

# Mathematical supplement

## What a description must preserve to compare system responses

Electronic Supplementary Material 1 for Foundations of Science

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### Purpose and conclusion

This reader supplies the assumptions, derivations and constructed comparisons needed to assess the mathematical argument of the accompanying article. In particular, it derives the exact history equation underlying Section 4.4, including its initial-state term. The calculations distinguish a preserved response from a closed dynamics, a calibrated response from an identified mechanism, and an exact invariant from an accurate prediction.

The mathematical implications are conditional deductions using established results. The supplied code and archived outputs support their calculable examples. They do not demonstrate a new theorem, empirical adequacy, biological memory, causal identification or predictive benefit. The later exploratory secondary analysis belongs to Electronic Supplementary Material 2 and is not part of this mathematical archive.

### How to use this supplement

Sections 1–8 develop the essential mathematics and its conditions. Section 9 distinguishes eight constructed attacks and controls from prospective empirical falsifiers. Section 10 maps arguments to portable scripts, archived outputs and source notes. The fifteen article equations retain their article numbering; additional displays use H, O or S labels local to this reader.

All 52 members of the accompanying mathematical archive are preserved byte for byte in materials/. The older notes record successive editorial stages, including earlier equation and source counts. This reader describes the consolidated fifteen-equation package; historical statements are not fresh executions. No scientific script was rerun to prepare this reader. The package was prepared locally and has no assigned repository DOI.

# 1 Response preservation and aggregation

Fix the candidate domain, input schedule  $u$ , horizon  $\tau$  and context  $c$ . The complete specification  $\xi$  may contain initial state and parameters. A retained description  $g$  is sufficient for a specified response  $R$  only if the response is constant on each admitted fiber:

$$g(\xi_A) = g(\xi_B) \Rightarrow R(\xi_A; u, \tau, c) = R(\xi_B; u, \tau, c).$$

Article equation 1

Define the response rule on the image of  $g$  by choosing any representative of a fiber. Constancy makes this choice unambiguous. It does not establish continuity, measurability, practical learnability or coverage of candidates absent from a dataset. Probabilistic use requires appropriate measurable response kernels.

If two candidates have the same description but responses differing by  $\Delta$ , the triangle inequality gives:

$$\max\{|\hat{R} - R_A|, |\hat{R} - R_B|\} \geq \frac{|\Delta|}{2}.$$

Article equation 2

For a nonempty bounded scalar response set  $S$  with  $L=\inf S$  and  $H=\sup S$ , the worst absolute error is  $\max(|L-p|, |H-p|)$ . Endpoint-approaching sequences prove the lower bound even when the endpoints are not attained. The midpoint attains  $(H-L)/2$ , assuming unrestricted scalar predictions. A finite observed range does not bound an entire candidate class.

For a differentiable summary of well-posed controlled dynamics  $x'=f(x,u,c)$ , instantaneous closure requires:

$$Dg(x)f(x, u, c) = F(g(x), u, c).$$

Article equation 3

The derivative must be constant on each fiber, and the target output must also factor through  $g$ . Shared endpoints do not establish closure. Time-varying inputs normally retain their explicit time dependence, unless they disappear from the reduced field or their evolution is separately included.

For the bilinear count  $y_i=o_i e_i$ , a fixed population of  $N$  units satisfies the exact identity:

$$\bar{y} = \bar{o}\bar{e} + \text{Cov}_N(o, e),$$

Article equation 4, with Cov divisor  $N$

$$\text{Cov}_N(o, e) = \frac{1}{N} \sum_i (o_i - \bar{o})(e_i - \bar{e}).$$

This identity describes pairing, not interaction between units. The count model assumes no saturation and fixed efficacy per opportunity; a binary response requires another response law.

## 2 Compartment balances and stationary response

Let  $x_1, x_2$  be nonnegative amounts. The input rates  $U \pm V$  have units of amount/time;  $d \pm \delta$  and  $k$  have units of inverse time. Assume constant known rates  $d > |\delta|$ ,  $k \geq 0$  and nonnegative inputs  $U \geq |V|$ . Conservative exchange and first-order losses give:

$$\begin{aligned}\dot{x}_1 &= U + V - (d + \delta)x_1 - k(x_1 - x_2), \\ \dot{x}_2 &= U - V - (d - \delta)x_2 + k(x_1 - x_2).\end{aligned}$$

Article equation 5, shown in two lines

Set  $s = (x_1 + x_2)/2$  and  $a = (x_1 - x_2)/2$ . Adding and subtracting the balances yields:

$$\dot{s} = U - ds - \delta a, \quad \dot{a} = V - \delta s - (d + 2k)a.$$

Article equation 6

The total stock is  $B = 2s$ , while the exit flow is  $J = (d + \delta)x_1 + (d - \delta)x_2$ . Thus  $B' = 2U - J$ . At equilibrium  $J^* = 2U$  independently of exchange. This is a flow balance, not equality of stock or a demonstrated improvement in biological processing.

Write  $D = d(d + 2k) - \delta^2 > 0$ . Solving the two stationary balances gives:

$$\begin{aligned}s^* &= \frac{(d + 2k)U - \delta V}{D}, \quad a^* = \frac{dV - \delta U}{D}, \\ \frac{\partial s^*}{\partial k} &= \frac{2\delta(dV - \delta U)}{D^2}.\end{aligned}$$

Article equation 7, shown in two lines

The sign is fixed as  $k$  varies with  $d, \delta, U, V$  held fixed: this model has no strict interior exchange optimum. Its eigenvalues are  $-d - k \pm \sqrt{(k^2 + \delta^2)}$ , both negative because  $(d + k)^2 - (k^2 + \delta^2) = D > 0$  and  $d + k > 0$ . Stability and physical nonnegativity are separate conditions.

A standardized redistribution compares two equilibria at  $V = +h$  and  $V = -h$ , with  $U \geq h \geq 0$ :

$$\Delta B^* = B^*(+h) - B^*(-h) = -\frac{4\delta h}{D}.$$

Article equation 8

It is neither a temporal rate nor a change from the basal equilibrium. For a sensor  $y = s + \epsilon a$  with  $|\epsilon| < 1$ , both compartment weights are positive and:

$$\Delta y^* = \frac{2h(\epsilon d - \delta)}{D}.$$

Article equation 9

### 3 Exact contrasts and observation limits

Use reference units  $m$  and  $t_0$ , with  $d=1/t_0$ ,  $U=1 \text{ m}/t_0$  and  $h=1/4 \text{ m}/t_0$ . The following cases are constructed, not samples from a population. Rates are expressed in  $1/t_0$ ,  $V$  in  $m/t_0$ , amounts in  $m$  and  $J$  in  $m/t_0$ .

| Case | $\delta$ | $k$ | Basal $V$ | Basal $(x_1^*, x_2^*)$ | $B^*$ | $J^*$ | $\Delta B^*$ |
|------|----------|-----|-----------|------------------------|-------|-------|--------------|
| A    | 0        | 1   | 0         | (1,1)                  | 2     | 2     | 0            |
| B    | 1/2      | 1   | 1/2       | (1,1)                  | 2     | 2     | -2/11        |
| C    | 1/2      | 0   | 0         | (2/3,2)                | 8/3   | 2     | -2/3         |

Cases A and B share basal amounts but differ in loss rates and basal inputs. Their stock-contrast difference is  $2/11 \text{ m}$ , so any shared prediction has worst absolute error at least  $1/11 \text{ m}$ . This establishes insufficiency of basal amounts within the pair; it does not isolate a single experimental cause called organization.

A stricter pair fixes  $d=U=1$ ,  $\delta=1/2$  and basal  $V=1/2$ , then changes only  $k$  from 0 to 1. Both basal states are (1,1), with inputs  $(3/2, 1/2)$ , loss rates  $(3/2, 1/2)$  and  $J^*=2$ . The imposed contrasts are  $-2/3$  and  $-2/11 \text{ m}$ ; the common minimax error is  $8/33 \text{ m}$ . Net exchange is zero at the shared basal state, so these data do not determine the exchange rate. A tracer measurement could separate bidirectional transfers.

#### Cancellation is not the same as unobservability

At  $\varepsilon=\delta/d$ , the sensor is  $y=(ds+\delta a)/d=J/(2d)$ , hence  $y^*=U/d$ . Its stationary contrast cancels because it measures a flow-proportional combination. For the state  $(s,a)$ , system matrix  $M$  and observation row  $C=(1,\varepsilon)$ :

$$M_{11} = -d, \quad M_{12} = M_{21} = -\delta, \quad M_{22} = -(d + 2k).$$

O1,  $C=(1,\varepsilon)$  and observability matrix  $O$  has rows  $C$  and  $CM$

$$\det O = \delta(\varepsilon^2 - 1) - 2k\varepsilon.$$

O2

At the cancelling  $\varepsilon=\delta/d$  this determinant is  $-\delta D/d^2$ , nonzero for  $\delta \neq 0$ . An ideal trajectory can therefore reconstruct state with known rates and inputs, despite zero stationary contrast. Conversely, case B at  $\varepsilon=2-\sqrt{5}$  has zero determinant but nonzero stationary contrast  $(3-2\sqrt{5})/11 \text{ m}$ . Neither implication holds in general. Ideal rank does not guarantee precision with noise or identification of unknown parameters.

## 4 Exact projected history

The complete compartment system is first order and instantaneous in its full two-dimensional state. History enters the total-only equation when the influential coordinate  $a$  is eliminated. This derivation is supplied in MULTISCALE\_COHERENCE.md and is the mathematical basis of article Section 4.4; it is included here in full.

For fixed known rates, let  $\gamma = d + 2k > 0$  and  $D = d\gamma - \delta^2 > 0$ . Allow admissible time-dependent inputs  $U(t) \geq |V(t)|$ , locally integrable so the first-order solution is well defined. Let  $a_0 = a(0)$ . The contrast equation is:

$$\dot{a} + \gamma a = V(t) - \frac{\delta}{2} B(t).$$

H1

Multiply by  $\exp(\gamma t)$ , integrate from 0 to  $t$  and divide by  $\exp(\gamma t)$ . Variation of constants gives the exact contrast:

$$a(t) = e^{-\gamma t} a_0 + \int_0^t e^{-\gamma(t-\tau)} [V(\tau) - \frac{\delta}{2} B(\tau)] d\tau.$$

H2

Substitute H2 into  $B' = 2U - dB - 2\delta a$ . The resulting total-only relation is:

$$\begin{aligned} \dot{B}(t) = & 2U(t) - dB(t) - 2\delta e^{-\gamma t} a_0 \\ & - 2\delta \int_0^t e^{-\gamma(t-\tau)} V(\tau) d\tau \\ & + \delta^2 \int_0^t e^{-\gamma(t-\tau)} B(\tau) d\tau. \end{aligned}$$

H3, displayed over three lines

The kernel on  $B$  has the positive coefficient  $\delta^2$ ; the input-split term has coefficient  $-2\delta$ . Every term in H3 has units of amount/time. The initial-state term cannot generally be omitted. Its value must be known, inferred with uncertainty, or its effect explicitly bounded. The exponential factor uses the relaxation rate of the eliminated coordinate conditional on its driving terms; feedback means  $\gamma$  need not be the slowest rate of the complete system.

In reference units  $d=U=k=1$ ,  $\delta=1/2$  and  $V=0$ , the initial states  $(2,0)$ ,  $(1,1)$  and  $(0,2)$  all have  $B=2$  but  $B'$  equal to  $-1, 0, +1$ . A first-order instantaneous total cannot encode these distinct initial slopes over that full state domain. Restrictions on initial states can change the domain, but do not establish closure over the omitted states.

H3 does not establish biological storage, adaptation, causality from observed histories or an irreducible organism-level memory. Retaining the internal coordinate, a suitable history, or explicit uncertainty are alternative representations of the same omitted distinction.

## 5 Higher order equations and initial compatibility

When  $U$  is differentiable on an interval, differentiate  $B' = 2U - dB - 2\delta a$ , substitute  $a' = V - \delta B/2 - \gamma a$ , and eliminate  $a$ . The exact second-order input-output equation is:

$$\ddot{B} + 2(d + k)\dot{B} + DB = 2\dot{U} + 2(d + 2k)U - 2\delta V. \quad \text{H4}$$

Every term has units of amount/time<sup>2</sup>. For piecewise bounded schedules, apply H4 on each smooth interval. At a bounded step  $\Delta U$ ,  $B$  is continuous and  $B'$  jumps by  $2\Delta U$ . A step  $\Delta V$  from equilibrium with  $U$  unchanged instead gives  $B'(0+) = 0$  and  $B''(0+) = -2\delta\Delta V$ . Treating a finite-window measurement as equilibrium requires a justified settling criterion.

For  $\delta \neq 0$ , known parameters and  $U$  allow reconstruction:

$$a = \frac{2U - dB - \dot{B}}{2\delta}, \quad s = \frac{B}{2}. \quad \text{H5}$$

Thus retaining  $(B, B')$  restores two state coordinates; it is not dimensional reduction. An input-independent state coordinate  $q = B' - 2U$  gives the equivalent driven system:

$$\dot{B} = 2U + q, \quad \dot{q} = -2(d + k)q - DB - 2dU - 2\delta V. \quad \text{H6}$$

The transformation  $(s, a) \rightarrow (B, q)$  has determinant  $-4\delta$ . Differentiating noisy measurements can amplify error, and reconstruction becomes sensitive as  $\delta$  approaches zero. No estimator or precision guarantee is supplied.

At  $\delta = 0$  the physical total already obeys  $B' = 2U - dB$ . H4 becomes:

$$\left(\frac{d}{dt} + \gamma\right)(\dot{B} + dB - 2U) = 0. \quad \text{H7}$$

It permits an extra residual  $E(t) = E(0)\exp(-\gamma t)$  unless  $B'(0) = 2U(0) - dB(0)$ . For  $d = k = 1$  and  $U = V = 0$ ,  $B(t) = \exp(-t) - \exp(-3t)$  solves H4 with  $B(0) = 0$ ,  $B'(0) = 2$ , but cannot be the physical total starting from zero nonnegative compartment amounts. Initial compatibility removes this spurious mode.

For  $\delta \neq 0$ , nonnegative initial amounts require  $B_0 \geq 0$  and  $|a_0| \leq B_0/2$ , equivalently:

$$|2U_0 - dB_0 - \dot{B}_0| \leq |\delta|B_0. \quad \text{H8}$$

The compatible state and input maps must also be declared when composing representations. At  $\delta = 0$ ,  $(x_1, x_2) \rightarrow (s, a)$  with inputs  $(u_1, u_2) \rightarrow (U, V)$ , followed by  $B = 2s$  with input  $2U$ , preserves total dynamics. Composition is valid only on the domain where both relations hold; a diagram alone is not a proof of multiscale biological coherence.

## 6 Calibration preserves a response within its domain

For  $x' = u - Lx$ , assume a positive, asymptotically stable linear compartment system with conservative transfers and nonnegative losses.  $L$  is invertible. The stationary total  $B^* = \mathbf{1}^T x^*$  is linear in  $u$ , and its response vector has units of time:

$$B^*(u + v) - B^*(u) = \mathbf{r}^T v, \quad \mathbf{r} = L^{-T} \mathbf{1}, \quad \mathbf{1}^T v = 0.$$

Article equation 11

The inverse transpose is essential when  $L$  is nonsymmetric. Since the integral of  $\exp(-Lt)$  from zero to infinity is  $L^{-1}$ ,  $r_i$  equals the integrated retained fraction of a unit pulse entering compartment  $i$ . This operational response need not identify individual exchange and loss rates.

If probe directions are columns of  $P$ , exact contrasts identify  $P^T r$ . For  $v = P\alpha$ , linearity predicts  $r^T v = \alpha^T P^T r$ . Outside  $\text{span}(P)$ , the measured probes alone do not fix the response; additional justified restrictions may do so. With fixed total input only the projection on  $\ker(\mathbf{1}^T)$  matters. Adding  $c\mathbf{1}$  leaves redistributions unchanged, while a basal observation at nonzero total can determine this offset for absolute responses.

The two parameter triples  $(d, \delta, k) = (1, 1/2, 0)$  and  $(5/4, 1, 3/8)$  both give  $B^*(U, V) = 8U/3 - 4V/3$  for every admissible stationary input. At  $U=1, V=0$ , both also give  $x^* = (2/3, 2)$ . After a step  $\Delta V$ , their initial total curvatures are  $-\Delta V$  and  $-2\Delta V$ ; at  $\Delta V = 1/4$  these are  $-1/4$  and  $-1/2$  m/to<sup>2</sup>. Complete stationary calibration of this total does not establish temporal equivalence.

A three-compartment constructed pair has response vectors  $(1, 2, 3)$  and  $(2, 3, 1)$ . Both give basal total 6 at  $u_0 = (1, 1, 1)$  and derivative  $-1$  along  $v_1 = (1, -1, 0)$ . Along  $v_2 = (0, 1, -1)$  the derivatives are  $-1$  and  $2$ . The admissible contrasts  $u_0 \pm v_2/4$  are  $-1/2$  and  $1$ : a common prediction from the matched basal and  $v_1$  data has worst error at least  $3/4$ . The physical matrices and checks are retained in `RESPONSE_GEOMETRY.md` and its script.

A channel  $y = w^T x$  calibrates  $L^{-T} w$ , not the true-total vector unless the observation map is independently justified. Full rank is an ideal condition; stipulated zero-mean channel error with covariance  $\Sigma$  gives reading variance  $\alpha^T \Sigma \alpha$ , which can differ greatly between equally sized directions.

Held-out directions test coverage, held-out amplitudes test fixed linear response and time-resolved tests examine transfer to a finite horizon. Nonnegative inputs constrain admissible changes; at a boundary they may form a cone. Saturation, changing rates or weights, and nonlinear curvature can invalidate extrapolation. These are proposed tests, not empirical results.

## 7 Information and target dependent summaries

Let  $X, Y, Z_1, Z_2$  be finite random variables under the same joint distribution, with  $Z_1 = g_1(X)$  and  $Z_2 = g_2(Z_1)$ . Logarithms have base two and information is in bits. Apply the chain rule at each deterministic summary:

$$I(X; Y) - I(Z_2; Y) = I(X; Y \mid Z_1) + I(Z_1; Y \mid Z_2).$$

Article equation 10

The two terms are nonnegative probability-weighted conditional divergences. The code checks finite tables using entropy and probability-ratio calculations separately. Zero loss means conditional independence on the positive-probability support; it does not cover candidates excluded from that support or certify that measured  $X$  exhausts relevant variables. Dynamical closure is a separate requirement.

For independent fair bits  $A, B$  and target  $Y = A \text{ XOR } B$ , each bit alone gives zero information while the joint pair gives one bit. Yet  $M = A + B$  retains  $Y$  through  $Y = M \bmod 2$ . This example needs linked information but admits a smaller readout. It does not require all records or the entire organism. For target  $A$ , the nested sequence  $(A, B) \rightarrow A + B \rightarrow (A + B) \bmod 2$  instead has mutual information  $1, 1/2, 0$  bits.

Identical copies of a target are redundant in the exact noiseless example. Independent bits predicting separate target components add information without joint-only synergy. A net joint-minus-individual difference can be zero while duplicated and joint-only components coexist. No general partial information decomposition or biological decoder is fitted in this package. Repeated noisy measurements require their own noise model.

### Predictability does not identify intervention effects

One model has independent fair exogenous  $U, V$  and endogenous  $A = U, B = V, Y = A \text{ XOR } B$ . Another has independent fair  $U, Q$  and endogenous  $A = U, Y = Q, B = A \text{ XOR } Y$ . They produce the same observational table of  $(A, B, Y)$ . Replacing the source equations by  $\text{do}(A=0, B=0)$  gives  $Y=0$  in the first and fair  $Y=Q$  in the second. Identical observational information cannot distinguish these effects.

### A geometric invariant omits a varying scale

For an ideal Euclidean circle, physical dilation  $r \rightarrow \lambda r$  with  $\lambda > 0$  preserves  $C/D = \pi$ , while circumference and area scale by  $\lambda$  and  $\lambda^2$ . Two radii sharing that ratio differ in circumference by  $2\pi|r_2 - r_1|$ . Equation 2 therefore gives a common worst-error lower bound  $\pi|r_2 - r_1|$ . Retaining radius repairs this geometric target; material mass needs additional variables. A fixed constant carries no information about the varying target merely because its decimal representation is long.

These finite comparisons distinguish mathematical reduction, association and causation. No empirical PID, biological mechanism or need for unrestricted complexity is demonstrated.

## 8 Change and prediction error

For constant finite-dimensional real generators  $A, A_r$  and a fixed dimensionally compatible summary  $P$ , induction gives  $PA^n = A_r^n P$ . The convergent matrix-exponential series then proves the forward identity below; differentiating at zero proves its converse:

$$PA = A_r P \Leftrightarrow P e^{tA} = e^{tA_r} P \quad \forall t.$$

Article equation 12

For driven systems  $x' = Ax + Hu$  and  $z' = A_r z + H_r u$ , the common input additionally requires  $PH = H_r$ . A target output must factor through  $P$ . Exact correspondence of specified models does not show that either model describes nature.

For  $J(q,p) = (-p,q)$ ,  $J^2 = -I$  and  $\exp(\theta J) = I \cos \theta + J \sin \theta$ . Multiplying the matrices yields the Cayley step:

$$C_h = (I - hJ/2)^{-1}(I + hJ/2) = R_{2\arctan(h/2)},$$

$$C_h^T C_h = I.$$

Article equation 13, shown in two lines

The quadratic norm is exact, but the angle per step is  $2 \arctan(h/2)$  rather than  $h$ . After  $N$  steps, the phase deficit is  $N[h - 2 \arctan(h/2)]$ , and a unit-radius position error is twice the absolute sine of half this deficit. At fixed  $T = Nh$  its leading phase deficit is  $Th^2/12$ . This is a linear-oscillator statement, not exact energy preservation for nonlinear Hamiltonian systems. Increasing horizon at fixed  $h$  and reducing  $h$  at fixed horizon are different comparisons.

For admitted discrete trajectories, suppose the one-step defect is uniformly at most  $\varepsilon$  and the reduced map  $\Psi$  is  $\ell$ -Lipschitz on all compared summary pairs. Adding and subtracting  $\Psi(g(x_n))$  gives:

$$e_{n+1} \leq \varepsilon + \ell e_n, \quad e_N \leq \ell^N e_0 + \varepsilon \sum_{j=0}^{N-1} \ell^j.$$

Article equation 14

Induction proves the bound. Both trajectories must remain in the stated domain through  $N$  steps and use the same specified input. For successive representation maps with defects  $\varepsilon_1, \varepsilon_2$  and second summary  $K$ -Lipschitz, the composite defect is at most  $K\varepsilon_1 + \varepsilon_2$ .  $K$  transforms sensitivity and units between descriptions; it differs from temporal amplification  $\ell$ .

A preserved invariant is not the requested response. A local error bound is not automatically a small accumulated error, and a finite Taylor calculation does not establish an infinite series outside its convergence assumptions. `CHANGE_ERROR.md` gives the analytic arguments rather than treating finite computational checks as all-order proofs.

## 8 Continued Conditional risk and biological units

Let  $W$  be square-integrable predictors,  $Z$  a function of  $W$ , and  $Y$  a square-integrable target under the same population distribution and squared loss. Write  $m_W = E[Y|W]$  and  $m_Z = E[Y|Z]$ . The tower property gives  $E[m_W|Z] = m_Z$ . Expanding  $Y - m_Z = (Y - m_W) + (m_W - m_Z)$  leaves a zero cross term, because the second factor is  $W$ -measurable:

$$\begin{aligned}\mathcal{R}_Z - \mathcal{R}_W &= E[(m_W - m_Z)^2] \geq 0, \\ \mathcal{R}_W &= E[(Y - m_W)^2].\end{aligned}$$

Article equation 15, shown in two lines

This identity concerns optimal population conditional means. A finite fitted predictor can perform worse after adding variables. Equal conditional means need not imply equal conditional distributions, and finite inconclusive performance does not demonstrate sufficiency or equivalence. Distribution shift, estimation error and different losses require separate comparisons.

In the supplied eight-atom example, the detailed optimal risk is  $15/4$ , the summarized risk is  $19/4$  and the conditional-mean information loss is 1. A control preserves both risks at  $15/4$  while changing conditional laws. No estimator is fitted. For four equally likely cardinal unit vectors  $W$ , norm  $Z=1$  omits the first coordinate after a known rotation: full optimal risk is zero, summarized risk is  $1/2$ . The risk remains invariant, even though the discrete population is not invariant under every rotation.

### A precise mean is not the response of a new unit

In the balanced model  $X_{ji} = \mu + U_j + \eta_{ji}$ ,  $m$  independent preparations each contribute  $k$  individuals. Let preparation effects and individual errors be mutually independent, zero-mean, with variances  $\tau^2$  and  $\sigma^2$ . Averaging gives:

$$\text{Var}(\bar{X}) = \frac{\tau^2}{m} + \frac{\sigma^2}{mk}.$$

S1 variance example

More individuals per preparation reduce the second component but do not remove the first. This variance concerns estimating  $\mu$ , not predicting a new individual. With dependence, covariance and the actual sampling structure must be specified; number of cells is not number of independent donors or preparations.

The article's repeated-efferocytosis comparison is prospective. Its target is new uptake after the second exposure, per phagocyte alive before the first; survival, absolute counts, adhesion and processing remain separate observables. Donors or independent preparations govern the holdout. Histories must be measured before prediction begins. Better observational prediction would not by itself identify the causal effect of an assigned history.

The synthesis has not been tested against a conventional workflow for incremental usefulness. Negative or inconclusive results remain admissible outcomes, and retaining a simpler description can be a decision under stated costs and error tolerances rather than evidence of its adequacy.

## 9 Falsification attempts and controls

The eight constructed attacks below were developed after the manuscript examples. They are exploratory stress tests, not preregistered empirical evidence. PASS in the archived JSON means that a specified construction was reproduced. It is neither an exhaustive search for contradictions nor biological validation.

### 1 An enriched basal description can still omit exchange

Fixing basal amounts, inputs and losses still fails for the exchange-only pair of Section 3: the shared basal state masks  $k$ , while the fixed redistribution produces contrasts  $-2/3$  and  $-2/11$ . This defeats a universal repair based only on those basal measurements. A tracer or an appropriate perturbation can distinguish transfer despite zero net basal exchange.

### 2 Individual stability does not bound an entire class

Take  $d=U=1$ ,  $k=0$  and basal  $V=\delta$ , with  $0<\delta<1$  and  $h=1/4$ . Every system has basal state  $(1,1)$ , but  $\Delta B^*=-\delta/(1-\delta^2)$  tends to minus infinity as  $\delta$  tends to 1. Each member is stable; its slow rate approaches zero. A finite pairwise lower bound is not a uniform error ceiling. At any fixed finite time  $t$  the contrast tends instead to  $2h[(1-\exp(-2t))/2-t]$ , which is finite. This contrast respects the distinction between equilibrium and finite horizon.

### 3 Changing a count into a binary outcome reverses the result

Efficiencies  $(1,1/3)$  paired with opportunity counts  $(1,3)$  versus  $(3,1)$  yield mean unsaturated counts 1 and  $5/3$ . If independent opportunities permit at most one retained response, the relevant law is  $1-(1-e)^o$  and the means are  $23/27$  and  $2/3$ : the second-minus-first contrast is  $-5/27$ . No between-unit interaction exists in either construction. The rival changes the target and capacity assumptions, not the algebra of the original count model.

### 4 A covariance repair is target specific

Efficiencies  $(0,1/2,1)$  paired with opportunity means  $(1,3,2)$  or  $(2,1,3)$  preserve both marginal sets, covariance  $1/6$  and mean count  $7/6$ . With independent Poisson opportunities, the probability of at least one event is  $1-\exp(-oe)$ ; its population means are about 0.547178 and 0.447894. Means and covariance repair the bilinear count, not every nonlinear outcome.

A counterexample outside a conditional claim's premises is a rival prediction, not a refutation of that conditional implication. A new target, summary or domain states a new claim; it does not retroactively restore a failed original claim.

## 9 Continued Observation and empirical falsifiers

### 5 Ideal rank does not ensure robust reconstruction

In dimensionless reference coordinates,  $d=k=1$  and  $\varepsilon=\delta$  give an observability determinant  $-\delta(3-\delta^2)$ , nonzero for  $0<\delta<1$ . The numerical condition number grows from about 666.67 at  $\delta=10^{-3}$  to about 666666.67 at  $\delta=10^{-6}$ . These values depend on coordinate and time scaling; they are not unit-independent precision thresholds or measured instrument noise. Unknown parameters are a separate identification problem.

### 6 An exchange cost permits an interior optimum

If exchange also changes  $d(k)=1+k/20$ , with  $\delta=1/2$ ,  $U=1$  and  $V=3/4$ , the stationary total becomes  $20(82k+25)/(41k^2+840k+300)$ . It has a unique positive maximum at  $(5\sqrt{313}-25)/82$ , approximately 0.774. This cost rival violates the original held-fixed loss assumption; it does not contradict its monotonicity formula. An interior optimum with independently verified fixed rates, inputs and measurement would challenge the original prediction.

### 7 Prospective tests separate balances from independent evidence

At fixed  $d, \delta, k, U$  and admissible  $V$ , the linear model predicts  $B^*(V+h)+B^*(V-h)-2B^*(V)=0$ . Reproducible curvature beyond uncertainty challenges it only after the held-fixed regime and equilibrium are checked. Independently measured flow can test  $J=(d+\delta)x_1+(d-\delta)x_2$  and  $J^*=2U$ . Defining  $J$  from the balance and recovering that balance is not an independent test of the loss law.

For the cancelling sensor  $\varepsilon=\delta/d$  and branches with common  $U$ , the balance gives  $\Delta y(t)=-\Delta B'(t)/(2d)$ . If the branches converge, integration gives:

$$\int_0^\infty \Delta y(t) dt = \frac{\Delta B(0) - \Delta B^*}{2d}.$$

F1 prospective sensor prediction

With equal initial totals, case B predicts 1/11 in reference amount×time units. A truly null sensor trajectory with an independently measured nonzero retention contrast contradicts the combined model, input and sensor assumptions under these conditions. It does not uniquely identify which premise failed. This prediction has not been tested empirically.

### 8 Controls where a simple summary succeeds

A linear response  $2+3b$  gives identical mean output for burdens (0,2) and (1,1). Constant efficiency 1/2 eliminates the opportunity-pairing difference. Equal losses and conservative exchange close the total. These controls defeat demanding distribution, pairing or exchange detail for every question.

A prospective utility study would reserve cases, specify a conventional competitor, give both strategies equal resources, and assess unjustified conclusions, discriminating contrasts and costs independently. No such study was performed. Unnecessary measurements, false causal attribution or no incremental benefit remain possible outcomes.

## 10 Reproducible map and archived evidence

Extract ESM\_1.zip into a new working directory. The folder materials/ contains the complete original scientific archive. The seven saved result files report PASS for their recorded constructions; these are historical execution receipts, not executions performed for this PDF. Mathematical reasoning and explicit assumptions remain necessary because rerunning code can reproduce an implementation error.

| Argument and source note                                     | Script                         | Archived output                   |
|--------------------------------------------------------------|--------------------------------|-----------------------------------|
| Balances, sensors, pairings;<br>MATHEMATICAL_VERIFICATION.md | verification.py                | verification_results.json         |
| Finite exchange-only contrast                                | verify_exchange_contrast.py    | exchange_contrast_results.json    |
| Eight attacks; FALSIFICATION_TESTS.md                        | falsification_tests.py         | falsification_results.json        |
| Information and scale;<br>INFORMATION_AND_SCALE.md           | verify_information_scale.py    | information_scale_results.json    |
| Calibration; RESPONSE_GEOMETRY.md                            | verify_response_geometry.py    | response_geometry_results.json    |
| History and compatibility;<br>MULTISCALE_COHERENCE.md        | verify_multiscale_coherence.py | multiscale_coherence_results.json |
| Error and risk; CHANGE_ERROR.md                              | verify_change_error.py         | change_error_results.json         |

The main verification records 62 named checks; history and compatibility record 22; response geometry 40; change and error 34. These counts identify the saved outputs and are not scores for scientific quality. All result files remain unchanged. Source notes preserve historical revisions and access limits; EQUATIONS.md supplies the fifteen editable article equations.

### Commands for a fresh mathematical reproduction

Use a new Python environment with the supplied requirements.txt. The recorded environment is Python 3.10.20, NumPy 2.2.6, SymPy 1.14.0 and Matplotlib 3.10.8; these are recorded versions, not a claim that every other version fails. No empirical dataset is needed.

```
cd materials
python -m pip install -r requirements.txt
python run_all.py
```

run\_all.py invokes the seven scientific checks and the figure generators. generate\_figures.py rebuilds Figures 2–3, generate\_roadmap.py Figure 1, and verify\_change\_error.py --figure-dir . Figure 4, in EN/ES formats. For individual checks, invoke the corresponding script above from materials/. Runs overwrite their local result files, so use an extracted working copy. The stored ZIP is not a write target.

Exact identities and rational values are distinguished from finite-precision matrix and conditioning comparisons. JSON timestamps and PDF/SVG metadata need not be byte-identical on reproduction. The archived pixel figures and symbolic result values provide the intended comparison; a new environment should record any difference rather than rewriting the delivered evidence.

## 11 Provenance and scope of source support

The derivations in this reader consolidate the author's mathematical notes and preserved code. The archive contains no original empirical dataset, private institutional source, full published paper or new scientific run. Figures 1–4 are author-created schematics or model calculations. Source-reading records identify material actually consulted and limitations; their existence is not evidence of complete reading or independent verification of all references.

Selected antecedents support the distinctions used in the accompanying article. The list below is a compact orientation; the full bibliography is in the principal manuscript and the historical 28-source access record is `materials/references_access.json`. Bibliographic metadata and bounded passage access must be distinguished from full-text review.

Li G, Rabitz H (1989). A general analysis of exact lumping in chemical kinetics. *Chemical Engineering Science* 44:1413–1430. [https://doi.org/10.1016/0009-2509\(89\)85014-6](https://doi.org/10.1016/0009-2509(89)85014-6)

Rasmussen M, Hastings A, Smith MJ, Agosto FB, Chen-Charpentier BM, Hoffman FM, Jiang J, Todd-Brown KEO, Wang Y, Wang YP, Luo Y (2016). Transit times and mean ages for nonautonomous and autonomous compartmental systems. *Journal of Mathematical Biology* 73:1379–1398. <https://doi.org/10.1007/s00285-016-0990-8>

Williams PL, Beer RD (2010). Nonnegative Decomposition of Multivariate Information. Preprint, arXiv:1004.2515. <https://arxiv.org/abs/1004.2515>

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Raue A, Kreutz C, Maiwald T, Bachmann J, Schilling M, Klingmüller U, Timmer J (2009). Structural and practical identifiability analysis of partially observed dynamical models by exploiting the profile likelihood. *Bioinformatics* 25:1923–1929. <https://doi.org/10.1093/bioinformatics/btp358>

Hairer E (2010). Geometric Numerical Integration. Lecture 2: Symplectic integrators. TU München, January–February 2010. Author lecture notes. [https://unige.ch/~hairer/poly\\_geoint/week2.pdf](https://unige.ch/~hairer/poly_geoint/week2.pdf)

Lazic SE, Clarke-Williams CJ, Munafò MR (2018). What exactly is ‘N’ in cell culture and animal experiments? *PLOS Biology* 16(4):e2005282. <https://doi.org/10.1371/journal.pbio.2005282>

Wolpert D, Libby E, Grochow JA, DeDeo S (2017). The Many Faces of State Space Compression. In: Walker SI, Davies PCW, Ellis GFR, editors. *From Matter to Life: Information and Causality*. Cambridge University Press, pp. 199–243. <https://doi.org/10.1017/9781316584200.010>

### Interpretation limits

Response factorization, scalar minimax, closure, information identities and conditional risk use established mathematical ideas. Constructed counterexamples can defeat a specified stronger reading without establishing how common its failure is in nature. Calibration can preserve an admitted response without identifying every rate; it does not certify responses outside its span or horizon. No claim of universal reduction, new theorem, empirical biological coherence, clinical efficacy or measured improvement of scientific decisions follows from these files.

The main article's contribution is the critical comparison of conditional choices: retain a consequential distinction, calibrate the required response, or change the observation. Its conceptual interest and originality remain matters for comparison with the relevant literature and editorial assessment; computational PASS does not settle them.

This reader was prepared as a journal-facing explanation of existing material. All scientific source members in `materials/` remain byte-identical to the supplied Supplement S1 copy. The root manifest records their hashes and those of the reader and README. The derivative packaging has not been submitted or deposited by this operation.