


Thermodynamic circuits: Modeling chemical reaction networks with nonequilibrium conductance matrices

Paul Raux ^{1,2} Christophe Goupil ² and Gatien Verley ¹

¹*Université Paris-Saclay, CNRS/IN2P3, IJCLab, 91405 Orsay, France*

²*Université Paris Cité, CNRS, LIED, F-75013 Paris, France*

 (Received 20 December 2024; revised 27 June 2025; accepted 5 August 2025; published 2 September 2025)

We derive the nonequilibrium conductance matrix for open stationary chemical reaction networks (CRNs) described by a deterministic mass action kinetic equation. As an illustration, we determine the nonequilibrium conductance matrix of a CRN made of two pseudolinear subnetworks, called chemical modules, in two different ways: First by computing the nonequilibrium conductances of the modules that are then serially connected and second by computing the nonequilibrium conductance of the CRN directly. The two approaches coincide, as expected from our theory of thermodynamic circuits.

DOI: [10.1103/PhysRevE.112.034112](https://doi.org/10.1103/PhysRevE.112.034112)

I. INTRODUCTION

Open chemical reaction networks (CRNs) are paradigmatic examples of complex out-of-equilibrium systems. In recent decades, they have attracted long-standing attention as they combine the theory of graphs and hypergraphs [1–3], dynamical systems theory [4,5], and thermodynamics [6–8]. Chemical reaction networks are of various complexity, from pseudolinear dynamics highly similar to Markov jump processes [9] to nonlinear dynamics with interacting species (beyond interaction through chemical reactions only) [10], passing by complex balance dynamics for deficiency zero CRNs [11]. Given their complexity, the circuit decomposition of CRNs is appealing to simplify the study of each chemical module separately. Once characterized, each chemical module can be reused in other CRNs without further studies, while the global investigation of a CRN requires one to restart from scratch upon any minor modification of the network. An existing circuit approach relies on chemical modules modeled by current-concentration characteristics [12]. In the latter work, constraints on internal species are dealt with the help of emergent cycles [13], i.e., a set of reactions that upon completion do not change the internal concentrations, but only transfer matter between chemostats. Moreover, couplings between chemical currents are not at the core of this theory, although they significantly constrain the efficiency of chemical transduction [14–17].

In the present work we extend our thermodynamic circuit theory (see Ref. [18]) to circuits of chemical modules. The description of chemical modules by nonequilibrium conductance matrices combines the simplification of circuit decomposition with the ability to extend the notion of coupling between reaction currents to the level of matter currents exchanged with the chemostats. Additionally, nonequilibrium resistance or conductance matrices provide a model for chemical transduction within irreversible thermodynamics that accounts for chemical currents coupling. Therefore, energy conversion (e.g., thermoelectric [19]) and chemical transduc-

tion are essentially studied on the same footing, illustrating the universality of concepts in the physics of conversion processes.

The paper is organized as follows. In Sec. II we derive the nonequilibrium resistance or conductance matrices at various levels of description of the open CRN. We start by recalling the theory of chemical kinetics, emphasizing its thermodynamic consistency [13]. Then, given their prominence in our work, we determine the conservation laws relating the chemostat currents, i.e., the physical currents corresponding to matter received by the CRN from the chemostats. This approach transfers Schnakenberg's decomposition of reaction currents on cycle currents [1] to a higher level where physical currents are decomposed on fundamental currents [18]. This allows for an effective description of the stationary CRN that does not rely on emergent cycles [12,13]. Instead, we consider conservation laws of physical currents (i.e., from chemostats). This simple change of viewpoint makes easier the connection with our theory of thermodynamic circuits and has greater similarity to the framework of Markov jump processes. In Sec. III we illustrate the calculation of the chemical nonequilibrium conductance matrix on the two first chemical modules appearing in Ref. [12]. Then we provide two derivations of the nonequilibrium conductance matrix of the CRN built upon their serial association. First, we apply our law of resistance addition for serial association of thermodynamic devices. Second, we derive the nonequilibrium conductance matrix directly for the whole network.

II. CHEMICAL NONEQUILIBRIUM CONDUCTANCE MATRIX

In this section we set the notation by recalling the thermodynamics of CRNs [13]. Whenever possible, we make a connection with stationary Markov jump processes as studied in the first section of Ref. [18]. In the same spirit, we review the description of conservation laws and conserved quantities existing in closed and opened CRNs. Finally, we build the

nonequilibrium conductance matrix describing the current-force characteristics of a CRN.

A. Chemical kinetics

We describe a chemical reaction network by a set of chemical species Z_α of concentration $[Z_\alpha]$, identified by $\alpha \in \mathcal{S} = \{1, 2, \dots, |\mathcal{S}|\}$, which are transformed by chemical reactions denoted by the index $\rho \in \mathcal{R} = \{1, 2, \dots, |\mathcal{R}|\}$. Each reaction ρ is arbitrarily oriented, is assumed to be reversible, and follows a chemical equation of the form

$$\sum_{\alpha \in \mathcal{S}} \nabla_{\alpha, \rho}^+ Z_\alpha \xrightleftharpoons[k_\rho^-]{k_\rho^+} \sum_{\alpha \in \mathcal{S}} \nabla_{\alpha, \rho}^- Z_\alpha \quad (1)$$

where $\nabla_{\alpha, \rho}^+$ ($\nabla_{\alpha, \rho}^-$) is the number of molecules α consumed (produced) for a given forward reaction ρ [8]. The evolution of the concentrations of species α follows the kinetic equation

$$\frac{d[\mathbf{Z}]}{dt} = \nabla \mathbf{j} + \mathcal{I}, \quad (2)$$

where $[\mathbf{Z}]$ is the concentration vector of components $[Z_\alpha]$, ∇ the stoichiometric matrix of components $\nabla_{\alpha, \rho} = \nabla_{\alpha, \rho}^- - \nabla_{\alpha, \rho}^+$, \mathbf{j} the vector of reaction currents, and \mathcal{I} the currents exchanged with the chemostats. We remark that Eq. (2) is a continuity equation for the species concentrations analogous to the master equation describing Markov processes. In this analogy, the species concentrations correspond to state probabilities, the stoichiometric matrix ∇ to the incidence matrix of the graph of the Markov jump process, and the reaction currents \mathbf{j} to the edge probability currents. The source term \mathcal{I} appears in the kinetic equation, but not in the master equation. This term is required to have fixed concentration of the external species. There is no such term for Markov jump processes: The reservoir constrains the transition rates and not the state occupancy directly. Another difference is that the master equation ruling the time evolution of the state probability for Markov jump processes is linear, while the kinetic equation ruling the time evolution of the concentrations can be nonlinear.

Assuming the mass action law, the reaction fluxes read

$$j_\rho \equiv k_\rho^+ [\mathbf{Z}]^{\nabla_\rho^+} - k_\rho^- [\mathbf{Z}]^{\nabla_\rho^-} \quad (3)$$

where we denote by k_ρ^\pm the kinetic rates and by ∇_ρ^\pm the ρ th column of matrix ∇^\pm . We use the notation $\mathbf{x}^y = \prod_\alpha x_\alpha^{y_\alpha}$. The kinetic rates are chosen according to the local detailed balance [9]

$$RT \log \frac{k_\rho^+}{k_\rho^-} = -[\nabla^T \boldsymbol{\mu}^0(T)]_\rho, \quad (4)$$

where ∇^T is the transpose of the stoichiometric matrix, $\boldsymbol{\mu}^0$ the column vector of standard chemical potential for species in \mathcal{S} , T the temperature of the isothermal CRN, and R the perfect gas constant. In other words, local detailed balance relates the dynamics to thermodynamics, i.e., kinetic rates to standard chemical potentials. It does so in order to ensure dynamically consistent equilibrium or stationary nonequilibrium states. We define the force conjugated to the reaction currents

j_ρ as

$$f_\rho \equiv RT \log \frac{k_\rho^+ [\mathbf{Z}]^{\nabla_\rho^+}}{k_\rho^- [\mathbf{Z}]^{\nabla_\rho^-}} = -(\nabla^T \boldsymbol{\mu})_\rho = -\Delta_\rho G, \quad (5)$$

where the vector $\boldsymbol{\mu}$ gathers the chemical potential of the species in \mathcal{S} and $\Delta_\rho G$ is the Gibbs free energy change caused by reaction ρ . The component α of the chemical potential vector $\boldsymbol{\mu}$ reads [9]

$$\mu_\alpha = \mu_\alpha^0 + RT \log[Z_\alpha]. \quad (6)$$

By definition, chemostats set to constant values the concentrations of external species denoted by $[Y_\alpha]$, with $\alpha \in \mathcal{S}_y$ the subset of chemostated species. The concentrations of internal species denoted $[X_\alpha]$ are free, i.e., species with $\alpha \in \mathcal{S}_x$ are not exchanged with any chemostat. The total set of species is the disjoint union of these two sets

$$\mathcal{S} = \mathcal{S}_x \cup \mathcal{S}_y. \quad (7)$$

Accordingly, the concentration vector and the stoichiometric matrix are written as

$$[\mathbf{Z}] = \begin{pmatrix} [X] \\ [Y] \end{pmatrix}, \quad \nabla = \begin{bmatrix} \nabla_x \\ \nabla_y \end{bmatrix}, \quad (8)$$

respectively. The rate equation is rewritten as

$$\frac{d[\mathbf{Z}]}{dt} = \begin{pmatrix} \frac{d[X]}{dt} \\ \mathbf{0} \end{pmatrix} = \begin{bmatrix} \nabla_x \\ \nabla_y \end{bmatrix} \mathbf{j} + \begin{pmatrix} \mathbf{0} \\ \mathbf{i} \end{pmatrix}, \quad (9)$$

where we use $\frac{d[Y]}{dt} = \mathbf{0}$ for external species. Hence, the splitting between external and internal species of Eq. (9) leads to a definition of the currents received by the open CRN from the chemostats

$$\mathbf{i} = -\nabla_y \mathbf{j} \quad (10)$$

and a kinetic equation for internal species with no source term

$$\frac{d[X]}{dt} = \nabla_x \mathbf{j} \quad (11)$$

since internal species are not exchanged with the environment, i.e., $\mathcal{I} = (\mathbf{0}, \mathbf{i})^T$ by definition. In this work, \mathbf{i} is the vector of chemostat currents as its components are matter currents only, as compared to Ref. [18], in which they are physical currents of any extensive quantity exchanged with a reservoir.

B. Conservation laws

Let us determine the conservation laws relating physical currents. We assume that the stoichiometric matrix ∇ has a nonzero cokernel, i.e., there exists an \mathbf{L} such that

$$\mathbf{L} \nabla = \mathbf{0}. \quad (12)$$

Then each row of matrix \mathbf{L} is a left eigenvector of the stoichiometric matrix with null eigenvalue. We denote by $|\mathcal{L}_{cl}|$ the number of rows of matrix \mathbf{L} and label them with $\lambda \in \{1, 2, \dots, |\mathcal{L}_{cl}|\}$. The subscript cl stands for close, as will become clear later on. Since we consider open CRNs, we can split \mathbf{L} blockwise by columns (splitting between the internal and external species)

$$\mathbf{L} = [\boldsymbol{\ell}_x \quad \boldsymbol{\ell}_y], \quad (13)$$

as the first lines of ∇ are for the internal species and the final ones for external species. Multiplying the rate equation (9) by L yields

$$\frac{dM}{dt} = \ell_y i, \quad (14)$$

where we have defined the moiety vector

$$M \equiv \ell_x [X]. \quad (15)$$

A way to interpret Eq. (14) is to consider the closed CRN case. Indeed, in this case $i = \mathbf{0}$ and Eq. (14) reveals that M gathers the conserved quantities of the dynamics. Thus L is the matrix whose lines are the conservation laws of the CRN if it were closed. This explains why L is usually called the matrix of conservation laws in the literature. For open CRNs, a conserved quantity M_λ remains conserved after opening the network if $(\ell_y i)_\lambda = 0$. However, for an open CRN, $i \neq \mathbf{0}$ by definition. Then M_λ is a conserved quantity of the dynamics only if for all $\alpha \in \mathcal{S}_y$, $(\ell_y)_{\lambda\alpha} = \mathbf{0}$ (case u) or if $(\ell_y i)_\lambda = 0$ with the λ th line of ℓ_y having at least one nonzero component. Note that without any assumptions about the chemostat currents, $(\ell_y i)_\lambda \neq 0$ (case b). The corresponding moieties are thus in general no longer conserved quantities of the dynamics. According to these two cases, we split linewise the matrix L and the vector M as

$$L = \begin{bmatrix} \ell^u \\ \ell^b \end{bmatrix}, \quad M = \begin{bmatrix} M^u \\ M^b \end{bmatrix}. \quad (16)$$

The matrix ℓ^u gathers the $|\mathcal{L}^u|$ conservation laws such that the components of M^u remain conserved whatever the current incoming from the reservoir: Opening the CRN always preserves the conservation laws ℓ^u that are said to be “unbroken.” By definition $\ell_y^u = \mathbf{0}$ and the unbroken conservation laws take the form

$$\ell^u = \begin{bmatrix} \ell_x^u & \ell_y^u \end{bmatrix} = \begin{bmatrix} \ell_x^u & \mathbf{0} \end{bmatrix}. \quad (17)$$

On the contrary, ℓ^b gathers the $|\mathcal{L}^b|$ conservation laws that can be associated with conserved quantities only when taking into account the matter exchanged with the chemostats. In this case, a particular combination of the currents incoming from the reservoirs is required to get a constant moiety. If not, the moiety is not conserved and opening the CRN has “broken” the conservation law. Applying now the broken conservation laws $\ell^b = \begin{bmatrix} \ell_x^b & \ell_y^b \end{bmatrix} = \begin{bmatrix} \ell_x^b & \ell \end{bmatrix}$ on Eq. (9), we obtain

$$\frac{dM^b}{dt} = \ell i. \quad (18)$$

We shorten the notation of ℓ_y^b to ℓ , for consistency with Ref. [18]. Indeed, when assuming that any species has reached its stationary concentration (as done in the following sections),

$$\ell i = \mathbf{0}. \quad (19)$$

Then ℓ stands for the conservation law matrix for physical currents flowing from the reservoirs. In the case of CRNs, one can check that the $|\mathcal{L}| = |\mathcal{L}^b| = |\mathcal{L}_{cl}| - |\mathcal{L}^u|$ rows of matrix ℓ are indeed the conservation laws that relate linearly the chemostat currents at stationary state. Hence, we have

exhibited in this section the block form of the matrix

$$L = \begin{bmatrix} \ell_x^u & \mathbf{0} \\ \ell_x^b & \ell \end{bmatrix}, \quad (20)$$

in which appears the submatrix ℓ of conservation laws for chemostat currents at the core of our theory of thermodynamic circuits. We provide in the next section a direct way of getting the conservation law matrix ℓ from the stoichiometric and cycle matrices.

C. Cycles and selection matrix

1. Cycles

From now on, we assume that the open CRN has reached a nonequilibrium stationary state. Then Eq. (11) reduces to

$$\nabla_x j = \mathbf{0} \quad (21)$$

and the reaction currents are linearly dependent: The lines of ∇_x contain the coefficients of a vanishing linear combination of reaction currents. Hence, sequences of reactions, called cycles, exist that leave the concentrations of internal species unchanged. We thus have

$$j = \mathcal{C} J, \quad (22)$$

where \mathcal{C} is the cycle matrix whose $|\mathcal{C}|$ columns are basis vectors of $\ker(\nabla_x)$ such that $\nabla_x j = \nabla_x \mathcal{C} J = \mathbf{0}$. We denote as usual the cycle currents by J , which is the vector of independent currents among the reaction currents in j . As already emphasized in Refs. [18,19], \mathcal{C} is also analogous to a selection matrix.

Now that we have the linearly independent cycle currents at hand, we can provide a direct computation of the matrix ℓ for the conservation laws constraining chemostat currents. Indeed, Eqs. (10), (19), and (22) lead to

$$\ell i = -\ell \nabla_y j = -\ell \nabla_y \mathcal{C} J = \mathbf{0}. \quad (23)$$

Since the currents J are linearly independent, the above equation imposes

$$\ell \phi = \mathbf{0} \quad \text{with } \phi \equiv \nabla_y \mathcal{C} \quad (24)$$

as the matrix of physical exchanges whose columns provide the matter exchanged with chemostats during each cycle. In other words, the rows of matrix ℓ are the row vectors of current conservation laws. They belong to the cokernel of ϕ . These row vectors indicate the exact proportion of chemostat currents that, when imposed on the system, does not change the internal species concentrations. Our approach of thermodynamic circuits based on current conservation laws is an alternative to the method relying on emergent cycles [12,13]. The vectors associated with such emergent cycles belong to the kernel of the stoichiometric submatrix for internal species, but are not in the kernel of the stoichiometric submatrix for external species. Said differently, emergent cycle are vectors (in the space of reactions) that indicate a set of reactions that upon completion do not change the internal concentrations but do change the external ones. In the end, conservation

laws for chemostat currents and emergent cycles are two different ways of keeping internal species fixed while transferring species between chemostats: The former focuses on the chemostat currents and the latter on cycles of reactions that only transfer species from one chemostat to another.

2. Selection matrix

Similarly to reaction currents being linear combination of independent cycle currents, we obtain below physical (chemostat) currents as linear combinations of the fundamental currents. The conservation laws are written $\ell i = 0$ and the physical currents are linearly dependent, as expected. We can select a subset of linearly independent currents as

$$i = SI, \quad (25)$$

where S is the selection matrix whose columns are basis vector of $\ker(\ell)$. As usual, we denote by I the fundamental currents; it is the vector of independent currents among the physical currents in i . By definition, the matrix S has linearly independent columns and admits a (left) pseudoinverse S^+ . The fundamental current vector then is written $I = S^+ i$. We emphasize that the fundamental currents are chosen as linearly independent currents among the chemostat currents. Depending on the CRN, we might have identical cycle and fundamental currents $J = I$, in which case $S = -\nabla_y \mathcal{C}$. However, this is not generally the case and happens only when the closed CRN has no cycle such that all cycles of the open CRN are emergent cycles (see the Appendix). Note that, as indicated in the Appendix, the selection matrix $S = -\nabla_y \mathcal{C}_{\text{em}}$ based solely on the set of emergent cycles leads to fundamental currents and forces associated with those along the chosen emergent cycles.

D. Entropy production and thermodynamic forces

In this section we determine the thermodynamic forces conjugated to reaction, cycle, chemostat, and fundamental currents for a stationary open CRN. This is done by ensuring thermodynamic consistency, i.e., an identical entropy production rate (EPR) at all levels of description of the CRN [1]. We start from the EPR σ at the level of reaction forces and currents given (up to the temperature factor) by

$$T\sigma = f^T j \quad (\text{reaction level}). \quad (26)$$

We switch to the cycle level by inserting the definition of the cycle currents (22) in the EPR (26). The EPR then reads

$$T\sigma = F^T J \quad (\text{cycle level}), \quad (27)$$

where we have introduced the cycle affinity

$$F^T = f^T \mathcal{C}. \quad (28)$$

Another decomposition of the EPR follows from inserting the definition of the reaction affinity (5) in Eq. (26). Using in addition that the rate equation in the stationary state yields $\mathcal{I} = -\nabla j$, we obtain

$$T\sigma = \mu^T \mathcal{I}, \quad (29)$$

in agreement with $f^T = -\mu^T \nabla$ of Eq. (5). This EPR further simplifies by noting that $\mathcal{I}^T = (\mathbf{0} \quad i)$ and by using the

internal-external splitting of $\mu^T = (\mu_x^T \quad a^T)$ as

$$T\sigma = a^T i \quad (\text{physical level}), \quad (30)$$

where $a = \mu_y$ is the vector of chemical potentials for external species. We can finally use the redundancy of the chemostat currents to write the EPR as

$$T\sigma = A^T I \quad (\text{fundamental level}), \quad (31)$$

where we have identified the fundamental force vector

$$A = S^T a \quad (32)$$

conjugated to the fundamental current vector I . This ends the identification of the four relevant current-force decompositions preserving the EPR.

E. Nonequilibrium conductance matrix

We now turn to the determination of the current-force characteristics based at each level of description on a nonequilibrium conductance matrix. We first define the reaction resistance matrix by the diagonal matrix

$$r = \text{diag}(r_1, \dots, r_{|\mathcal{R}|}) \quad \text{with} \quad r_\rho = \frac{f_\rho}{j_\rho}. \quad (33)$$

The thermodynamic force at the level of reactions is written as a function of reaction currents

$$f = r j. \quad (34)$$

Then the cycle currents and forces are related by

$$F = R J \quad \text{with} \quad R \equiv \mathcal{C}^T r \mathcal{C} \quad (\text{cycle level}) \quad (35)$$

since

$$F = \mathcal{C}^T f = \mathcal{C}^T r j = (\mathcal{C}^T r \mathcal{C}) J, \quad (36)$$

where we use Eqs. (22) and (28). The matrix R is symmetric and positive definite by non-negativity of the EPR. Hence an inverse matrix exists, we call R^{-1} the cycle conductance matrix. It relates the cycle currents to its conjugated affinities as

$$J = R^{-1} F. \quad (37)$$

Another conductance matrix exists relating stationary currents \mathcal{I} and chemical potential via

$$\mathcal{I} = \mathcal{G} \mu \quad \text{with} \quad \mathcal{G} \equiv \nabla r^{-1} \nabla^T, \quad (38)$$

since

$$\mathcal{I} = -\nabla j = -\nabla r^{-1} f = (\nabla r^{-1} \nabla^T) \mu. \quad (39)$$

In a similar way, we obtain the conductance matrices at the level of physical forces and currents

$$i = g a \quad \text{with} \quad g \equiv \phi R^{-1} \phi^T \quad (\text{physical level}). \quad (40)$$

To do so, we start from Eq. (10) and use Eqs. (22), (37), and (28) to get

$$i = -\nabla_y \mathcal{C} R^{-1} \mathcal{C}^T f. \quad (41)$$

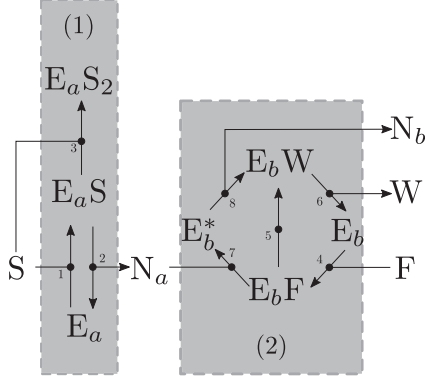


FIG. 1. CRN decomposed into chemical modules 1 and 2 as proposed in Ref. [12]. The modules are associated in series. Module 1 has two external species S and N_a and three internal species E_a , E_aS , and E_aS_2 . Module 2 has four external species N_a , F , W , and N_b and four internal species E_b , E_bF , E_b^* , and E_bW . The serial association is implemented by ensuring the conservation of the reaction currents $j_2 = j_7$ and the equality of the stationary concentration of N_a computed in modules 1 and 2.

The last step involves the reaction affinity of Eq. (5) in vector notation

$$f = -\nabla_x^T \mu_x - \nabla_y^T a \Rightarrow \mathcal{C}^T f = -\mathcal{C}^T \nabla_y^T a \quad (42)$$

since $\nabla_x \mathcal{C} = 0$ by definition. We notice that the nonequilibrium conductance matrix at the physical level takes the same expression as for Markov jump processes [17,18] once the relevant physical matrix ϕ has been identified. We remark that the physical conductance matrix is explicitly written as $g = \nabla_y \mathcal{C} \mathcal{C}^+ r^{-1} (\mathcal{C} \mathcal{C}^+)^T \nabla_y^T$, in which $\mathcal{C} \mathcal{C}^+$ is a projector and not the identity since \mathcal{C}^+ is a left inverse only.

Finally, the conductance for fundamental currents and forces is written

$$I = GA \quad \text{with } G \equiv S^+ g S^{T+} \quad (\text{fundamental level}). \quad (43)$$

Indeed, assuming that G exists such that $I = GA$ and using Eqs. (25) and (32) yields

$$i = SI = SGS^T a \Rightarrow g = SGS^T, \quad (44)$$

which leads to the fundamental conductance matrix of Eq. (43) since S^+ is a (left) pseudoinverse. This concludes our derivation of the nonequilibrium conductance matrix associated with a CRN at any level of description. In the end, an analogy with Markov jump processes is clear due to the identification of the matrix of physical exchanges ϕ on one side and, on another side, considering that the cycle matrix \mathcal{C} must be in the kernel of ∇_x , the stoichiometric submatrix for internal species only.

III. ILLUSTRATION

We now derive the nonequilibrium conductance matrix for the CRNs of Fig. 1. Then, building on these matrices, we apply our theory of thermodynamic circuits [18] to obtain the

nonequilibrium conductance matrix of the serial association of the two CRNs. To conclude this illustration, we verify that the derivation of the nonequilibrium conductance matrix from the full network gives the same result.

This section is organized as follows. We start by describing the modules by providing their stoichiometric matrices and their submatrices for internal or external species. Then we determine the currents and their conjugated forces at all levels of description by exploiting cycles and conservation laws. As the modules have pseudo-first-order dynamics, the stationary concentrations can be computed exactly, either by using the Kirchhoff theorem as in Appendix B of Ref. [12] or through purely linear algebraic steps as in Ref. [20]. Using those, the resistance matrix at the reaction level follows. We propagate it to get the conductance matrices at all levels of description. Finally, using the law of resistance matrix addition derived in [18], we determine the conductance matrix for the serial association of modules 1 and 2. We compare our result with the direct computation of the conductance matrix at the fundamental level.

A. Stoichiometry and reaction currents

The stoichiometric matrices describing the reactions for modules 1 and 2 read

$$\nabla^{(1)} = \begin{bmatrix} \nabla_x^{(1)} \\ \nabla_y^{(1)} \end{bmatrix} = \begin{bmatrix} -1 & 1 & 0 \\ 1 & -1 & -1 \\ 0 & 0 & 1 \\ -1 & 0 & -1 \\ 0 & 1 & 0 \end{bmatrix}, \quad (45)$$

$$\nabla^{(2)} = \begin{bmatrix} \nabla_x^{(2)} \\ \nabla_y^{(2)} \end{bmatrix} = \begin{bmatrix} -1 & 0 & 1 & 0 & 0 & 0 \\ 1 & -1 & 0 & -1 & 0 & 0 \\ 0 & 1 & -1 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 & -1 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ -1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \end{bmatrix}. \quad (46)$$

The columns (reaction number ρ) are ordered as

$$\begin{aligned} \mathcal{R}^{(1)} &= \{1, 2, 3\}, \\ \mathcal{R}^{(2)} &= \{4, 5, 6, 7, 8\}, \end{aligned} \quad (47)$$

respectively. The rows (species labels Z_α) are ordered as

$$\mathcal{S}^{(1)} = \{E_a, E_aS, E_aS_2, S, N_a\}, \quad (48)$$

$$\mathcal{S}^{(2)} = \{E_b, E_bF, E_bW, E_b^*, N_a, N_b, F, W\}, \quad (49)$$

respectively. The internal and external species are

$$\begin{aligned} \mathcal{S}_x^{(1)} &= \{E_a, E_aS, E_aS_2\}, & \mathcal{S}_x^{(2)} &= \{E_b, E_bF, E_bW, E_b^*\}, \\ \mathcal{S}_y^{(1)} &= \{S, N_a\}, & \mathcal{S}_y^{(2)} &= \{N_a, N_b, F, W\}. \end{aligned} \quad (50)$$

The horizontal line in the stoichiometric matrices separates them into two submatrices: The upper block $\nabla_x^{(m)}$ and the lower block $\nabla_y^{(m)}$ for $m = 1, 2$. In the next two sections, we

express the stationary currents at all levels of description in terms of the reaction currents

$$\mathbf{j}^{(1)} = \begin{pmatrix} j_1 \\ j_2 \\ j_3 \end{pmatrix} = \begin{pmatrix} k_1^+ S[E_a] - k_1^- [E_a S] \\ k_2^+ [E_a S] - k_2^- N_a[E_a] \\ k_3^+ S[E_a S] - k_3^- [E_a S_2] \end{pmatrix}, \quad (51)$$

$$\mathbf{j}^{(2)} = \begin{pmatrix} j_4 \\ j_5 \\ j_6 \\ j_7 \\ j_8 \end{pmatrix} = \begin{pmatrix} k_4^+ F[E_b] - k_4^- [E_b F] \\ k_5^+ [E_b F] - k_5^- [E_b W] \\ k_6^+ [E_b W] - k_6^- W[E_b] \\ k_7^+ N_a[E_b F] - k_7^- [E_b^*] \\ k_8^+ [E_b^*] - k_8^- N_b[E_b W] \end{pmatrix}, \quad (52)$$

where the concentrations of external species are denoted without square brackets to emphasize that they are parameters for the effective rate constants.

B. From reaction to cycle currents

As mentioned previously, the reaction currents are linearly dependent; a basis of linearly independent cycle currents can thus be chosen. Looking for a basis of the kernel of $\nabla_x^{(m)}$ for $m = 1, 2$, we choose the cycle matrices

$$\mathcal{C}^{(1)} = \begin{pmatrix} 1 \\ 1 \\ 0 \end{pmatrix}, \quad \mathcal{C}^{(2)} = \begin{bmatrix} 0 & 1 \\ -1 & 1 \\ 0 & 1 \\ 1 & 0 \\ 1 & 0 \end{bmatrix}. \quad (53)$$

Applying Eq. (21) to both modules yields the following relation between their reaction currents:

$$j_1 = j_2, \quad j_3 = 0, \quad (54)$$

$$j_4 = j_6, \quad j_5 = j_6 - j_8, \quad j_7 = j_8. \quad (55)$$

We remark that the equation $j_3 = 0$ is due to our assumption of stationary state; a nonzero current would lead to an accumulation of $E_a S_2$ in the system. We notice also that these relations between reaction currents are an instance of Kirchhoff's current law applied to each species of the CRN. Then, since the cycle matrices are pseudoinvertible ($\mathcal{C}^{(1)}$ is a vector and $\mathcal{C}^{(2)}$ has linearly independent columns), we can invert Eq. (22) for both modules and obtain the cycle currents

$$\mathbf{J}^{(1)} = \mathcal{C}^{(1)+} \mathbf{j}^{(1)} = j_1, \quad (56)$$

$$\mathbf{J}^{(2)} = \mathcal{C}^{(2)+} \mathbf{j}^{(2)} = \begin{pmatrix} j_8 \\ j_6 \end{pmatrix}, \quad (57)$$

which are compatible with $\mathbf{j}^{(m)} = \mathcal{C}^{(m)} \mathbf{J}^{(m)}$ by using the constraints of Eqs. (54) and (55).

From the cycle matrices and the stoichiometric submatrix for external species, we find the matrices of physical exchanges

$$\Phi^{(1)} = \begin{pmatrix} -1 \\ 1 \end{pmatrix}, \quad \Phi^{(2)} = \begin{bmatrix} -1 & 0 \\ 1 & 0 \\ 0 & -1 \\ 0 & 1 \end{bmatrix}, \quad (58)$$

whose lines are associated with external species as ordered in Eq. (50).

C. From physical to fundamental currents

The left null eigenvectors of $\nabla^{(m)}$ for $m = 1, 2$ constitute the rows of matrices

$$\mathbf{L}^{(1)} = \left[\begin{array}{ccc|cc} 1 & 1 & 1 & 0 & 0 \\ -2 & -1 & 0 & 1 & 1 \end{array} \right] = \begin{bmatrix} \ell_x^{(1)u} & \mathbf{0} \\ \ell_x^{(1)b} & \ell^{(1)} \end{bmatrix}, \quad (59)$$

$$\mathbf{L}^{(2)} = \left[\begin{array}{cccc|cccc} 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 \\ -1 & -1 & -1 & 0 & 1 & 1 & 0 & 0 \\ -1 & 0 & 0 & 0 & 0 & 0 & 1 & 1 \end{array} \right] = \begin{bmatrix} \ell_x^{(2)u} & \mathbf{0} \\ \ell_x^{(2)b} & \ell^{(2)} \end{bmatrix}. \quad (60)$$

We separate the unbroken and broken conservation laws (internal and external species) by a horizontal (vertical) line. We identify the matrices $\ell^{(m)}$ of conservation laws for the chemical currents received from the chemostats

$$\ell^{(1)} = (1 \quad 1), \quad \ell^{(2)} = \begin{bmatrix} 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 \end{bmatrix}. \quad (61)$$

Those matrices are in the cokernel of the matrices of physical exchanges given in Eq. (58). The physical currents follow from Eq. (10) and read for both modules

$$\mathbf{i}^{(1)} = -\nabla_y^{(1)} \mathbf{j}^{(1)} = \begin{pmatrix} j_1 \\ -j_1 \end{pmatrix}, \quad (62)$$

$$\mathbf{i}^{(2)} = -\nabla_y^{(2)} \mathbf{j}^{(2)} = \begin{pmatrix} j_8 \\ -j_8 \\ j_6 \\ -j_6 \end{pmatrix}. \quad (63)$$

Their components follow the order of external species in $\mathcal{S}_y^{(m)}$ of Eq. (50). They are chosen to be positive when matter flows from the chemostat to the module, as one can check in Fig. 2. Finally, we can select linearly independent currents called fundamental currents by choosing a vector basis for the kernels of the conservation law matrices in Eq. (61). This leads to selection matrices

$$\mathbf{S}^{(1)} = \begin{pmatrix} 1 \\ -1 \end{pmatrix}, \quad \mathbf{S}^{(2)} = \begin{bmatrix} 1 & 0 \\ -1 & 0 \\ 0 & 1 \\ 0 & -1 \end{bmatrix}. \quad (64)$$

One can check Eq. (25) with the above selection matrices for the fundamental currents

$$\mathbf{I}^{(1)} = j_1, \quad \mathbf{I}^{(2)} = \begin{pmatrix} j_8 \\ j_6 \end{pmatrix}. \quad (65)$$

In the end, module 1 is described by an effective reaction converting S into N_a and one reaction current j_1 . Similarly, module 2 is described by two coupled effective reactions and two reaction currents j_6 and j_8 . Figure 2 summarizes this effective description for modules 1 and 2 in serial association [12].

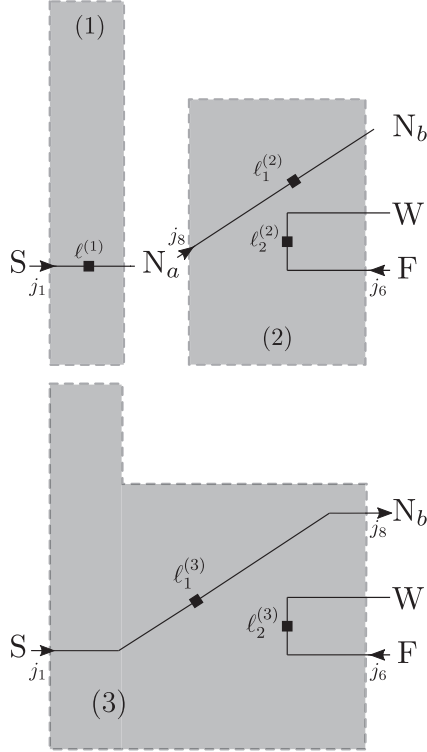


FIG. 2. Effective description of modules 1, 2, and 3. In modules 2 and 3, a coupling exists between currents j_6 and j_8 , although it does not appear in this graphical representation of conservation laws.

D. Thermodynamic forces

We now turn to the derivation of the conjugated thermodynamics forces in terms of the reaction affinities defined in Eq. (5) which read, for modules 1 and 2,

$$\mathbf{f}^{(1)} = \begin{pmatrix} f_1 \\ f_2 \\ f_3 \end{pmatrix} = \begin{pmatrix} \mu_{E_a} + \mu_S - \mu_{E_a S} \\ \mu_{E_a S} - \mu_{N_a} - \mu_{E_a} \\ \mu_{E_a S} + \mu_S - \mu_{E_a S_2} \end{pmatrix}, \quad (66)$$

$$\mathbf{f}^{(2)} = \begin{pmatrix} f_4 \\ f_5 \\ f_6 \\ f_7 \\ f_8 \end{pmatrix} = \begin{pmatrix} \mu_{E_b} + \mu_F - \mu_{E_b F} \\ \mu_{E_b F} - \mu_{E_b W} \\ \mu_{E_b W} - \mu_W - \mu_{E_b} \\ \mu_{E_b F} + \mu_{N_a} - \mu_{E_b}^* \\ \mu_{E_b}^* - \mu_{N_b} - \mu_{E_b W} \end{pmatrix}. \quad (67)$$

Using these reaction affinities for modules 1 and 2 in the definition of cycle forces (28), we obtain

$$\mathbf{F}^{(1)} = \mathbf{C}^{(1)T} \mathbf{f}^{(1)} = f_1 + f_2 = \mu_S - \mu_{N_a}, \quad (68)$$

$$\mathbf{F}^{(2)} = \mathbf{C}^{(2)T} \mathbf{f}^{(2)} = \begin{pmatrix} f_7 + f_8 - f_5 \\ f_4 + f_5 + f_6 \end{pmatrix} = \begin{pmatrix} \mu_{N_a} - \mu_{N_b} \\ \mu_F - \mu_W \end{pmatrix}. \quad (69)$$

Those cycle forces are conjugated to the currents of Eqs. (56) and (57). The physical forces are the chemical potential associated with the external species

$$\mathbf{a}^{(1)T} = (\mu_S \quad \mu_{N_a}), \quad (70)$$

$$\mathbf{a}^{(2)T} = (\mu_{N_a} \quad \mu_{N_b} \quad \mu_F \quad \mu_W). \quad (71)$$

Finally, the fundamental forces are obtained by applying the definition of Eq. (32) with the selection matrices of Eq. (64) and the physical forces of Eqs. (70) and (71),

$$\mathbf{A}^{(1)T} = \mathbf{a}^{(1)T} \mathbf{S}^{(1)} = \mu_S - \mu_{N_a}, \quad (72)$$

$$\mathbf{A}^{(2)T} = \mathbf{a}^{(2)T} \mathbf{S}^{(2)} = (\mu_{N_a} - \mu_{N_b} \quad \mu_F - \mu_W). \quad (73)$$

Note that with this choice of selection matrices, the fundamental forces for both modules are equal to the cycle forces.

E. Conductance matrices

We compute now the resistance and conductance matrices at all levels for modules 1 and 2. First, at the reactions level, the resistance matrices are

$$\mathbf{r}^{(1)} = \begin{bmatrix} r_1 & 0 & 0 \\ 0 & r_2 & 0 \\ 0 & 0 & r_3 \end{bmatrix}, \quad (74)$$

$$\mathbf{r}^{(2)} = \begin{bmatrix} r_4 & 0 & 0 & 0 & 0 \\ 0 & r_5 & 0 & 0 & 0 \\ 0 & 0 & r_6 & 0 & 0 \\ 0 & 0 & 0 & r_7 & 0 \\ 0 & 0 & 0 & 0 & r_8 \end{bmatrix}, \quad (75)$$

with the r_ρ obtained from Eqs. (51), (52), (66), and (67). Using Eq. (35), the cycle resistance matrices for each module read

$$\mathbf{R}^{(1)} = r_1 + r_2, \quad (76)$$

$$\mathbf{R}^{(2)} = \begin{bmatrix} r_5 + r_7 + r_8 & -r_5 \\ -r_5 & r_4 + r_5 + r_6 \end{bmatrix}. \quad (77)$$

As expected, since there is a single-cycle current for module 1, the cycle resistance is scalar. Module 2 has two cycles; its resistance matrix is thus a 2×2 matrix. Its diagonal elements display the resistance addition of the reaction involved in each cycle. Its off-diagonal elements characterize the coupling between the transport of chemical species along the cycles' pathways. Looking at the CRN of module 2 in Fig. 1, one expects that reaction for $\rho = 5$ couples the two reaction cycles. Using Eq. (40), the conductance matrices at physical level read

$$\mathbf{g}^{(1)} = \frac{1}{r_1 + r_2} \mathbf{U} \quad \text{with } \mathbf{U} = \begin{bmatrix} 1 & -1 \\ -1 & 1 \end{bmatrix}, \quad (78)$$

$$\mathbf{g}^{(2)} = \frac{1}{\det \mathbf{R}^{(2)}} \begin{bmatrix} (r_4 + r_5 + r_6) \mathbf{U} & r_5 \mathbf{U} \\ r_5 \mathbf{U} & (r_5 + r_7 + r_8) \mathbf{U} \end{bmatrix}. \quad (79)$$

Finally, the conductance matrices at the fundamental level are obtained from Eq. (43):

$$\mathbf{G}^{(1)} = \frac{1}{r_1 + r_2}, \quad (80)$$

$$\mathbf{G}^{(2)} = \frac{1}{\det \mathbf{R}^{(2)}} \begin{bmatrix} r_4 + r_5 + r_6 & r_5 \\ r_5 & r_5 + r_7 + r_8 \end{bmatrix}. \quad (81)$$

In other words, the cycle and fundamental resistance matrices are equal for these CRNs.

F. Conductance matrix of the full network

We refer to module 3 as the serial association of modules 1 and 2 via the chemical species N_a . Therefore, N_a , which was an external species for modules 1 and 2 when they were studied separately, is now an internal species from the point of view of module 3. In this section we present two alternative derivations of the nonequilibrium conductance matrix of module 3. First, we explain how our law of resistance addition for serially connected thermodynamic devices applies to this example. Then we apply the procedure developed in this paper to the larger network of module 3. We obtain the same result from the two derivations.

1. Law of resistance matrix addition

In the previous sections, modules 1 and 2 were studied separately, i.e., as if reactions occur into separate reactors. We now turn to the serial association of modules 1 and 2 to give module 3. Upon connection, all reactions occur in the same reactor with conservation of the chemical current corresponding to exchanges of N_a between the two modules. Moreover, the concentration $[N_a]$ at the “interface” between the modules reaches a unique nonequilibrium stationary state. In other words, the serial connection implies $j_1 = j_8$ and chemical potential continuity at the module’s interface for N_a .

On this basis, we can apply our general method to compute the nonequilibrium conductance matrix of module 3 (see Ref. [18]). As a start, we determine the conservation laws of module 3 and provide the currents at the interface between the two modules as a function of the chemostat currents of module 3. The left-right splitting of physical currents reads

$$\mathbf{i}^{(1)} = \begin{pmatrix} i_l^{(1)} \\ i_r^{(1)} \end{pmatrix} = \begin{pmatrix} j_1 \\ -j_1 \end{pmatrix}, \quad (82)$$

$$\mathbf{i}^{(2)} = \begin{pmatrix} i_l^{(2)} \\ i_r^{(2)} \end{pmatrix} = \begin{pmatrix} j_8 \\ -j_8 \\ j_6 \\ -j_6 \end{pmatrix}, \quad (83)$$

where $i_r^{(2)}$ is the vector made with the last three components of $\mathbf{i}^{(2)}$. By construction, the physical currents from the chemostats of module 3 are

$$\mathbf{i}^{(3)} = \begin{pmatrix} i_l^{(1)} \\ i_r^{(2)} \end{pmatrix} = \begin{pmatrix} j_1 \\ -j_8 \\ j_6 \\ -j_6 \end{pmatrix}, \quad (84)$$

since the current leaving module 1 from the right and entering module 2 on the left is eliminated from our description after serial connection of the two modules. The conservation laws of Eq. (61) can be reformulated to separate interface and chemostat currents for module 3. In the equation below, we place on the left-hand side the interface currents and on the right-hand side the chemostat currents

$$L_i i_r^{(1)} = L_e i^{(3)}, \quad (85)$$

with

$$L_i = \begin{bmatrix} -1 \\ 1 \\ 0 \end{bmatrix}, \quad L_e = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 \end{bmatrix} \quad (86)$$

the matrices resulting from this transformation of conservation laws [see Eq. (40) in Ref. [18]]. Equation (85) allows us to obtain the conservation laws for module 3: We denote by

$$\mathbf{v} = \begin{bmatrix} 1 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} \quad (87)$$

the matrix whose lines are basis vectors of the cokernel of L_i [see Eq. (45) in Ref. [18]]. Left multiplying Eq. (85) by \mathbf{v} produces the conservation laws for physical currents of module 3,

$$\ell^{(3)} \mathbf{i}^{(3)} = \mathbf{0}, \quad (88)$$

where

$$\ell^{(3)} = \mathbf{v} L_e = \begin{bmatrix} 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 \end{bmatrix}. \quad (89)$$

It turns out that the conservation law matrices for modules 2 and 3 are equal. This is expected since a single pin connection does not decrease the number of external species. In practice, module 1 puts one pin of module 2 in mixed boundary conditions. A choice of selection matrix associated with the conservation law matrix of Eq. (89) is thus

$$\mathbf{S}^{(3)} = \mathbf{S}^{(2)}. \quad (90)$$

In the same line, the equivalent description of module 3 is very similar to the one of module 2, as shown in Fig. 2. Returning to Eq. (85), we can solve for $i_r^{(1)}$ to express it in terms of $\mathbf{i}^{(3)}$ as $i_r^{(1)} = \pi \mathbf{i}^{(3)} = -i_l^{(2)}$ with

$$\pi = L_i^+ L_e = \frac{1}{2} \begin{bmatrix} -1 & 1 & 0 & 0 \end{bmatrix}. \quad (91)$$

Inserting this relation in Eqs. (82) and (83) yields the relation between the physical currents of modules 1 and 2 in terms of those of module 3,

$$\mathbf{i}^{(m)} = \pi^{(m,3)} \mathbf{i}^{(3)} \quad (92)$$

for $m = 1, 2$, where

$$\pi^{(1,3)} = \begin{bmatrix} 1 & 0 & 0 & 0 \\ -\frac{1}{2} & \frac{1}{2} & 0 & 0 \end{bmatrix}, \quad (93)$$

$$\pi^{(2,3)} = \begin{bmatrix} \frac{1}{2} & -\frac{1}{2} & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}. \quad (94)$$

Finally, the relation between the fundamental currents of modules 1 and 2 and those of module 3 is obtained by using Eq. (25) with the selection matrix of Eq. (90) in Eq. (92),

$$\mathbf{i}^{(m)} = \pi^{(m,3)} \mathbf{S}^{(3)} \mathbf{I}^{(3)}. \quad (95)$$

Then, since the selection matrices for modules 1 and 2 are pseudoinvertible, we finally obtain

$$\mathbf{I}^{(m)} = \mathbf{\Pi}^{(m,3)} \mathbf{I}^{(3)}, \quad (96)$$

with $\mathbf{\Pi}^{(m,3)} \equiv \mathbf{S}^{(m)+} \mathbf{\pi}^{(m,3)} \mathbf{S}^{(3)}$, giving

$$\mathbf{\Pi}^{(1,3)} = [1 \ 0], \quad \mathbf{\Pi}^{(2,3)} = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}. \quad (97)$$

Using the additive structure for resistance matrices [see Eq. (34) in Ref. [18]]

$$\mathbf{G}^{(3)-1} = \sum_{m=1}^2 \mathbf{\Pi}^{(m,3)T} \mathbf{G}^{(m)-1} \mathbf{\Pi}^{(m,3)}, \quad (98)$$

we get the fundamental resistance matrix of module 3,

$$\mathbf{G}^{(3)-1} = \begin{bmatrix} r_1 + r_2 + r_5 + r_7 + r_8 & -r_5 \\ -r_5 & r_4 + r_5 + r_6 \end{bmatrix}, \quad (99)$$

describing the force-current characteristics. Interestingly the coupling between the fundamental currents for module 3, i.e., the off-diagonal elements in $\mathbf{G}^{(3)-1}$, emerges solely from the chemical reaction coupling the two cycles of module 2. The intensity of the first diagonal element is the sum of the resistance of the two cycles involved in the serial association. The second diagonal coefficient is equal to the cycle resistance of the cycle that is not involved in the serial association.

2. Direct derivation

In this section we provide an alternative derivation of the conductance matrix of Eq. (99) for module 3. We compute this matrix directly from the stoichiometric matrix of the entire CRN. The latter reads

$$\mathbf{\nabla}^{(3)} = \begin{bmatrix} \mathbf{\nabla}_x^{(3)} \\ \mathbf{\nabla}_y^{(3)} \end{bmatrix} = \begin{bmatrix} -1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & -1 & -1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & -1 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & -1 & 0 & -1 & 0 \\ 0 & 0 & 0 & 0 & 1 & -1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & -1 \\ \hline -1 & 0 & -1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \end{bmatrix}. \quad (100)$$

In this matrix, the columns are numbered by the reaction index $\rho = 1, \dots, 8$. The rows correspond to the chemical species ordered as in

$$\mathcal{S}^{(3)} = \{E_a, E_a S, E_a S_2, N_a, E_b, E_b F, E_b W, E_b^*, S, N_b, F, W\}. \quad (101)$$

The upper left 3×3 submatrix is $\mathbf{\nabla}_x^{(1)}$. The lower right 4×5 submatrix above the horizontal line is $\mathbf{\nabla}_x^{(2)}$. The lower right 3×5 submatrix is $\mathbf{\nabla}_y^{(2)}$. The fourth row that corresponds to N_a appears now in the internal species (upper part) of the stoichiometric matrix. The ninth row that corresponds to S remains in the external species (lower part). The whole networks admits the two following cycles

$$\mathbf{C}^{(3)} = \begin{bmatrix} 1 & 0 \\ 1 & 0 \\ 0 & 0 \\ 0 & 1 \\ -1 & 1 \\ 0 & 1 \\ 1 & 0 \\ 1 & 0 \end{bmatrix}. \quad (102)$$

The reaction resistance matrix is the diagonal matrix

$$\mathbf{r}^{(3)} = \text{diag}(r_1, r_2, r_3, r_4, r_5, r_6, r_7, r_8). \quad (103)$$

The cycle resistance matrix thus reads

$$\mathbf{R}^{(3)} = \begin{bmatrix} r_1 + r_2 + r_5 + r_7 + r_8 & -r_5 \\ -r_5 & r_4 + r_5 + r_6 \end{bmatrix}. \quad (104)$$

To obtain the conservation laws, we look for the cokernel of the stoichiometric matrix, which takes the form

$$\mathbf{L}^{(3)} = \left[\begin{array}{cccccc|cccc} 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 \\ 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -2 & -1 & 0 & 1 & -1 & -1 & -1 & 0 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & -1 & 0 & 0 & 0 & 0 & 0 & 1 & 1 \end{array} \right]. \quad (105)$$

The two last line correspond to the broken conservation laws since they have nonzero coefficients for the external species. The conservation laws for chemostat currents are recovered as the lower right block in $\mathbf{L}^{(3)}$. We emphasize that we chose for $\mathbf{L}^{(3)}$ an appropriate row ordering of the left null eigenvectors so as to get a matrix of conservation laws in the form of Eq. (20). Given that matrix of current conservation law is identical to the one found in the serial approach, the same choice of selection matrix can be made, leading to the fundamental resistance matrix given in Eq. (99). Therefore, we conclude that, for the simple CRNs studied in this section, the serial connection of chemical modules leads to the same results as the direct approach on the full network.

IV. CONCLUSION

In this work we have defined (for the four levels of description: reaction, cycle, physical, and fundamental) the nonequilibrium conductance matrix of a CRN in its (unique) stationary nonequilibrium state. This definition involves the

reaction cycles for internal species, the matter exchanged with the chemostats for each cycle, and the conservation laws of the CRN leading to a choice of selection matrix associated with a given basis of fundamental currents and forces. Once these concepts have been identified in the framework of CRNs, the definition for the conductance matrix is analogous to the one for Markov jump processes [17,18]. This approach leads to a synthetic description of a CRN in terms of its nonequilibrium conductance matrix and conservation laws for physical currents, in the spirit of Ref. [18], as compared to the approach based on emergent cycles of Refs. [12,13].

The nonequilibrium conductance matrix is uniquely defined when assuming that the CRN reaches a unique nonequilibrium stationary state. This is guaranteed for pseudo-first-order kinetics which are linear, although we remark that the notion of linearity depends on the decomposition of the CRN into chemical modules. It may happen that nonlinearity reappears upon connection of linear modules, as it is the case for our illustrative example. In this case, the problem of nonuniqueness may reappear when solving for the concentration of the species at the module's interface. This problem of multiple solutions deserves further investigation, for instance, regarding stability criteria. Borrowing from the theory of electronic circuits will certainly be useful in this direction, all the more so for emergent phenomena commonly appearing in nonlinear systems. This may help to advance the description of nonequilibrium phase transitions given the crucial lack of nonequilibrium thermodynamic potentials and associated variational principles.

DATA AVAILABILITY

No data were created or analyzed in this study.

APPENDIX: RELATIVE DIMENSION OF CYCLE AND FUNDAMENTAL FORCES

The main text examples have cycle and fundamental vectors that share the same dimension. This is possible only when the closed CRN has no cycle, i.e., when $|\mathcal{C}_{cl}| \equiv \dim(\ker \nabla) = 0$, with \mathcal{C}_{cl} denoting the set of cycles of the closed CRN. We show this property in this appendix with a proof that relies on several uses of the rank nullity theorem for matrices ∇_x and ∇ and their transposes. This theorem states that the number of

columns of a matrix is equal to the rank of the matrix plus the dimension of its kernel, i.e.,

$$|\mathcal{R}| = \text{rk } \nabla_x + |\mathcal{C}|, \quad (\text{A1})$$

$$|\mathcal{S}_x| = \text{rk } \nabla_x^T + |\mathcal{L}^u|, \quad (\text{A2})$$

$$|\mathcal{R}| = \text{rk } \nabla + |\mathcal{C}_{cl}|, \quad (\text{A3})$$

$$|\mathcal{S}| = \text{rk } \nabla^T + |\mathcal{L}_{cl}|. \quad (\text{A4})$$

Since a matrix and its transpose have identical rank, we obtain

$$|\mathcal{C}| = -|\mathcal{S}_x| + |\mathcal{L}^u| + |\mathcal{R}|, \quad (\text{A5})$$

$$= |\mathcal{S}_y| - |\mathcal{L}^b| + |\mathcal{L}_{cl}| - |\mathcal{S}| + |\mathcal{R}|, \quad (\text{A6})$$

$$= |\mathcal{S}_y| - |\mathcal{L}^b| + |\mathcal{C}_{cl}|. \quad (\text{A7})$$

Hence, given that $|\mathcal{C}|$ is the number of cycle forces and $|\mathcal{S}_y| - |\mathcal{L}^b|$ the number of fundamental forces, the two are different when $|\mathcal{C}_{cl}| \neq 0$, i.e., for nonzero kernel of the stoichiometric matrix.

We remark that Eq. (A7) shows that the number of fundamental forces is equal to the number of emergent cycles denoted by $|\mathcal{C}_{em}|$. Indeed, the number of cycles in the open CRN satisfies

$$|\mathcal{C}| = |\mathcal{C}_{cl}| + |\mathcal{C}_{em}| \quad (\text{A8})$$

by definition of emergent cycles [13]. Intuitively, there are in general fewer cycles in the closed CRN than in the open CRN, $|\mathcal{C}_{cl}| \leq |\mathcal{C}|$, since there are fewer right eigenvectors of ∇ than of ∇_x (the latter having fewer rows). The difference in these numbers of cycles corresponds precisely to the number of emergent cycles. Given this equivalence between the fundamental level of description and the one based on emergent cycles, it is possible to select as fundamental currents those along emergent cycles. In this case, separating the cycle matrix $\mathcal{C} = (\mathcal{C}_{cl}, \mathcal{C}_{em})$ into the cycle matrices for the closed CRN \mathcal{C}_{cl} (whose columns are in $\ker \nabla$) and for emergent cycles \mathcal{C}_{em} (whose columns are not in $\ker \nabla$), the selection matrix can be chosen as $S = -\nabla_y \mathcal{C}_{em}$. This choice is compatible with the fact that the columns of S define a basis of $\ker \ell$ since emergent cycles are independent and as many as the number of fundamental currents. Moreover, this choice leads, as required, to $\ell S = 0$ since by definition $0 = \ell \phi = \ell \nabla_y \mathcal{C}$, which allows us to write $\ell \nabla_y \mathcal{C}_{em} = 0$.

- [1] J. Schnakenberg, *Rev. Mod. Phys.* **48**, 571 (1976).
- [2] T. L. Hill, *Free Energy Transduction and Biochemical Cycle Kinetics* (Springer, New York, 1989).
- [3] S. Dal Cengio, V. Lecomte, and M. Polettini, *Phys. Rev. X* **13**, 021040 (2023).
- [4] J. Ross, in *Thermodynamics and Fluctuations Far from Equilibrium*, edited by S. R. Berry and K. Yamanouchi, Springer Series in Chemical Physics Vol. 90 (Springer, Berlin, 2008).
- [5] N. Van Kampen, *Stochastic Processes in Physics and Chemistry*, 3rd ed. (North-Holland, Amsterdam, 2007).
- [6] G. Nicolis and I. Prigogine, *Self-Organization in Nonequilibrium Systems: From Dissipative Structures to Order Through Fluctuations* (Wiley, New York, 1977).

- [7] T. Schmiedl and U. Seifert, *J. Chem. Phys.* **126**, 044101 (2007).
- [8] R. Rao and M. Esposito, *Phys. Rev. X* **6**, 041064 (2016).
- [9] F. Avanzini, M. Bilancioni, V. Cavina, S. D. Cengio, M. Esposito, G. Falasco, D. Forastiere, N. Freitas, A. Garilli, P. E. Harunari, V. Lecomte, A. Lazarescu, S. G. M. Srinivas, C. Moslonka, I. Neri, E. Penocchio, W. D. Pineros, M. Polettini, A. Raghu, P. Raux, K. Sekimoto, and A. Soret, *SciPost Phys. Lect. Notes* **80** (2024).
- [10] F. Avanzini, G. Falasco, and M. Esposito, *New J. Phys.* **22**, 093040 (2020).
- [11] D. F. Anderson, G. Craciun, M. Gopalkrishnan, and C. Wiuf, *Bull. Math. Biol.* **77**, 1744 (2015).

- [12] F. Avanzini, N. Freitas, and M. Esposito, [Phys. Rev. X **13**, 021041 \(2023\)](#).
- [13] M. Polettini and M. Esposito, [J. Chem. Phys. **141**, 024117 \(2014\)](#).
- [14] R. S. Caplan, [J. Theor. Biol. **10**, 209 \(1966\)](#).
- [15] A. Wachtel, R. Rao, and M. Esposito, [J. Chem. Phys. **157**, 024109 \(2022\)](#).
- [16] M. Bilancioni and M. Esposito, [Nat. Commun. **16**, 5765 \(2025\)](#).
- [17] H. Vroylandt, D. Lacoste, and G. Verley, [J. Stat. Mech. \(2018\) 023205](#).
- [18] P. Raux, C. Goupil, and G. Verley, [Phys. Rev. E **110**, 014134 \(2024\)](#).
- [19] P. Raux, C. Goupil, and G. Verley, preceding paper, [Phys. Rev. E **112**, 034111 \(2025\)](#).
- [20] P. Raux, Circuit theory for thermodynamic engines in stationary nonequilibrium, Ph.D. thesis, Université Paris Cité, 2024.