1 \theta_3)}{r_1 r_2^2 \theta_2 \theta_3^2} b^2 + O(b^3), \quad (\text{S69b})$$

$$Y_3 = \theta_1 - \frac{\theta_1 (\theta_1 r_1^2 r_2 \theta_2^2 \theta_3 + \theta_1 r_1 r_2^2 \theta_2 \theta_3^2)}{r_1^2 r_2^2 \theta_2^2 \theta_3^2} b \quad (\text{S69c})$$

$$+ \frac{\theta_1 (r_1^2 \theta_1^2 \theta_2^2 + r_1 r_2 \theta_1^2 \theta_2 \theta_3 + r_2^2 \theta_1^2 \theta_3^2)}{r_1^2 r_2^2 \theta_2^2 \theta_3^2} b^2 + O(b^3). \quad (\text{S69d})$$

Lagrange multipliers can be used to solve for the optimal θ values in this limit.

$$\frac{\partial L}{\partial \theta_1} = b - \frac{2\theta_1 r_1^2 r_2 \theta_2^2 \theta_3 + 2\theta_1 r_1 r_2^2 \theta_2 \theta_3^2}{r_1^2 r_2^2 \theta_2^2 \theta_3^2} b^2 \quad (\text{S70a})$$

$$+ \frac{3r_1^2 \theta_1^2 \theta_2^2 + 3r_1 r_2 \theta_1^2 \theta_2 \theta_3 + 3r_2^2 \theta_1^2 \theta_3^2}{r_1^2 r_2^2 \theta_2^2 \theta_3^2} b^3 + O(b^4) - \mu = 0, \quad (\text{S70b})$$

$$\frac{\partial L}{\partial \theta_2} = \frac{\theta_1^2}{r_1 \theta_2^2} b^2 - \frac{\theta_1^2 (r_1 \theta_1 \theta_2 + 2r_2 \theta_1 \theta_3)}{r_1^2 r_2 \theta_2^3 \theta_3} b^3 + O(b^4) - \mu = 0, \quad (\text{S70c})$$

$$\frac{\partial L}{\partial \theta_3} = \frac{\theta_1^2}{r_2 \theta_3^2} b^2 - \frac{\theta_1^2 (2r_1 \theta_1 \theta_2 + r_2 \theta_1 \theta_3)}{r_1 r_2^2 \theta_2 \theta_3^3} b^3 + O(b^4) - \mu = 0. \quad (\text{S70d})$$

C. Derivation of Partition Strengths in the Overabundance Limit

We expand the protein fractions as a series in $1/b$.

$$Y_1 = 1 - \frac{r_1 \theta_2}{\theta_1 b} + \frac{r_1^2 \theta_2^2}{\theta_1^2 b^2} + O(b^{-3}), \quad (\text{S71a})$$

$$Y_2 = \frac{r_1 \theta_2}{\theta_1 b} - \frac{r_1^2 \theta_2^2 + r_1 r_2 \theta_2 \theta_3}{\theta_1^2 b^2} + O(b^{-3}), \quad (\text{S71b})$$

$$Y_3 = \frac{r_1 r_2 \theta_2 \theta_3}{\theta_1 b^2} + O(b^{-3}). \quad (\text{S71c})$$

Lagrange multipliers can be used to solve for the optimal θ values in this limit. Since the leading term is already $O(b^{-3})$, we keep terms up to order b^{-4} .

$$\frac{\partial Y_1}{\partial \theta_1} = \frac{r_1 r_2 \theta_2 \theta_3 (2r_1 \theta_2 - b\theta_1 + 2r_2 \theta_3)}{b^2 \theta_1^3} + O(b^{-3}) - \mu = 0, \quad (\text{S72a})$$

$$\frac{\partial Y_2}{\partial \theta_2} = -\frac{r_1 r_2 \theta_3 (2r_1 \theta_2 - b\theta_1 + r_2 \theta_3)}{b^2 \theta_1^2} + O(b^{-3}) - \mu = 0, \quad (\text{S72b})$$

$$\frac{\partial Y_3}{\partial \theta_3} = -\frac{r_1 r_2 \theta_2 (r_1 \theta_2 - b\theta_1 + 2r_2 \theta_3)}{b^2 \theta_1^2} + O(b^{-3}) - \mu = 0. \quad (\text{S72c})$$

D. Derivation of Partition Strengths with Bottleneck Reactions

We first expand the protein fractions as a series in r_1 .

$$Y_1 = 1 - \left(\frac{\theta_2}{b \theta_1} \right) r_1 + \frac{\theta_2^2}{b^2 \theta_1^2} r_1^2 + O(r_1^3), \quad (\text{S73a})$$

$$Y_2 = \frac{\theta_2}{b \theta_1 + r_2 \theta_3} r_1 - \frac{\theta_2^2}{b \theta_1 (b \theta_1 + r_2 \theta_3)} r_1^2 + O(r_1^3), \quad (\text{S73b})$$

$$Y_3 = \frac{r_2 \theta_2 \theta_3}{b (b \theta_1 + r_2 \theta_3)} r_1 - \frac{r_2 \theta_2^2 \theta_3}{b^2 \theta_1 (b \theta_1 + r_2 \theta_3)} r_1^2 + O(r_1^3). \quad (\text{S73c})$$

Lagrange multipliers can be used to solve for the optimal θ values in this limit.

$$\frac{\partial Y_1}{\partial \theta_1} = \frac{b r_2 \theta_2 \theta_3}{(b \theta_1 + r_2 \theta_3)^2} r_1 + \frac{r_2 \theta_2 \theta_3 (2b \theta_1 \theta_2 + r_2 \theta_2 \theta_3)}{b \theta_1^2 (b \theta_1 + r_2 \theta_3)^2} r_1^2 + O(r_1^3) - \mu = 0, \quad (\text{S74a})$$

$$\frac{\partial Y_2}{\partial \theta_2} = \frac{r_2 \theta_3}{b \theta_1 + r_2 \theta_3} r_1 - \frac{2r_2 \theta_2 \theta_3}{b \theta_1 (b \theta_1 + r_2 \theta_3)} r_1^2 + O(r_1^3) - \mu = 0, \quad (\text{S74b})$$

$$\frac{\partial Y_3}{\partial \theta_3} = \frac{b r_2 \theta_1 \theta_2}{(b \theta_1 + r_2 \theta_3)^2} r_1 - \frac{r_2 \theta_2^2}{(b \theta_1 + r_2 \theta_3)^2} r_1^2 + O(r_1^3) - \mu = 0. \quad (\text{S74c})$$

Similarly, we can expand the protein fractions as a series in r_2 .

$$Y_1 = \frac{b\theta_1}{b\theta_1 + r_1\theta_2} + O(r_2^3), \quad (\text{S75a})$$

$$Y_2 = \frac{r_1\theta_2}{b\theta_1 + r_1\theta_2} - \frac{r_1\theta_2\theta_3}{b\theta_1(b\theta_1 + r_1\theta_2)} r_2 + \frac{r_1\theta_2\theta_3^2}{b^2\theta_1^2(b\theta_1 + r_1\theta_2)} r_2^2 + O(r_2^3), \quad (\text{S75b})$$

$$Y_3 = \frac{r_1\theta_2\theta_3}{b(b\theta_1 + r_1\theta_2)} r_2 - \frac{r_1\theta_2\theta_3^2}{b^2\theta_1(b\theta_1 + r_1\theta_2)} r_2^2 + O(r_2^3). \quad (\text{S75c})$$

Lagrange multipliers can be used to solve for the optimal θ values in this limit.

$$\frac{\partial Y_1}{\partial \theta_1} = -\frac{b r_1 \theta_2 \theta_3}{(b \theta_1 + r_1 \theta_2)^2} r_2 + \frac{r_1 \theta_2 \theta_3 (2 \theta_3 b^2 \theta_1^2 + r_1 \theta_2 \theta_3 b \theta_1)}{b^2 \theta_1^3 (b \theta_1 + r_1 \theta_2)^2} r_2^2 + O(r_2^3) - \mu = 0, \quad (\text{S76a})$$

$$\frac{\partial Y_2}{\partial \theta_2} = \frac{b r_1 \theta_1 \theta_3}{(b \theta_1 + r_1 \theta_2)^2} r_2 - \frac{r_1 \theta_3^2}{(b \theta_1 + r_1 \theta_2)^2} r_2^2 + O(r_2^3) - \mu = 0, \quad (\text{S76b})$$

$$\frac{\partial Y_3}{\partial \theta_3} = \frac{r_1 \theta_2}{b \theta_1 + r_1 \theta_2} r_2 - \frac{2 r_1 \theta_2 \theta_3}{b \theta_1 (b \theta_1 + r_1 \theta_2)} r_2^2 + O(r_2^3) - \mu = 0. \quad (\text{S76c})$$

4. NUMERICAL METHODS

A. Simulation Parameters

Here is a detailed estimate of the average number of total molecules involved in the synthesis of a protein in an *E. coli* cell. The molecules will include both small molecules such as metabolic intermediates and amino acids, and large molecules such as proteins and other polymeric compounds.

For a ribosome to synthesize a protein, it requires the following ingredients: amino acids (≈ 350), tRNA (≈ 350), ATP/GTP ≈ 1050 , ribosomes (≈ 350). The average protein length in *E. coli* is 350 amino acids. Although ribosomes are not consumed, each protein needs one ribosome to synthesize. The above is summarized in table S1, and we find that on average about 2100 molecules are involved (though not necessarily *consumed*).

Table S1. Estimated counts of total molecules involved in the synthesis of a protein on average in a typical *E. coli* Cell

Molecule type	Count	Notes
Amino acids (N_{AA})	≈ 350	The average protein length is 350 amino acids, while the longest is a helicase encoded by the <i>lhr</i> gene, comprising 1,538 amino acids.
tRNA molecules (N_{tRNA})	≈ 350	Each amino acid is delivered to the ribosome by a specific tRNA molecule.
ATP/GTP ($N_{ATP/GTP}$)	≈ 1050	Amino acid activation: Each amino acid is activated by an aminoacyl-tRNA synthetase, consuming 1 ATP per amino acid. Translation steps: Each elongation cycle consumes 2 GTP, respectively for the binding of aminoacyl-tRNA to the A site and the translocation step [??].
Ribosomes (N_{rib})	≈ 350	Ribosomes are not consumed, but each protein needs one ribosome to synthesize.
Total molecule count (N_{mol})	≈ 2100	

B. Optimization

We can solve for the θ value corresponding to optimal growth rate by numerical optimization using 4th-order Runge-Kutta or with the analytic solution in a simplex. To speed up the parameter sweep, we use a softmax transformation of the following form to formulate it as an unconstrained problem,

$$\theta_1 \rightarrow \frac{e^u}{1 + e^u + e^v}, \quad \theta_2 \rightarrow \frac{1}{1 + e^u + e^v}, \quad \theta_3 \rightarrow \frac{e^v}{1 + e^u + e^v}, \quad (S77)$$

and optimize over the region $(u, v) \in (-\infty, 0]^2$. The simulation speed is greatly enhanced with the python optimization package `scipy.optimize import minimize`, compared to traditional two-stage minimization. Parallel processing is used for different b values by calling from `joblib import Parallel, delayed`.

The difference between different methods is shown in figure S1.

C. Numerical Simulations

Here are additional graphs that did not make it into the summary document.

C.1. Comparisons and Contrasts

Expression using the approximate theory for the starvation and abundant nutrient limits are shown in figures S3, S2 and S4. The approximate expressions do not seem to match well, but the growth rate to nutrient level curve fits the theory well. See figure S5 for a comparison.

Trajectories (fractions) for the biomass associated with each node are shown and compared in figures S6 and S7. The trends for Y_j are different in the small and large b limits, and we can summarize them as

$$\text{low } b: Y_1 \nearrow Y_2 \nearrow Y_3 \searrow Y_4 \nearrow Y_5 \nearrow, \quad (S78)$$

$$\text{high } b: Y_1 \searrow Y_2 \searrow Y_3 \searrow Y_4 \searrow Y_5 \searrow. \quad (S79)$$

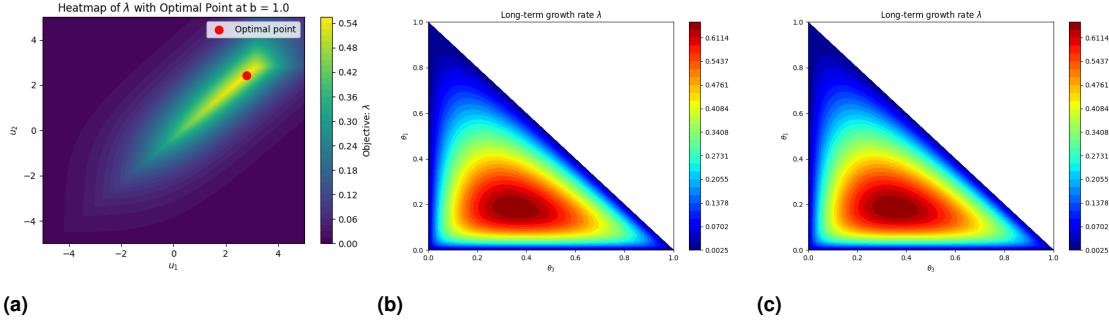


Fig. S1. (a) Unconstrained optimization in $(-\infty, 0]^2$ after SoftMax transformation. (b) Constrained optimization in simplex using the analytical solution, as in [1]. (c) Numerical solution of the system of coupled ODEs using the python optimization package.

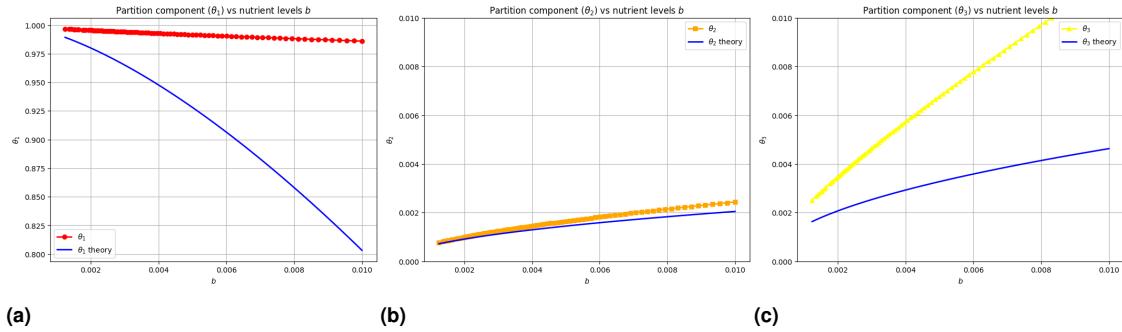


Fig. S2. The partition strength follows square root trend with changing nutrient level during starvation. (a) Transport proteins θ_1 (b) Metabolic proteins θ_2 (c) Ribosomal and translational proteins θ_3 . Here we compare the numerical result to theory.

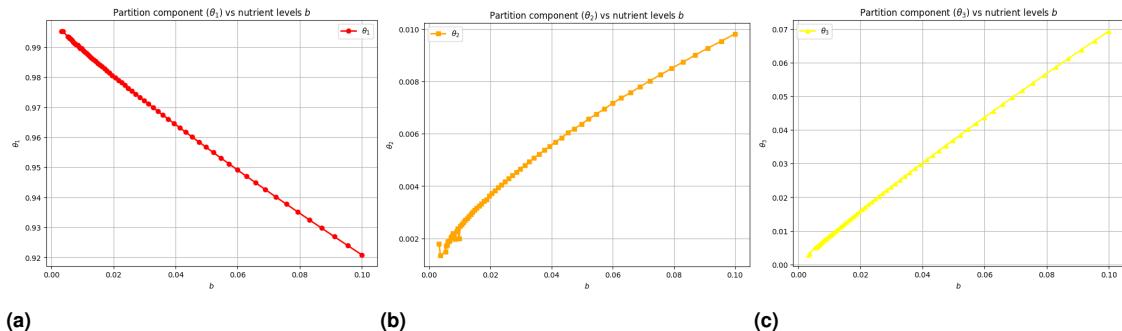


Fig. S3. Partition strength follows square root trend with changing nutrient level during starvation. (a) Transport proteins θ_1 (b) Metabolic proteins θ_2 (c) Ribosomal and translational proteins θ_3 .

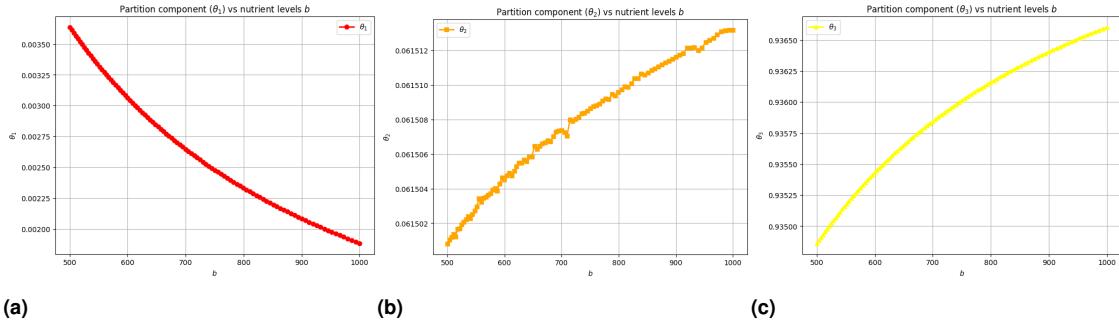


Fig. S4. Partition strength during abundant nutrients. (a) Transport proteins θ_1 (b) Metabolic proteins θ_2 (c) Ribosomal and translational proteins θ_3 .

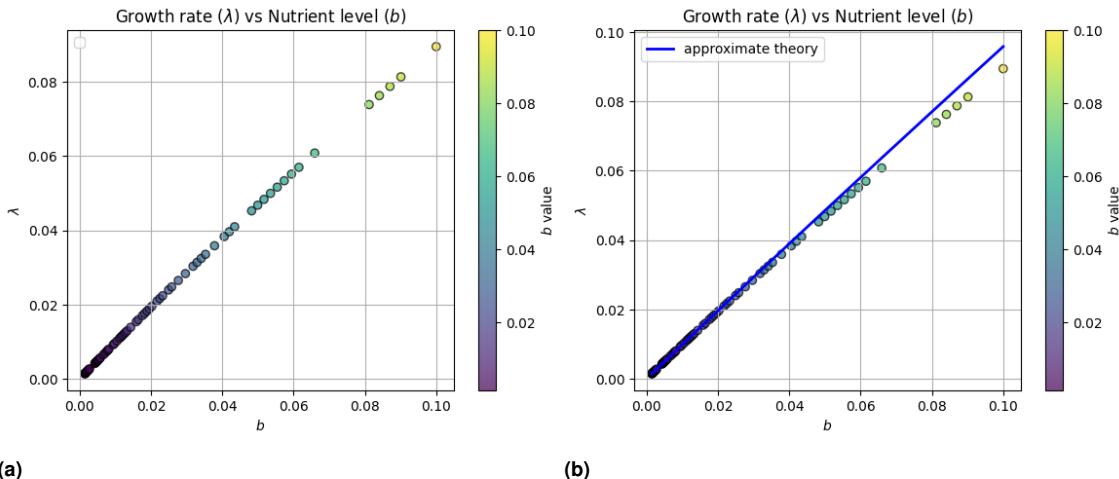


Fig. S5. (a) Growth rate to nutrient level curve, without theory prediction. (b) Same curve, with theory prediction.

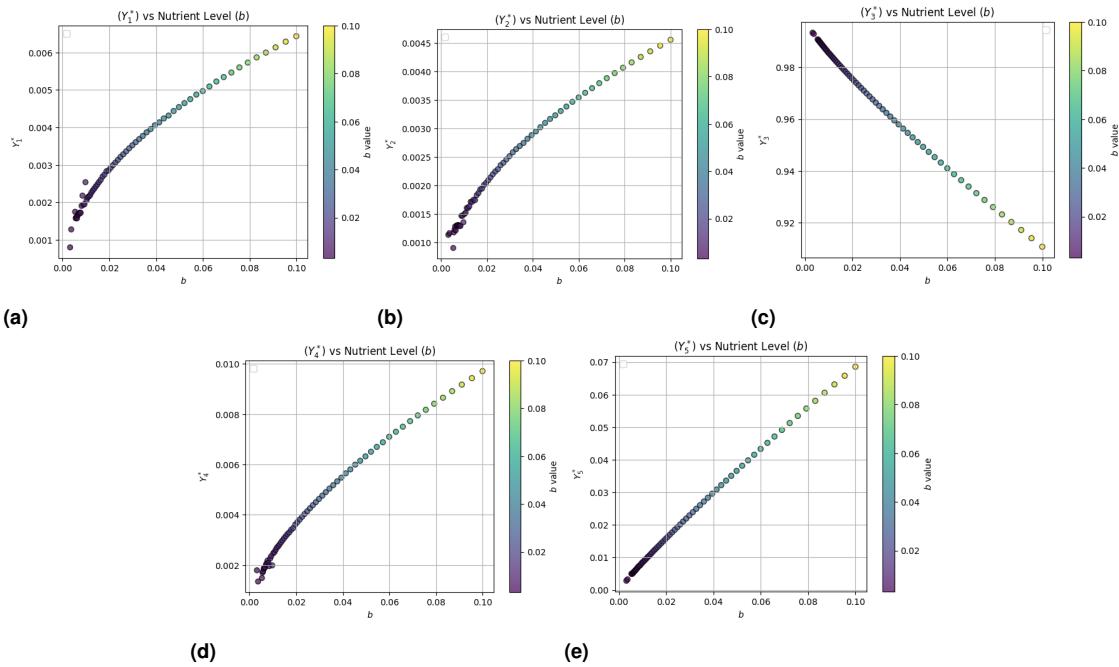


Fig. S6. Trajectories for Y_j during starvation. (a) Metabolites Y_1 (b) Metabolites Y_2 (c) Transport proteins Y_3 (d) Metabolic proteins Y_4 (e) Ribosomal and translational proteins Y_5 .

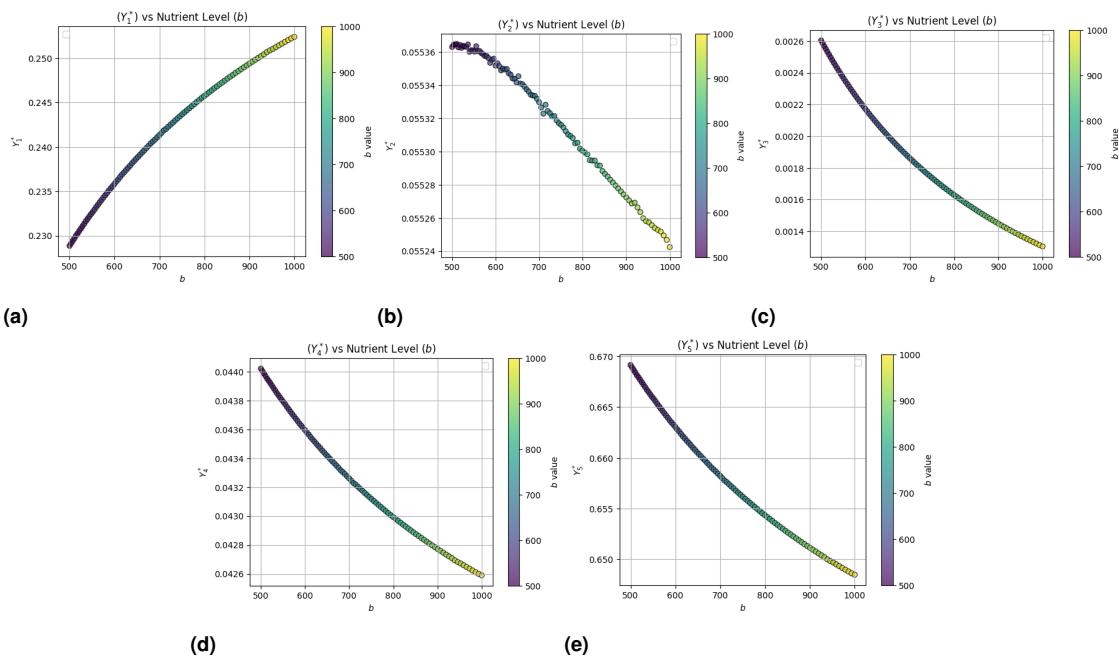


Fig. S7. Trajectories for Y_j during abundant nutrient supply. (a) Metabolites Y_1 (b) Metabolites Y_2 (c) Transport proteins Y_3 (d) Metabolic proteins Y_4 (e) Ribosomal and translational proteins Y_5 .

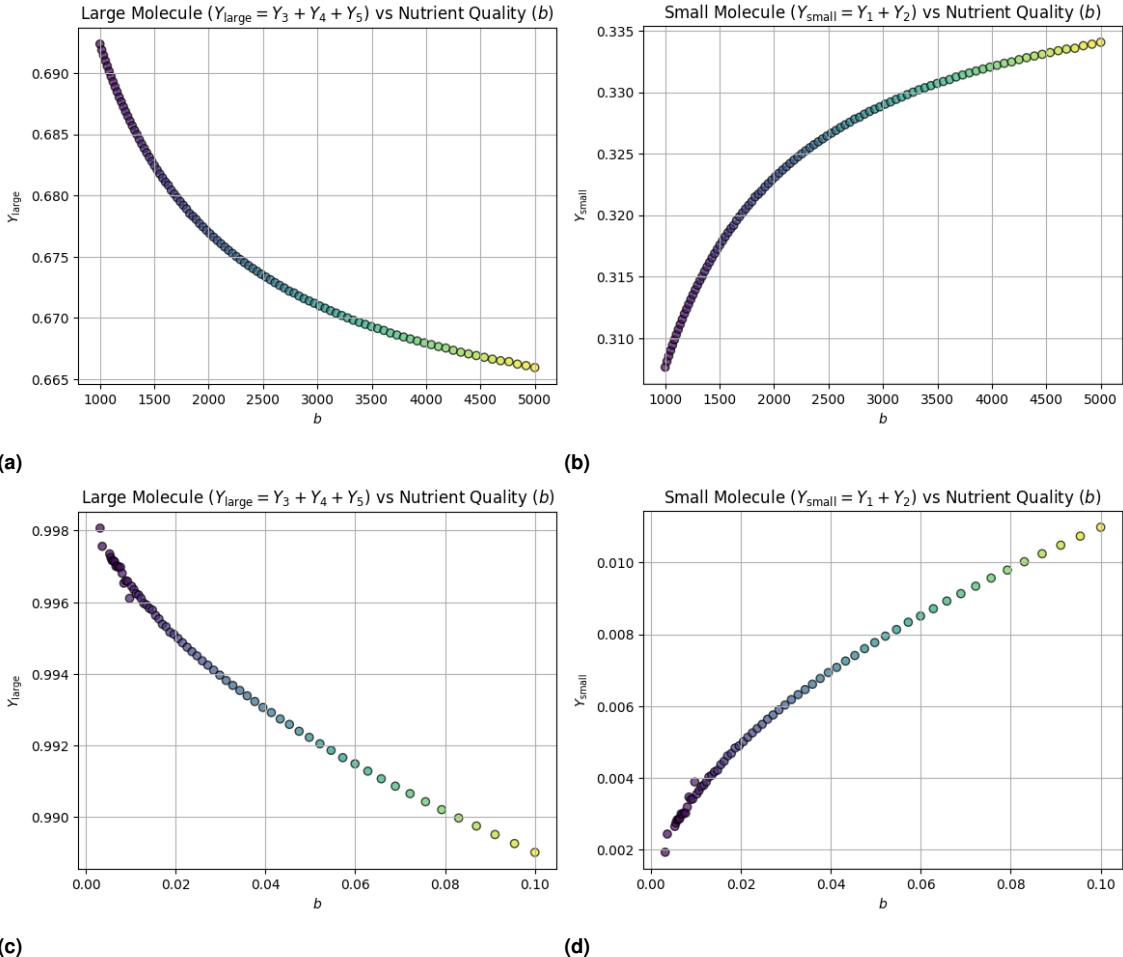


Fig. S8. The trends for Small and Large with respect to nutrient level remains similar in both limits, but .
 (a) (b) (c) (d)

C.2. Some Similarities

The trends in the small and large molecule fraction remains similar for b in the small and large limits. However, the fraction of large molecules is very high (~ 0.995) when nutrient is low, while it is only moderately high (~ 0.675) when nutrient is abundant. Refer to figure S8 for the graphs.

C.3. More Than Three Partitions

The relationships between growth rate, nutrient level, and protein/molecule fractions remain the same in the starvation limit when we generalize to more partitions, figure S9.

Differences emerge when we increase b . Also, b in the high nutrient limit has qualitatively different behavior compared to the $n = 3$ case. Figure S10.

D. Correlation Between Biomass Fraction vs. Rate Constants

We can also explore the correlation between biomass fractions Y_i and the corresponding rate constants a_i . Here we show some examples in figure ??.

5. APPENDIX

A. Steady State Protein Fraction in the Overabundance Limit

The steady-state protein fractions in the overabundance limit were given in symbolic form only, without explicitly giving the coefficients due to the complexity. Also, the expressions may not be very enlightening. Here we provide the full expressions.

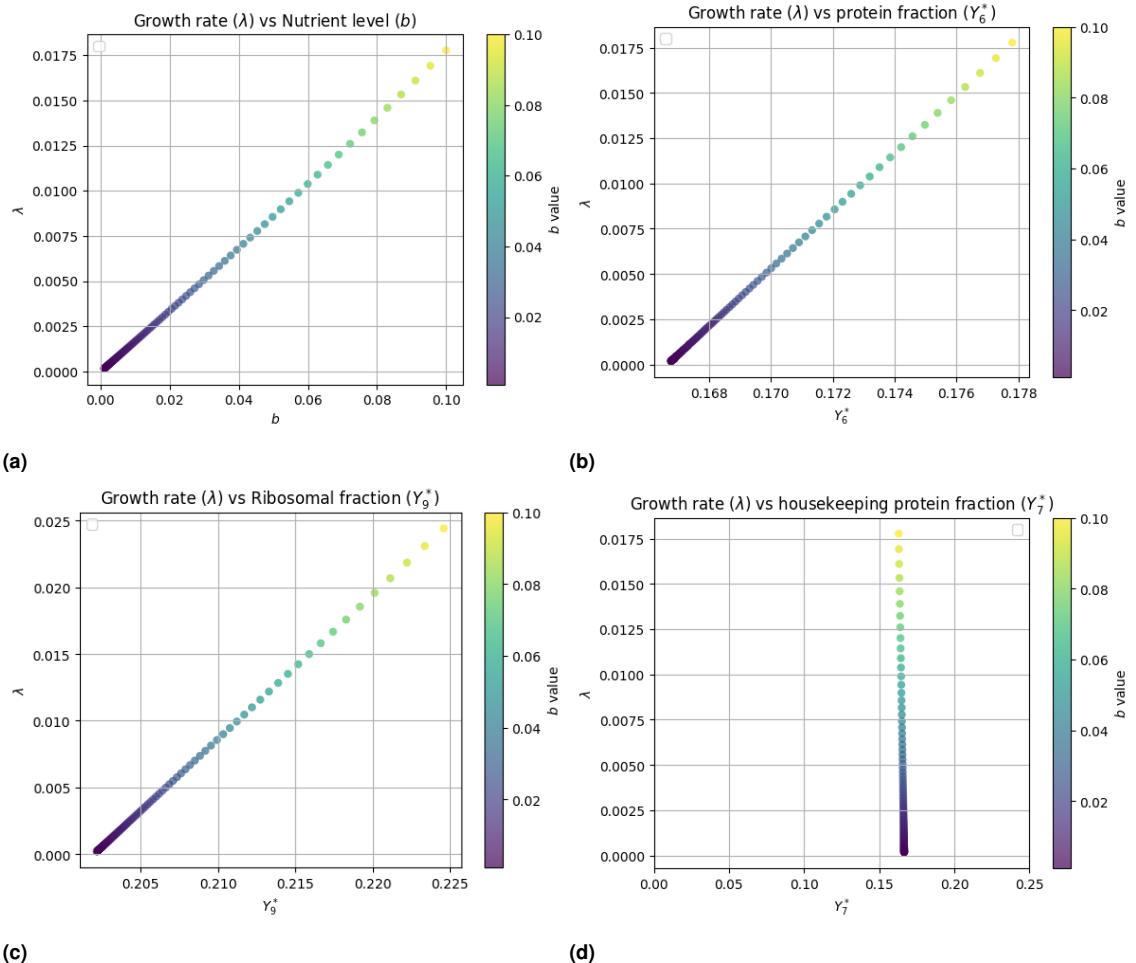


Fig. S9. Starvation. (a) Growth rate to b relationship for six-sector model. This model has been considered in [2], [3] as a model for bacteria growth. (b) Growth rate vs Y_6 for six-sector model. (c) Ribosomal fraction Y_9 for four-sector model. (d) Growth rate vs housekeeping protein fraction Y_7 in six-sector model.

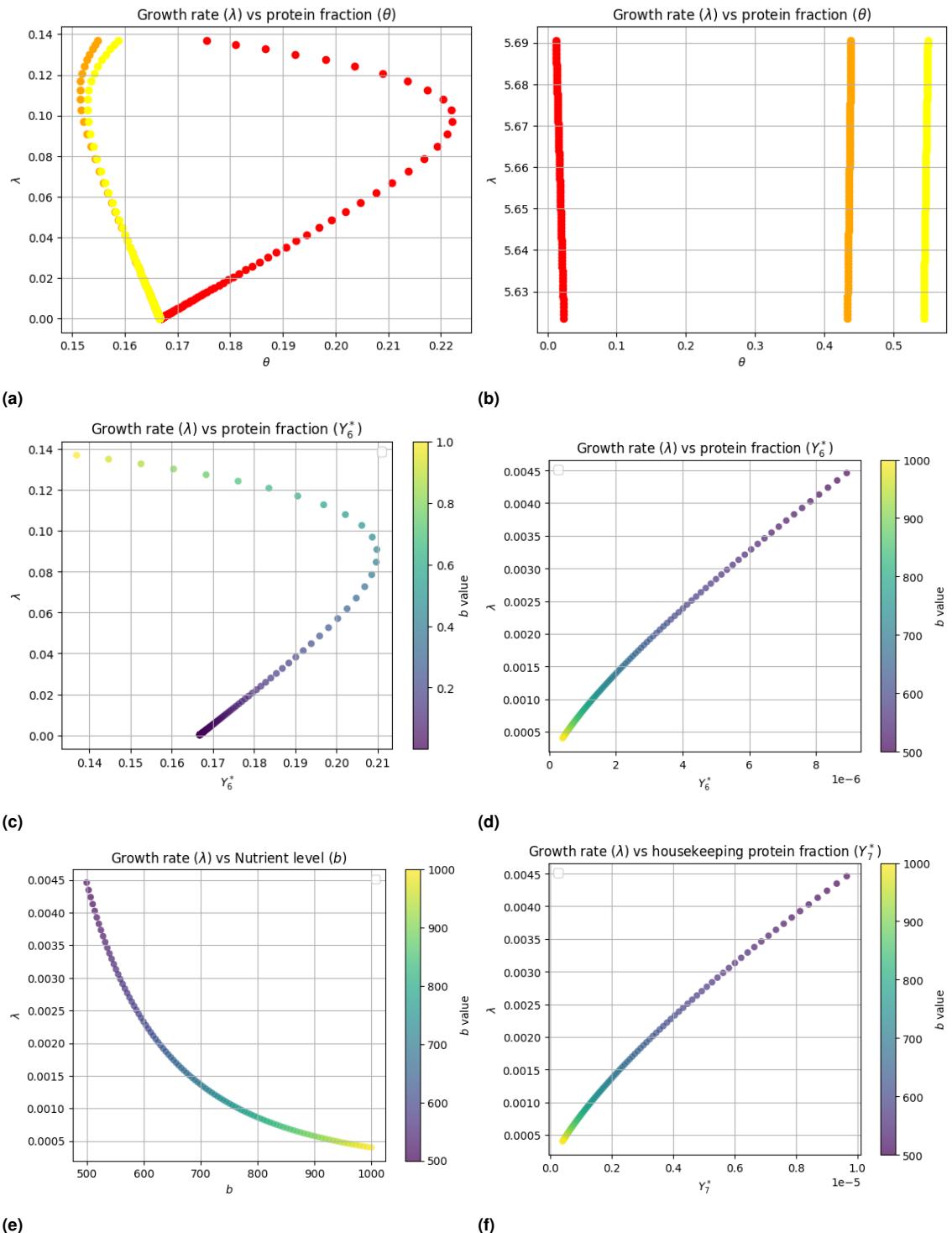
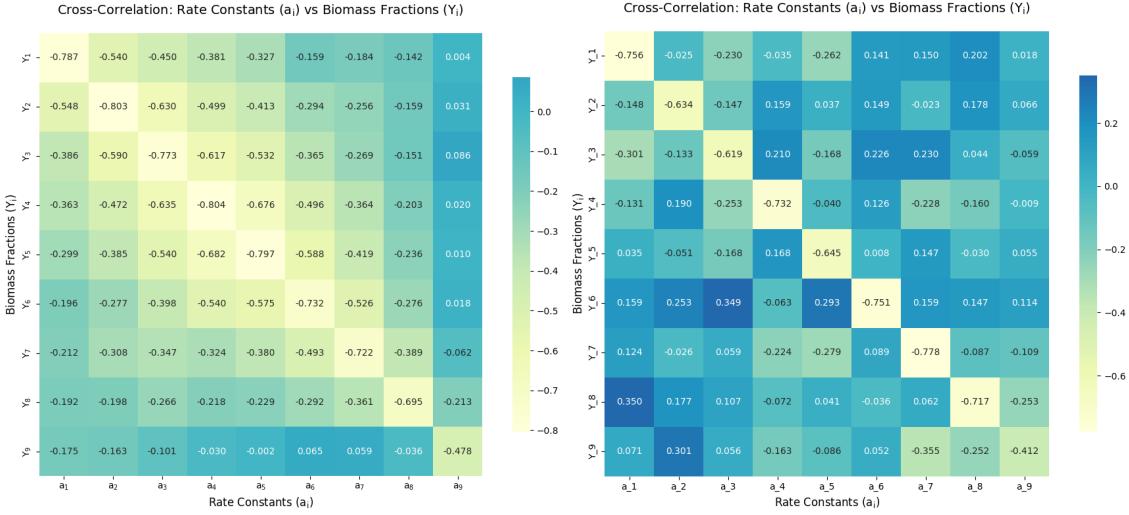


Fig. S10. High or medium abundance of nutrients, with the six-sector model [2]. (a) Growth rate vs θ for medium nutrient levels. (b) Growth rate vs θ for high nutrient levels. (c) Growth rate vs (one of the) metabolite(s) fraction. (d) Growth rate vs Y_6 . (e) Growth rate vs b relationship. (f) Growth rate vs one of the metabolic protein fractions.



(a) Correlation between Y_1 and a_1 with $b = 0.01$, where a_i are sorted.
(b) Correlation between Y_1 and a_1 with $b = 10.0$, where a_i are unsorted and randomized.

The trajectories are given by

$$Y_1 = 1 + \frac{\alpha^2 a_1^2 k_1}{(k_1 + 1)^3} - \frac{\alpha a_1}{k_1 + 1} - \frac{a_1 (2k_1 + k_1^2 - 2\alpha a_1 k_1 + 1)}{\alpha(\alpha\beta + 2)^2(k_1 + 1)^3 b^2} + O(b^{-3}), \quad (\text{S80})$$

$$Y_2 = \frac{\alpha a_1}{k_1 + 1} - \frac{\alpha^2 a_1^2 \left(k_1 + \frac{\alpha_2(\alpha\beta + 1)(k_1 + 1)^2}{a_1 k_2} \right)}{(k_1 + 1)^3} - \frac{a_1 (2\alpha a_2 - k_2 - 2k_1 k_2 - k_1^2 k_2 + 4\alpha a_2 k_1 + 2\alpha^2 \beta a_2 + 2\alpha a_2 k_1^2 + 4\alpha^2 \beta a_2 k_1 + 2\alpha^2 \beta a_2 k_1^2 + 2\alpha a_1 k_1 k_2)}{\alpha k_2 (\alpha\beta + 2)^2 (k_1 + 1)^3 b^2} \quad (\text{S81})$$

$$+ O(b^{-3}) \quad (\text{S82})$$

$$= \frac{\alpha a_1^2 [k_2 - \alpha(1 + \alpha\beta)a_2]}{(1 + k_1)k_2 a_1} - \frac{\alpha^2 k_1 a_1^2}{(1 + k_1)^3} + \frac{a_1 [(k_2 - 2\alpha a_2(1 + \alpha\beta))(1 + k_1)^2 - 2\alpha k_1 k_2 a_1]}{\alpha k_2 (\alpha\beta + 2)^2 (k_1 + 1)^3 b^2} + O(b^{-3}), \quad (\text{S83})$$

$$Y_3 = \frac{\left(a_1 a_2 (\alpha\beta + 1) (4\alpha^3 a_1 + 4\alpha^3 a_2 - 4\alpha^2 k_2 + 4\alpha^3 a_2 k_1^2 - 4\alpha^2 k_1^2 k_2 + 4\alpha^4 \beta a_1 + 8\alpha^4 \beta a_2 - 4\alpha^3 \beta k_2 + 4\alpha^3 a_1 k_1 + 8\alpha^3 a_2 k_1 - 8\alpha^2 k_1 k_2 + \alpha^5 \beta^2 a_1 + 5\alpha^5 \beta^2 a_2 + \alpha^6 \beta^3 a_2 - \alpha^4 \beta^2 k_2 - 8\alpha^3 \beta k_1 k_2 + 4\alpha^3 a_1 k_1 k_2 + 8\alpha^4 \beta a_2 k_1^2 + \alpha^5 \beta^2 a_1 k_1 + 10\alpha^5 \beta^2 a_2 k_1 + 2\alpha^6 \beta^3 a_2 k_1 - 4\alpha^3 \beta k_2^2 k_2 - 2\alpha^4 \beta^2 k_1 k_2 + 5\alpha^5 \beta^2 a_2 k_1^2 + \alpha^6 \beta^3 a_2 k_1^2 - \alpha^4 \beta^2 k_2^2 k_2 + 4\alpha^4 \beta a_1 k_1 + 16\alpha^4 \beta a_2 k_1 + 4\alpha^4 \beta a_1 k_1 k_2 + \alpha^5 \beta^2 a_1 k_1 k_2) \right)}{\alpha b k_2^2 (\alpha\beta + 2)^3 (k_1 + 1)^3} \\ + \frac{\left(a_1 a_2 (\alpha\beta + 1) (2\alpha k_2 - 2\alpha^2 a_1 - 2\alpha^2 a_2 - \alpha^3 \beta a_1 - 3\alpha^3 \beta a_2 + \alpha^2 \beta k_2 - 2\alpha^2 a_1 k_1 - 4\alpha^2 a_2 k_1 + 2\alpha k_1^2 k_2 - \alpha^4 \beta^2 a_2 - 2\alpha^2 a_2 k_1^2 + \alpha^2 \beta k_1^2 k_2 - \alpha^4 \beta^2 a_2 k_1^2 - \alpha^3 \beta a_1 k_1 - 6\alpha^3 \beta a_2 k_1 + 2\alpha^2 \beta k_1 k_2 - 2\alpha^2 a_1 k_1 k_2 - 3\alpha^3 \beta a_2 k_1^2) \right)}{\alpha b^2 k_2^2 (\alpha\beta + 2)^3 (k_1 + 1)^3} \\ + \frac{\left(a_1 a_2 (\alpha\beta + 1) (3\alpha a_1 - 2k_2 + 3\alpha a_2 - 4k_1 k_2 - 2k_1^2 k_2 + 3\alpha a_1 k_1 + 6\alpha a_2 k_1 + 3\alpha^2 \beta a_2) + (3\alpha a_2 k_1^2 + 6\alpha^2 \beta a_2 k_1 + 3\alpha^2 \beta a_2 k_1^2 + 3\alpha a_1 k_1 k_2 + 4\alpha b k_1 k_2 - 2\alpha^4 \beta^2 a_2 b k_1 - \alpha^3 \beta a_1 b k_1 k_2) \right)}{\alpha b^3 k_2^2 (\alpha\beta + 2)^3 (k_1 + 1)^3} \quad (\text{S84})$$

$$= \frac{G_3}{b} + \frac{H_3}{b^2} + O(b^{-3}), \quad (\text{S85})$$

$$\begin{aligned}
Y_4 &= \frac{\left(a_1 a_2 (\alpha \beta + 1) (+4\alpha^3 a_1 + 4\alpha^3 a_2 - 4\alpha^2 k_2 + 4\alpha^3 a_2 k_1^2 - 4\alpha^2 k_1^2 k_2 + 4\alpha^4 \beta a_1 + 8\alpha^4 \beta a_2 + 4\alpha^3 a_1 k_1 \right.} \\
&\quad \left. + 8\alpha^3 a_2 k_1 - 8\alpha^2 k_1 k_2 + \alpha^5 \beta^2 a_1 + 5\alpha^5 \beta^2 a_2 + \alpha^6 \beta^3 a_2 - \alpha^4 \beta^2 k_2 + \alpha^5 \beta^2 a_1 k_1 + 10\alpha^5 \beta^2 a_2 k_1 \right. \\
&\quad \left. + 2\alpha^6 \beta^3 a_2 k_1 - 4\alpha^3 \beta k_1^2 k_2 - 2\alpha^4 \beta^2 k_1 k_2 - 4\alpha^3 \beta k_2 - 8\alpha^3 \beta k_1 k_2 + 4\alpha^3 a_1 k_1 k_2 + 8\alpha^4 \beta a_2 k_1^2 \right. \\
&\quad \left. + 5\alpha^5 \beta^2 a_2 k_1^2 + \alpha^6 \beta^3 a_2 k_1^2 - \alpha^4 \beta^2 k_1^2 k_2 + 4\alpha^4 \beta a_1 k_1 + 16\alpha^4 \beta a_2 k_1 + 4\alpha^4 \beta a_1 k_1 k_2 + \alpha^5 \beta^2 a_1 k_1 k_2)) \right)}{\alpha k_2^2 (\alpha \beta + 2)^3 (k_1 + 1)^3} \\
&+ \frac{\left(a_1 a_2 (\alpha \beta + 1) (2\alpha k_2 - 2\alpha^2 a_1 - 2\alpha^2 a_2 - \alpha^3 \beta a_1 - 3\alpha^3 \beta a_2 + \alpha^2 \beta k_2 - 2\alpha^2 a_1 k_1 \right.} \\
&\quad \left. - 4\alpha^2 a_2 k_1 + 2\alpha k_1^2 k_2 - 6\alpha^3 \beta a_2 k_1 + 2\alpha^2 \beta k_1 k_2 - 2\alpha^2 a_1 k_1 k_2 - \alpha^4 \beta^2 a_2 k_1^2 - \alpha^3 \beta a_1 k_1 \right. \\
&\quad \left. + 4\alpha k_1 k_2 + \alpha^2 \beta k_1^2 k_2 - \alpha^4 \beta^2 a_2 - 2\alpha^2 a_2 k_1^2 - 3\alpha^3 \beta a_2 k_1^2 - 2\alpha^4 \beta^2 a_2 k_1 - \alpha^3 \beta a_1 k_1 k_2) \right)}{\alpha b k_2^2 (\alpha \beta + 2)^3 (k_1 + 1)^3} \\
&+ \frac{\left(a_1 a_2 (\alpha \beta + 1) (4\alpha a_1 - 3k_2 + 4\alpha a_2 - 6k_1 k_2 - 3k_1^2 k_2 + 4\alpha a_1 k_1 + 8\alpha a_2 k_1 + 4\alpha^2 \beta a_2 + 4\alpha a_2 k_1^2 \right.} \\
&\quad \left. + 8\alpha^2 \beta a_2 k_1 + 4\alpha^2 \beta a_2 k_1^2 + 4\alpha a_1 k_1 k_2) \right)}{\alpha b^2 k_2^2 (\alpha \beta + 2)^3 (k_1 + 1)^3} \tag{S86}
\end{aligned}$$

$$= G_4 + \frac{H_4}{b} + O(b^{-2}), \tag{S87}$$

$$\begin{aligned}
Y_5 &= \frac{\left(a_1 a_2 (\alpha \beta + 1) (4\alpha^4 \beta a_1 k_1 k_2 + \alpha^5 \beta^2 a_1 k_1 k_2 + \alpha^5 \beta^2 a_1 k_1 + 10\alpha^5 \beta^2 a_2 k_1 + 2\alpha^6 \beta^3 a_2 k_1 \right.} \\
&\quad \left. - 4\alpha^3 \beta k_1^2 k_2 - 2\alpha^4 \beta^2 k_1 k_2 - 8\alpha^3 \beta k_1 k_2 + 4\alpha^3 a_1 k_1 k_2 + 8\alpha^4 \beta a_2 k_1^2 + 4\alpha^3 a_1 + 4\alpha^3 a_2 \right. \\
&\quad \left. - 4\alpha^2 k_2 + 4\alpha^3 a_2 k_1^2 - 4\alpha^2 k_1^2 k_2 + 4\alpha^4 \beta a_1 + 8\alpha^4 \beta a_2 + \alpha^5 \beta^2 a_1 + 5\alpha^5 \beta^2 a_2 + \alpha^6 \beta^3 a_2 \right. \\
&\quad \left. - \alpha^4 \beta^2 k_2 + 5\alpha^5 \beta^2 a_2 k_1^2 + \alpha^6 \beta^3 a_2 k_1^2 - \alpha^4 \beta^2 k_1^2 k_2 + 4\alpha^4 \beta a_1 k_1 + 16\alpha^4 \beta a_2 k_1 + 4\alpha^3 a_1 k_1 \right. \\
&\quad \left. + 8\alpha^3 a_2 k_1 - 8\alpha^2 k_1 k_2 - 4\alpha^3 \beta k_2) \right)}{\alpha k_2^2 (\alpha \beta + 2)^3 (k_1 + 1)^3} \\
&+ \frac{\left(a_1 a_2 (\alpha \beta + 1) (\alpha^2 \beta k_2 - 2\alpha^2 a_1 k_1 - 4\alpha^2 a_2 k_1 + 2\alpha k_1^2 k_2 - 2\alpha^2 a_1 - 2\alpha^2 a_2 - \alpha^3 \beta a_1 \right.} \\
&\quad \left. - 3\alpha^3 \beta a_2 + \alpha^2 \beta k_1^2 k_2 - \alpha^4 \beta^2 a_2 k_1^2 - \alpha^3 \beta a_1 k_1 - 6\alpha^3 \beta a_2 k_1 + 2\alpha^2 \beta k_1 k_2 - 2\alpha^2 a_1 k_1 k_2 + 2\alpha k_2 \right. \\
&\quad \left. - \alpha^4 \beta^2 a_2 + 4\alpha k_1 k_2 - 3\alpha^3 \beta a_2 k_1^2 - 2\alpha^4 \beta^2 a_2 k_1 - \alpha^3 \beta a_1 k_1 k_2) \right)}{\alpha b k_2^2 (\alpha \beta + 2)^3 (k_1 + 1)^3} \\
&+ \frac{\left(a_1 a_2 (\alpha \beta + 1) (4\alpha a_1 - 3k_2 + 4\alpha a_2 - 6k_1 k_2 - 3k_1^2 k_2 + 4\alpha a_1 k_1 + 8\alpha a_2 k_1 + 4\alpha^2 \beta a_2 \right.} \\
&\quad \left. + 4\alpha a_2 k_1^2 + 8\alpha^2 \beta a_2 k_1 - 2\alpha^2 a_2 b k_1^2 + 4\alpha^2 \beta a_2 k_1^2 + 4\alpha a_1 k_1 k_2) \right)}{\alpha b^2 k_2^2 (\alpha \beta + 2)^3 (k_1 + 1)^3} \tag{S88}
\end{aligned}$$

$$= G_5 + \frac{H_5}{b} + O(b^{-2}), \tag{S89}$$

Then the growth rate is

$$\lambda = bY_3 \quad (\text{S90})$$

$$= \frac{\left(a_1 a_2 (\alpha\beta + 1) (4\alpha^3 a_1 + 4\alpha^3 a_2 - 4\alpha^2 k_2 + 4\alpha^3 a_2 k_1^2 - 4\alpha^2 k_1^2 k_2 + 4\alpha^4 \beta a_1 + 8\alpha^4 \beta a_2 - 4\alpha^3 \beta k_2 + 4\alpha^3 a_1 k_1 + 8\alpha^3 a_2 k_1 - 8\alpha^2 k_1 k_2 + \alpha^5 \beta^2 a_1 + 5\alpha^5 \beta^2 a_2 + \alpha^6 \beta^3 a_2 - \alpha^4 \beta^2 k_2 - 8\alpha^3 \beta k_1 k_2 + 4\alpha^3 a_1 k_1 k_2 + 8\alpha^4 \beta a_2 k_1^2 + \alpha^5 \beta^2 a_1 k_1 + 10\alpha^5 \beta^2 a_2 k_1 + 2\alpha^6 \beta^3 a_2 k_1 - 4\alpha^3 \beta k_1^2 k_2 - 2\alpha^4 \beta^2 k_1 k_2 + 5\alpha^5 \beta^2 a_2 k_1^2 + \alpha^6 \beta^3 a_2 k_1^2 - \alpha^4 \beta^2 k_1^2 k_2 + 4\alpha^4 \beta a_1 k_1 + 16\alpha^4 \beta a_2 k_1 + 4\alpha^4 \beta a_1 k_1 k_2 + \alpha^5 \beta^2 a_1 k_1 k_2) \right)}{\alpha k_2^2 (\alpha\beta + 2)^3 (k_1 + 1)^3} \\ + \frac{\left(a_1 a_2 (\alpha\beta + 1) (2\alpha k_2 - 2\alpha^2 a_1 - 2\alpha^2 a_2 - \alpha^3 \beta a_1 - 3\alpha^3 \beta a_2 + \alpha^2 \beta k_2 - 2\alpha^2 a_1 k_1 - 4\alpha^2 a_2 k_1 + 2\alpha k_1^2 k_2 - \alpha^4 \beta^2 a_2 - 2\alpha^2 a_2 k_1^2 + \alpha^2 \beta k_1^2 k_2 - \alpha^4 \beta^2 a_2 k_1^2 - \alpha^3 \beta a_1 k_1 - 6\alpha^3 \beta a_2 k_1 + 2\alpha^2 \beta k_1 k_2 - 2\alpha^2 a_1 k_1 k_2 - 3\alpha^3 \beta a_2 k_1^2) \right)}{\alpha b k_2^2 (\alpha\beta + 2)^3 (k_1 + 1)^3} \\ + \frac{\left(a_1 a_2 (\alpha\beta + 1) (3\alpha a_1 - 2k_2 + 3\alpha a_2 - 4k_1 k_2 - 2k_1^2 k_2 + 3\alpha a_1 k_1 + 6\alpha a_2 k_1 + 3\alpha^2 \beta a_2 + 3\alpha a_2 k_1^2 + 6\alpha^2 \beta a_2 k_1 + 3\alpha^2 \beta a_2 k_1^2 + 3\alpha a_1 k_1 k_2 + 4\alpha b k_1 k_2 - 2\alpha^4 \beta^2 a_2 b k_1 - \alpha^3 \beta a_1 b k_1 k_2) \right)}{\alpha b^2 k_2^2 (\alpha\beta + 2)^3 (k_1 + 1)^3} \quad (\text{S91})$$

$$= \lambda_0 - \frac{\lambda_1}{b} + O(b^{-2}). \quad (\text{S92})$$

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