Unifying mass-action kinetics and Newtonian mechanics by means of Nambu brackets

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Abstract We demonstrate that elementary biochemical reactions defined by mass-action kinetics satisfy a particular Nambu structure. To this end, we express biochemical reaction equations in terms of Nambu brackets and certain ω -factors. The ω -factors account for the fact that mass-action kinetics exhibits in general flow fields with finite divergence. The proposed approach by means of Nambu brackets and ω -factors unifies divergence free flow fields of Newtonian mechanics and flow fields with finite divergence of mass-action kinetics.

Keywords Mass-action kinetics · Nambu brackets · Divergence of flow fields

1 Introduction

Hamiltonian mechanics can be defined by means of Poisson brackets [1]. In the case of a two-dimensional phase space (x, p) , the Poisson bracket $\{A, B\}$ of two functions $A(x, p)$ and $B(x, p)$ is defined by $\{A, B\} = \partial A / \partial x \partial B / \partial p - \partial A / \partial p \partial B / \partial x$. In this two-dimensional case, the evolution of the state vector $\mathbf{r} = (x, p)$ of a dynamical system is given by $d\mathbf{r}/dt = \{\mathbf{r}, H\}$, where $H(x, p)$ is the Hamiltonian of the system. Moreover, any function $f(\mathbf{r})$ defined on (x, p) evolves as $df/dt = \{f, H\}$. If we set $f = H$, then we obtain $dH/dt = \{H, H\} = 0$, which states that H is constant. Nambu mechanics [2] can be introduced by generalizing the Poisson brackets such that they apply to systems that are characterized by a set of

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Hamiltonian functions $H_1, \dots, H_{n-1}$ and evolve on n -dimensional state spaces with state vectors $\mathbf{r} = (r_1, \dots, r_n)$. Explicitly, the Nambu bracket $\{A_1, \dots, A_n\}$ for the functions $A_1(\mathbf{r}), \dots, A_n(\mathbf{r})$ is defined by

$$\{A_1, \dots, A_n\} = \sum_{i_1, \dots, i_n=1}^n \epsilon_{i_1, \dots, i_n} \frac{\partial A_1}{\partial r_{i_1}} \frac{\partial A_2}{\partial r_{i_2}} \dots \frac{\partial A_n}{\partial r_{i_n}}, \quad (1)$$

where $\epsilon_{i_1, \dots, i_n}$ is the n -dimensional epsilon tensor. Nambu mechanics [2]

$$\frac{d}{dt} \mathbf{r}_k = \sum_{i_2, \dots, i_n=1}^n \epsilon_{k, i_2, \dots, i_n} \frac{\partial H_1}{\partial r_{i_2}} \dots \frac{\partial H_{n-1}}{\partial r_{i_n}} \quad (2)$$

can then be alternatively expressed in terms of $d\mathbf{r}/dt = \{\mathbf{r}, H_1, \dots, H_{n-1}\}$. Moreover, any function $f(\mathbf{r})$ evolves as $df/dt = \{f, H_1, \dots, H_{n-1}\}$ (in this context note that for Nambu brackets we have $\nabla f \cdot \{\mathbf{r}, H_1, \dots, H_{n-1}\} = \{f, H_1, \dots, H_{n-1}\}$). If we set $f = H_k$ for any $k = 1, \dots, n-1$, then it follows that $dH_k/dt = \{H_k, H_1, \dots, H_{n-1}\} = 0$, i.e., the Hamiltonian-like functions are invariants of the dynamics (Eq. 2). The force $\mathbf{I}$ defined by the n -dimensional vector $\mathbf{I}(\mathbf{r}) = \{\mathbf{r}, H_1, \dots, H_{n-1}\}$ is divergence free, i.e., we have $\nabla \cdot \mathbf{I} = 0$ with $\nabla = (\partial/\partial r_1, \dots, \partial/\partial r_n)$. This property implies that the density function $\rho(\mathbf{r}, t)$ for a many particle system with particles evolving like $d\mathbf{r}/dt = \{\mathbf{r}, H_1, \dots, H_{n-1}\}$ satisfies the Liouville equation: $\partial\rho/\partial t = -\nabla \cdot (\mathbf{I}\rho)$.

In the field of classical physics, Nambu mechanics has found several applications. Rigid body rotations satisfying Euler equations [2–8] and particles moving on two spheres [9–13] can be described in terms of Eq. 2. Certain electrodynamic problems (e.g., a charged particle moving in a magnetic field) have been addressed by means of Nambu mechanics [7, 14–18]. The Kepler problem (with its six-dimensional phase space and five invariants) exemplifies another Nambu system [19]. Chiral models [10] as well as the Calogero–Moser system [20, 21] have been investigated. The harmonic oscillator of classical Hamiltonian mechanics has been generalized to yield an elliptic oscillator [22] and multi-oscillator dynamics have been examined from the perspective of Nambu mechanics [19, 23] (for further oscillatory Nambu systems, see also [14, 16]). Likewise, the motion of a free particle from a Nambu perspective has been examined [14, 16]. Some suggestions concerning perturbation theoretical calculations of energy levels can be found in the literature as well [7]. Finally, it has been shown that Nambu mechanics, just as Hamiltonian mechanics, can be generalized to address so-called canonical-dissipative systems [3, 12] (see also [24]).

Our objective is to exploit Nambu brackets in order to study the evolution of biochemical reactions defined by mass-action kinetics. As we will show in Section 2, biochemical reactions exhibit invariants that can be regarded as counterparts to Hamiltonian functions occurring in Nambu mechanics. However, in general, the state space flows representing biochemical reaction kinetics are not divergence free. Therefore, we will need to introduce a factor into Eq. 2 that accounts for the flow field divergence. The motivation for our approach is at least threefold. First, our approach allows the identification of commonalities and differences between the dynamics of Newtonian (Nambu) systems and the dynamics of biological systems. Second, approaching biochemical reactions from a classical mechanics perspective facilitates the introduction of concepts and tools from classical mechanics that might yield new insights into the behavior and characteristic properties of biological systems. Third, the classical mechanics perspective may be used as departure point for introducing analysis methods that simplify the study of reaction kinetics in biology.

2 Nambu bracket formulation of elementary reactions

2.1 Mass-action kinetics for single reactions

The evolution of chemical and biochemical reactions are typically formulated in terms of dynamic systems [25]. As an example, we may consider a chemical reaction of two molecules A and B producing a molecule C : $A + B \rightleftharpoons C$, where, as indicated, we are dealing with a reversible reaction such that both forward and reverse reactions are possible. In general, we consider a single (reversible) reaction that involves $L + R$ molecules (macromolecules, biomolecules, or species). We have L components that react together in order to produce another R components such that

Note that we consider only elementary reactions for which stoichiometric coefficients are either unity or zero [25]. In Eq. 3 the parameters $k_1 > 0$ and $k_2 \geq 0$ denote the reaction rates for the forward and reverse reactions, respectively. In the special case $k_2 = 0$, we are dealing with a nonreversible reaction (for an example, see Section 2.3). Let a_i and b_j denote the concentrations of the molecules A_i and B_j , respectively. From the law of mass action, it follows that the reaction kinetics reads [25]

$$\frac{d}{dt}a_i = k_2 \prod_{j=1}^R b_j - k_1 \prod_{m=1}^L a_m, \quad \frac{d}{dt}b_j = k_1 \prod_{i=1}^L a_i - k_2 \prod_{m=1}^R b_m \quad (4)$$

with $i = 1, \dots, L$ and $j = 1, \dots, R$. For example, the reaction $A + B \rightleftharpoons C$ yields

$$\frac{d}{dt}a = -k_1 ab + k_2 c, \quad \frac{d}{dt}b = -k_1 ab + k_2 c, \quad \frac{d}{dt}c = k_1 ab - k_2 c, \quad (5)$$

where a , b , and c denote the concentrations of molecules A , B , and C .

Equation 4 is a $n = L + R$ dimensional dynamical system with state vector $\mathbf{r} = (r_1, \dots, r_n) = (a_1, \dots, a_L, b_1, \dots, b_R)$. Most importantly, there are $n - 1$ independent invariants. In view of our objective to take advantage of Nambu brackets, we will consider them as counterparts to Hamiltonian functions and denote them by $H_1, \dots, H_{n-1}$. Let us illustrate the existence of $n - 1$ independent invariants. To this end, we use a first set of L invariants defined by

$$H_i = a_i + b_1 \quad (6)$$

for $i = 1, \dots, L$. Clearly, they are linearly independent of each other. In addition, we define another set of $R - 1$ independent invariants: $H_{L+1} = b_2 + a_1, \dots, H_{L+R-1} = b_R + a_1$. That is, we use

$$H_{L-1+j} = b_j + a_1 \quad (7)$$

for $j = 2, \dots, R$. Again, it is obvious that the invariants in Eq. 7 are linearly independent from each other. Moreover, the invariants in Eq. 7 are linearly independent from those defined in Eq. 6. All other invariants of the reaction kinetics (Eq. 4) can be expressed in terms of the invariants $H_1, \dots, H_{n-1}$ (e.g., the invariant $a_i - a_{i^*}$ with $i \neq i^*$ can be expressed by $a_i - a_{i^*} = H_i - H_{i^*}$).

Having defined the invariants $H_1, \dots, H_{n-1}$, we evaluate next the vector-valued Nambu bracket $\mathbf{I} = \{\mathbf{r}, H_1, \dots, H_{n-1}\}$. We first consider I_k for $k = 2, \dots, L$ (the case $k = 1$ requires a special treatment). In this case, we have

$$I_k = \sum_{i_2, \dots, i_n=1}^n \epsilon_{k, i_2, \dots, i_n} \frac{\partial H_1}{\partial r_{i_2}} \cdots \frac{\partial H_{n-1}}{\partial r_{i_n}}. \quad (8)$$

We are interested in identifying the nonzero terms occurring on the right-hand side (we will see that there is exactly one such term). In order to obtain such a nonvanishing term, the indices $i_2, \dots, i_n$ must be different from k . Consequently, $\partial/\partial r_k$ (which is $\partial/\partial a_k$ for $k = 2, \dots, L$) is not at our disposal. The only way to obtain, for $H_k = a_k + b_1$, a factor $\partial H_k/\partial r_{i_2} \neq 0$ is to differentiate H_k with respect to b_1 . Consequently, the index i_{k+1} is given by $i_{k+1} = L + 1$ and we obtain:

$$I_k = \frac{\partial H_k}{\partial b_1} \sum_{i_2, \dots, i_k, i_{k+2}, \dots, i_n=1}^n \epsilon_{k, i_2, \dots, i_k, L+1, i_{k+2}, \dots, i_n} \frac{\partial H_1}{\partial r_{i_2}} \cdots \frac{\partial H_{k-1}}{\partial r_{i_k}} \frac{\partial H_{k+1}}{\partial r_{i_{k+2}}} \cdots \frac{\partial H_{n-1}}{\partial r_{i_n}} \quad (9)$$

with $\partial H_k/\partial b_1 = 1$. For the sake of readability, we replace in what follows integer values such as k and $L + 1$ by their corresponding coordinates $r_k = a_k$ and $r_{L+1} = b_1$:

$$I_{a_k} = \sum_{i_2, \dots, i_k, i_{k+2}, \dots, i_n=1}^n \epsilon_{a_k, i_2, \dots, i_k, b_1, i_{k+2}, \dots, i_n} \frac{\partial H_1}{\partial r_{i_2}} \cdots \frac{\partial H_{k-1}}{\partial r_{i_k}} \frac{\partial H_{k+1}}{\partial r_{i_{k+2}}} \cdots \frac{\partial H_{n-1}}{\partial r_{i_n}}. \quad (10)$$

Next, we note that in any nonvanishing term all partial derivatives $\partial/\partial b_2, \dots, \partial/\partial b_R$ must be present. If we do not use all coordinates $b_2, \dots, b_R$ as partial derivatives, then one of the remaining coordinates r_k would occur at least two times in the expression

$$\frac{\partial H_1}{\partial r_{i_2}} \cdots \frac{\partial H_{k-1}}{\partial r_{i_k}} \frac{\partial H_{k+1}}{\partial r_{i_{k+2}}} \cdots \frac{\partial H_{n-1}}{\partial r_{i_n}}. \quad (11)$$

The ϵ -tensor for such an expression would be zero. In view of this remark, we are next looking for $R - 1$ indices $w_1, \dots, w_{R-1}$ such that the expression $\partial H_{w_1}/\partial b_2 \cdots \partial H_{w_{R-1}}/\partial b_R$ does not vanish. Moreover, all indices $w_1, \dots, w_{R-1}$ must be different. There is only one solution: $(w_1, \dots, w_{R-1}) = (L + 1, \dots, L + R - 1)$. That is,

$$\frac{\partial H_{L+1}}{\partial b_2} \cdots \frac{\partial H_{L+R-1}}{\partial b_R} = 1. \quad (12)$$

Substituting this result into Eq. 9, we can fix $R - 1$ indices and obtain

$$\begin{aligned} I_{a_k} &= \frac{\partial H_{L+1}}{\partial b_2} \cdots \frac{\partial H_{L+R-1}}{\partial b_R} \sum_{i_2, \dots, i_k, i_{k+2}, \dots, i_{L+1}} \epsilon_{a_k, i_2, \dots, i_k, b_1, i_{k+2}, \dots, i_{L+1}, b_2, \dots, b_R} Z \\ &= \sum_{i_2, \dots, i_k, i_{k+2}, \dots, i_{L+1}} \epsilon_{a_k, i_2, \dots, i_k, b_1, i_{k+2}, \dots, i_{L+1}, b_2, \dots, b_R} Z \end{aligned} \quad (13)$$

with

$$Z = \frac{\partial H_1}{\partial r_{i_2}} \cdots \frac{\partial H_{k-1}}{\partial r_{i_k}} \frac{\partial H_{k+1}}{\partial r_{i_{k+2}}} \cdots \frac{\partial H_L}{\partial r_{i_{L+1}}}. \quad (14)$$

The remaining $L - 1$ Hamiltonian functions $H_1, \dots, H_{k-1}, H_{k+1}, \dots, H_L$ depend on the variables b_1 and a_j ($j \neq k$). In order to obtain a nonvanishing expression Z , we cannot use

b_1 for one of the r_j coordinates (the ϵ -tensor would become zero). Consequently, we need to use factors of the form $\partial H_j / \partial a_j$. In doing so, we fix all remaining indices:

$$\begin{aligned} I_{a_k} &= \frac{\partial H_1}{\partial a_1} \cdots \frac{\partial H_{k-1}}{\partial a_{k-1}} \frac{\partial H_{k+1}}{\partial a_{k+1}} \cdots \frac{\partial H_L}{\partial a_L} \epsilon_{a_k, a_1, \dots, a_{k-1}, b_1, a_{k+1}, \dots, a_L, b_2, \dots, b_R} \\ &= \epsilon_{a_k, a_1, \dots, a_{k-1}, b_1, a_{k+1}, \dots, a_L, b_2, \dots, b_R} . \end{aligned} \quad (15)$$

We exchange the indices a_k and b_1 by means of one transposition:

$$I_{a_k} = \epsilon_{a_k, a_1, \dots, a_{k-1}, b_1, a_{k+1}, \dots, a_L, b_2, \dots, b_R} = -\epsilon_{b_1, a_1, \dots, a_L, b_2, \dots, b_R} . \quad (16)$$

We need to carry out L exchanges of index pairs (transpositions) in order to rearrange the sequence $b_1, a_1, \dots, a_L$ into $a_1, \dots, a_L, b_1$. That is, we have

$$I_{a_k} = -\epsilon_{b_1, a_1, \dots, a_L, b_2, \dots, b_R} = (-1)^{L+1} \epsilon_{a_1, \dots, a_L, b_1, b_2, \dots, b_R} = (-1)^{L+1} . \quad (17)$$

The special case $k = 1$ can be treated by similar arguments and we find the same result as in Eq. 17: if L is odd (even), we have $I_{a_1} = 1$ ($I_{a_1} = -1$). We determine next the coefficients I_k for $k = L + 2, \dots, L + R$ related to the coordinates $r_k = b_2, \dots, b_R$ (the case $k = L + 1$ for b_1 requires a separate treatment). That is, we consider

$$I_{b_k} = \sum_{i_2, \dots, i_n=1}^n \epsilon_{b_k, i_2, \dots, i_n} \frac{\partial H_1}{\partial r_{i_2}} \cdots \frac{\partial H_{n-1}}{\partial r_{i_n}} \quad (18)$$

and identify all nonzero terms on the right-hand side (as we will see, there is only one such term). In analogy to the previous case, the variable b_k cannot be used as partial derivative, which implies that, for the invariant $H_{L-1+k} = b_k + a_1$, we can obtain a nonvanishing factor $\partial H_{L-1+k} / \partial r_w$ only by putting $r_w = a_1$. Equation 18 becomes

$$\begin{aligned} I_{b_k} &= \frac{\partial H_{L-1+k}}{\partial a_1} \sum_{i_2, \dots, i_{L-1+k}, i_{L+1+k}, \dots, i_n} \epsilon_{b_k, i_2, \dots, i_{L-1+k}, a_1, i_{L+1+k}, \dots, i_n} Z' \\ &= \sum_{i_2, \dots, i_{L-1+k}, i_{L+1+k}, \dots, i_n} \epsilon_{b_k, i_2, \dots, i_{L-1+k}, a_1, i_{L+1+k}, \dots, i_n} Z' \end{aligned} \quad (19)$$

with

$$Z' = \frac{\partial H_1}{\partial r_{i_2}} \cdots \frac{\partial H_{L-2+k}}{\partial r_{i_{L-1+k}}} \frac{\partial H_{L+k}}{\partial r_{i_{L+1+k}}} \cdots \frac{\partial H_{n-1}}{\partial r_{i_n}} . \quad (20)$$

By analogy to the previous case, we next note that a necessary condition for a nonvanishing expression in the sum of Eq. 19 is that the expression involves all partial derivatives $\partial / \partial a_2, \dots, \partial / \partial a_L$. If we do not use up all coordinates $a_2, \dots, a_L$ as partial derivatives, then we need to use another coordinate at least two times, which would make the ϵ -tensor zero. The only way to use up all variables $a_2, \dots, a_L$ and to obtain a nonzero term is to construct the factor

$$\frac{\partial H_2}{\partial a_2} \cdots \frac{\partial H_L}{\partial a_L} = 1 . \quad (21)$$

Consequently, Eq. 19 reduces to

$$I_{b_k} = \sum_{i_2, i_{L+1}, \dots, i_{L-1+k}, i_{L+1+k}, \dots, i_n} \epsilon_{b_k, i_2, a_2, \dots, a_L, i_{L+1}, \dots, i_{L-1+k}, a_1, i_{L+1+k}, \dots, i_n} Z'' \quad (22)$$

with

$$Z'' = \frac{\partial H_1}{\partial r_{i_2}} \frac{\partial H_{L+1}}{\partial r_{i_{L+2}}} \dots \frac{\partial H_{L-2+k}}{\partial r_{i_{L-1+k}}} \frac{\partial H_{L+k}}{\partial r_{i_{L+1+k}}} \dots \frac{\partial H_{n-1}}{\partial r_{i_n}}. \quad (23)$$

For $H_1 = a_1 + b_1$ we obtain a nonvanishing term Z'' involving the factor $\partial H_1 / \partial r_{i_2}$ only if we put $r_{i_2} = b_1$. This implies

$$I_{b_k} = \sum_{i_{L+1}, \dots, i_{L-1+k}, i_{L+1+k}, \dots, i_n} \epsilon_{b_k, b_1, a_2, \dots, a_L, i_{L+1}, \dots, i_{L-1+k}, a_1, i_{L+1+k}, \dots, i_n} \frac{\partial H_{L+1}}{\partial r_{i_{L+2}}} \dots \frac{\partial H_{L-2+k}}{\partial r_{i_{L-1+k}}} \frac{\partial H_{L+k}}{\partial r_{i_{L+1+k}}} \dots \frac{\partial H_{n-1}}{\partial r_{i_n}}. \quad (24)$$

The remaining $R - 2$ Hamiltonian functions $H_{L+1}, \dots, H_{L-2+k}, H_{L+k}, \dots, H_{L+R-1}$ depend on the variables a_1 and b_j ($j \neq k$). In order to obtain a nonvanishing term in the sum of Eq. 24, we cannot use a_1 for any of the coordinates r_j (the ϵ -tensor would become zero). Consequently, we need to use factors of the form $\partial H_j / \partial b_j$. In doing so, we fix all remaining indices:

$$\begin{aligned} I_{b_k} &= \frac{\partial H_{L+1}}{\partial b_2} \dots \frac{\partial H_{L-2+k}}{\partial b_{k-1}} \frac{\partial H_{L+k}}{\partial b_{k+1}} \dots \frac{\partial H_{n-1}}{\partial b_R} \epsilon_{b_k, b_1, a_2, \dots, a_L, b_2, \dots, b_{k-1}, a_1, b_{k+1}, \dots, b_R} \\ &= \epsilon_{b_k, b_1, a_2, \dots, a_L, b_2, \dots, b_{k-1}, a_1, b_{k+1}, \dots, b_R}. \end{aligned} \quad (25)$$

We exchange the indices a_1 and b_k by means of one transposition such that

$$I_{b_k} = -\epsilon_{a_1, b_1, a_2, \dots, a_L, b_2, \dots, b_R}. \quad (26)$$

By means of $L - 1$ transpositions, we rearrange the index-sequence $b_1, a_2, \dots, a_L$ into $a_2, \dots, a_L, b_1$. In doing so, we obtain

$$I_{b_k} = (-1)^L \epsilon_{a_1, \dots, a_L, b_1, \dots, b_R} = (-1)^L. \quad (27)$$

For the special case I_{b_1} , a similar calculation reveals that we obtain the same result as shown in Eq. 27: if L is even (odd), we have $I_{b_1} = 1$ ($I_{b_1} = -1$). Combining the results from Eqs. 17 and 27, we eventually find

$$\mathbf{I} = \pm \underbrace{(1, \dots, 1)}_L, \underbrace{(-1, \dots, -1)}_R)^T, \quad (28)$$

where the plus (minus) sign holds for odd (even) L (and the superscript T means that we take the transpose, i.e., we have a column vector). Equation 4 can equivalently be expressed in terms of

$$\frac{d}{dt} \mathbf{r} = \pm \omega(\mathbf{r}) \mathbf{I} \quad (29)$$

with the factor

$$\omega(\mathbf{r}) = k_2 \prod_{j=1}^R b_j - k_1 \prod_{i=1}^L a_i. \quad (30)$$

Since we have $\mathbf{I} = \{\mathbf{r}, H_1, \dots, H_{n-1}\}$, Eq. 29 can be cast into the form

$$\frac{d}{dt} \mathbf{r} = \pm \omega(\mathbf{r}) \{\mathbf{r}, H_1, \dots, H_{n-1}\}. \quad (31)$$

Equation 31 provides us with a formulation of mass-action kinetics (Eq. 4) in terms of Nambu brackets. This formulation highlights two different aspects. First, the Nambu bracket in Eq. 31 points out that the reaction dynamics involves invariants. Second, the ω -factor indicates that the reaction dynamics in general will not be divergence free. In particular, for the force term $\mathbf{g}(\mathbf{r}) = \pm\omega(\mathbf{r})\{\mathbf{r}, H_1, \dots, H_{n-1}\}$, we obtain

$$\nabla \cdot \mathbf{g} = \pm(\nabla\omega) \cdot \{\mathbf{r}, H_1, \dots, H_{n-1}\} = (\nabla\omega) \cdot \underbrace{(1, \dots, 1)}_L, \underbrace{(-1, \dots, -1)}_R^T. \quad (32)$$

The divergence can inform us to a certain extent about the stability of attractors (e.g., fixed points) of biochemical reactions. Let $V(t) \geq 0$ denote a volume in the state space spanned by $r_1, \dots, r_n$. Then, the integral over the divergence of $\mathbf{g}$ determines to rate of change of that volume [26, 27]:

$$\frac{d}{dt} V(t) = \int_{V(t)} \nabla \cdot \mathbf{g} d^n r. \quad (33)$$

Recall that for Nambu systems we have $\nabla \cdot \mathbf{g} = 0$, which reflects the fact that state space volumes are preserved under the dynamics of Nambu systems. In contrast, for biochemical reactions we may observe contractions of state space volumes.

Let us illustrate Eq. 31 with an example. For $A + B \rightleftharpoons C$, we have $L = 2$ and $R = 1$. The state vector is $\mathbf{r} = (a, b, c)$ and the invariants read $H_1 = a + c$ and $H_2 = b + c$, such that the Nambu bracket (Eq. 28) becomes $\{\mathbf{r}, H_1, H_2\} = (-1, -1, 1)^T$. Alternatively, we first note that $\nabla H_1 = (1, 0, 1)^T$ and $\nabla H_2 = (0, 1, 1)^T$ (with $\nabla = (\partial/\partial a, \partial/\partial b, \partial/\partial c)$) and then compute $\{\mathbf{r}, H_1, H_2\} = \nabla H_1 \times \nabla H_2 = (-1, -1, 1)^T$. From Eq. 30, we obtain $\omega(\mathbf{r}) = -k_1 ab + k_2 c$. Consequently, Eq. 31 reads

$$\frac{d}{dt} \mathbf{r} = -\omega(\mathbf{r}) \{\mathbf{r}, H_1, H_2\} = (k_1 ab - k_2 c) \nabla H_1 \times \nabla H_2, \quad (34)$$

which is equivalent to Eq. 5 and gives us the dynamics of the reaction $A + B \rightleftharpoons C$ in terms of a Nambu bracket. In what follows, we assume $k_2 > 0$. The divergence of the force term $\mathbf{g} = (k_1 ab - k_2 c) \nabla H_1 \times \nabla H_2$ is $\nabla \cdot \mathbf{g} = -k_2 - k_1(a(t) + b(t))$ and depends in general on the evolution of the concentrations $a(t)$ and $b(t)$. In any case, the divergence is negative, that is, we have $\nabla \cdot \mathbf{g} < -k_2$ for all $\mathbf{r} = (a, b, c)$. From Eq. 33, it follows that

$$\frac{d}{dt} V(t) = - \int_{V(t)} \{k_2 + k_1(a + b)\} da db dc \leq -k_2 V(t). \quad (35)$$

Consequently, we have $V(t) \leq \tilde{V}(t)$ with

$$\tilde{V}(t) = V(0) \exp\{-k_2 t\}. \quad (36)$$

In words, any state space volume decays to zero, which indicates that the biochemical reaction approaches an attractor in the limit $t \rightarrow \infty$. For the $A + B \rightleftharpoons C$ reaction, this attractor is given by a fixed point that satisfies $\omega = 0$. Equation (34) highlights commonalities and differences between the reaction $A + B \rightleftharpoons C$ and conservative systems of classical (Nambu) mechanics. Just as can be observed in Nambu systems, the reaction $A + B \rightleftharpoons C$ corresponds to a dynamical system of order n that involves $n - 1$ invariants or Hamiltonians (here, $n = 3$). Unlike systems of classical mechanics, the system is nonconservative, which is indicated by the ω -factor in Eq. 34. This implies that, in general, perturbations will not persist. Moreover, this implies that the biological system can exhibit more than neutral stability. It can exhibit an attractor. Equations 35 and 36 illustrate that the

second observation (the violation of the classical mechanics scenario) allows us to introduce a concept of nonlinear physics that has been developed for systems that violate Hamiltonian dynamics: the concept of the contraction of state space volumes. For the biochemical $A + B \rightleftharpoons C$ reaction, we find that state space volumes $V(t)$ shrink in the limit $t \rightarrow \infty$ to a single point such that $V \rightarrow 0$.

2.2 Coupled biochemical reactions

For coupled biochemical reactions, similar considerations can be carried out. In the general case, we consider M reversible reactions involving n species (i.e., n different types of biomolecules) $X_1, \dots, X_n$. These reactions read

for $j = 1, \dots, M$. The parameters $l_i^{(j)}$ and $r_i^{(j)}$ correspond to stoichiometric coefficients equal to unity or zero for the elementary reactions under consideration [25]. In our context, the stoichiometric coefficients indicate whether or not in the reaction j a molecule X_i occurs on the left or right-hand side of the reaction dynamics. We introduce the index sets of all left and right participating molecules $D_l^{(j)} = \{k \mid l_k^{(j)} = 1\}$ and $D_r^{(j)} = \{k \mid r_k^{(j)} = 1\}$. Let $|\{\cdot\}|$ denote the size of a set. Accordingly, we define the set sizes $L^{(j)} = |D_l^{(j)}|$, $R^{(j)} = |D_r^{(j)}|$, and $n^{(j)} = L^{(j)} + R^{(j)}$. That is, $n^{(j)}$ is the total number of different components (or reagents) involved in the reaction j . We have $n^{(j)} \leq n$ and define the difference $d^{(j)} = n - n^{(j)}$. That is, there are $d^{(j)}$ components not involved in the reaction j . Each reaction contributes to a change of the n -dimensional state vector $\mathbf{r} = (x_1, \dots, x_n)$, where x_i is the concentration of molecules X_i . In order to describe each reaction separately by means of a Nambu bracket, let us define next $n - 1$ independent invariants. The first $n^{(j)} - 1$ (or $L^{(j)} + R^{(j)} - 1$) invariants are those defined in the context of the single reaction (Eq. 3). In doing so, we obtain the functions $H_1^{(j)}, \dots, H_{n^{(j)}-1}^{(j)}$. In addition, we define $d^{(j)}$ independent invariants on the basis of the components not involved in the reaction j :

$$H_{n^{(j)}}^{(j)} = x_{k_1}, \dots, H_{n-1}^{(j)} = x_{k_{d^{(j)}}}. \quad (38)$$

As a result, we obtain a total of $n^{(j)} - 1 + d^{(j)} = n - 1$ independent invariants. Formally, we may define the indices k_u in Eq. 38 as follows. First, we define the index set $D_0^{(j)} = \{k \mid l_k^{(j)} = 0 \wedge r_k^{(j)} = 0\}$ of all indices of reagents not involved in the reaction j . Subsequently, we sort the index set in ascending order and thus obtain $D_{0,\text{sort}}^{(j)}$. The indices in (38) can then be identified with the indices in $D_{0,\text{sort}}^{(j)}$ such that $H_{n^{(j)}-1+u}^{(j)} = x_{k_u}$ for $u = 1, \dots, d^{(j)}$ and $k_u \in D_{0,\text{sort}}^{(j)}$. The reaction equations of the coupled reactions (Eq. 37) can then be written by means of Nambu brackets as

$$\frac{d}{dt} \mathbf{r} = \sum_{j=1}^M (-1)^{L^{(j)}+1} \omega^{(j)}(\mathbf{r}) \{ \mathbf{r}, H_1^{(j)}, \dots, H_{n-1}^{(j)} \}, \quad (39)$$

where the factors $\omega^{(j)}(\mathbf{r})$ are determined from the single reactions (in analogy to the results derived in Section 2.1). From a mathematical perspective, Eq. 39 describes n -coupled first-order differential equations that involve polynomial functions. In doing so, there is a striking

similarity with Haken networks studied in the context of pattern recognition and multistable competitive systems [28–32].

2.3 Further generalization

Our proposed approach may be generalized in various ways. For example, we may consider so-called clamped variables. That is, we may consider substances whose concentrations are determined externally (and are held constant over time). Let A'_i and B'_i denote such substances and a'_i and b'_i their concentrations. Then Eq. 3 becomes

$$\sum_{i=1}^L A_i + \sum_{i=1}^{L'} A'_i \xrightleftharpoons[k_2]{k_1} \sum_{j=1}^R B_j + \sum_{j=1}^{R'} B'_j. \quad (40)$$

Likewise, (4) reads

$$\begin{aligned} \frac{d}{dt} a_i &= k_2 \prod_{j=1}^R \prod_{k=1}^{R'} b_j b'_k - k_1 \prod_{j=1}^L \prod_{k=1}^{L'} a_j a'_k, \\ \frac{d}{dt} b_i &= k_1 \prod_{j=1}^L \prod_{k=1}^{L'} a_j a'_k - k_2 \prod_{j=1}^R \prod_{k=1}^{R'} b_j b'_k. \end{aligned} \quad (41)$$

The formulation in terms of Nambu brackets defined by Eq. 31 still holds, provided we generalize Eq. 30 as

$$\omega(\mathbf{r}) = k_2 \prod_{j=1}^R \prod_{k=1}^{R'} b_j b'_k - k_1 \prod_{j=1}^L \prod_{k=1}^{L'} a_j a'_k. \quad (42)$$

Analogous considerations can be made for coupled reaction equations. We restrict ourselves to giving an example in this regard. We consider a cyclic of three nonreversible reactions that involves the substances X , Y , Z , and three molecules C'_1 , C'_2 , and C'_3 whose concentrations are held constant. The reactions are

Let x , y , z denote the concentrations of X , Y , Z . Then the invariants of the first reaction are $H_1^{(1)} = x + y$ and $H_2^{(1)} = z$. Likewise, for the second and third reactions, we obtain $H_1^{(2)} = y + z$, $H_2^{(2)} = x$, $H_1^{(3)} = x + z$, and $H_2^{(3)} = y$. For the reaction dynamics in Eq. 43, we obtain from Eq. 39

$$\frac{d}{dt} \mathbf{r} = \omega^{(1)} \nabla H_1^{(1)} \times H_2^{(1)} + \omega^{(2)} \nabla H_1^{(2)} \times H_2^{(2)} + \omega^{(3)} \nabla H_1^{(3)} \times H_2^{(3)}, \quad (44)$$

where $\omega^{(k)}$ can be determined from the single reactions listed in Eq. 43 and $\mathbf{r} = (x, y, z)$. We find $\omega^{(1)} = -k_1 c_1 x$, $\omega^{(2)} = -k_2 c_2 y$, and $\omega^{(3)} = -k_3 c_3 z$. Here, the parameters c_k are the concentrations of the substances C'_k . Substituting the variables $\omega^{(k)}$ and the Hamiltonian invariants into Eq. 44 gives us

$$\frac{d}{dt} \mathbf{r} = \mathbf{g}(\mathbf{r}) = -k_1 c_1 x \begin{pmatrix} 1 \\ -1 \\ 0 \end{pmatrix} - k_2 c_2 y \begin{pmatrix} 0 \\ 1 \\ -1 \end{pmatrix} - k_3 c_3 z \begin{pmatrix} -1 \\ 0 \\ 1 \end{pmatrix}. \quad (45)$$

The divergence of the force vector $\mathbf{g}$ is given by $\nabla \cdot \mathbf{g} = -(k_1c_1 + k_2c_2 + k_3c_3)$ such that any state space volume $V(t)$ decays as $V(t) = V(0) \exp\{-bt\}$ with $b = k_1c_1 + k_2c_2 + k_3c_3 > 0$.

3 Conclusions

We established to some extent a unification of classical Newtonian mechanics and mass-action kinetics. Newtonian mechanics can be expressed in terms of Hamiltonian mechanics. The latter is based on Poisson brackets which can be generalized to Nambu brackets in order to address multi-Hamiltonian systems. We showed that biochemical mass-action kinetics in turn can be described in terms of such multi-Hamiltonian Nambu brackets. This line of arguments puts Newtonian mechanics and reaction kinetics into a unified framework based on Nambu brackets.

We considered single and coupled reactions. Our main results in terms of Eqs. 31 and 39 point out two key aspects of biochemical reaction kinetics. On the one hand, biochemical reactions exhibit invariants as indicated by the Nambu brackets. On the other hand, when interpreting biochemical reactions in terms of dynamical systems, the respective state space flows in general are not divergence free, as indicated by the state-dependent ω -factors. In doing so, we pointed out commonalities and differences between systems of classical mechanics and biological systems satisfying mass-action kinetics.

The framework involving Nambu brackets provides a basis for introducing concepts and tools of classical mechanics into biology. For example, when force fields are not divergence free, then the deviation from the divergence free condition has both a qualitative and quantitative aspect.

First, at a fixed point $\mathbf{r}$, we have $\nabla \cdot \mathbf{g} = \sum_{k=1}^n \lambda_k$, where λ_k are Lyapunov exponents. Consequently, a necessary condition for the existence of a stable fixed point is that the divergence is negative [26]. Second, when $\nabla \cdot \mathbf{g} < 0$ then $\nabla \cdot \mathbf{g}$ determines the rate of volume contraction: $\chi = V^{-1}dV/dt$. Quantitatively, χ may be used as a measure for dissipation rate [27]. In our context, χ quantifies how far away a system is from being an ordinary Nambu system with $\chi = 0$ and $\nabla \cdot \mathbf{g} = 0$ (i.e., χ serves as a distance measure).

Finally, as mentioned in the introduction, the classical mechanics perspective may be exploited in order to develop analysis methods that simplify the study of reaction kinetics in biology. For example, Eq. 39 illustrates that M biochemical reactions involve M different ω -factors irrespective of the number n of species involved in those reactions. In particular, when we have more species than reaction steps ($n > M$), then, from Eq. 39, we may derive a dynamic description for the variables $\omega^{(j)}(t) = \omega^{(j)}(\mathbf{r}(t))$. If the system under consideration is such that, from Eq. 39, a closed description in $\omega^{(j)}(t)$ can be obtained, then the dynamical description in terms of ω -factors reduces the dimensionality of the problem at hand from n to M . It might be beneficial to study the system in the (lower) M -dimensional space rather than in the original (higher) n -dimensional space.

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