

1                    Reachability, Persistence, and  
2 Constructive Chemical Reaction Networks (Part II):  
3                    A Formalism for Species Composition  
4                    in Chemical Reaction Network Theory  
5                    and Application to Persistence

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10                    **Abstract**

11                    Chemical Reaction Network Theory uses mathematics to study sys-  
12                    tems of reactions and infer their properties from their structure. At  
13                    the onset is an abstract definition of a chemical reaction network which  
14                    is very general and is pertinent beyond chemistry, e.g. in modeling in-  
15                    teractions of microscopic and macroscopic living species. This allows  
16                    the theory to provide widely applicable theorems. It also results in that  
17                    the idea of chemical composition is mostly used implicitly in examples  
18                    to illustrate theorems, not explicitly to establish new properties. In this  
19                    paper we propose a formalism for species composition in a way that  
20                    generalizes the idea of atomic composition – for instance, elementary  
21                    species will extend the idea of atoms. We envision that this formalism  
22                    could lead to more theorems on classes of networks that are of inter-  
23                    est in biochemistry. Toward that prospect, we prove that if there is  
24                    no isomerism among elementary species, and if a newly formalized and  
25                    widely applicable reversibility condition holds, then a reaction network  
26                    is vacuously persistent: no species will tend to extinction if all species  
27                    are implicitly present at initial time. This paper is the second in a  
28                    series of three articles. The first paper studies vacuous persistence and  
29                    the third one probes a class of enzymatic networks.

30 **Keywords.** Chemical Reaction Network; Species Composition; Constructive Network; Vacuous  
31 Persistence; Reachability.

32 **Mathematics Subject Classification (2010).** Primary: 92C42. Secondary: 92C45, 34D05.

## 33 1 Introduction

34 This paper is the second in a series of three articles on the persistence of  
35 chemical reaction networks. A reaction network is persistent provided no  
36 species tend to extinction if all species are present at initial time. Persistence  
37 is inherently interesting and has implications for the global asymptotic sta-  
38 bility of positive equilibrium states. In Gnacadja [3], the first article in this  
39 series, we introduce and characterize vacuous persistence, a stronger form of  
40 persistence in which the initial state is merely required to implicitly have all  
41 species. A major motivation for this three-part work was the intuition that  
42 persistence should apply to chemical reaction networks in which species are  
43 made of building blocks that are conserved and processes are fundamentally  
44 reversible. Proving this requires specific and relevant definitions of notions  
45 of building blocks, of fundamentally reversible processes, etc. This paper  
46 addresses these prerequisites.

47  
48 We develop a theory of species composition inspired by the idea of atomic  
49 composition of molecules – for instance, our concept of elementary species  
50 extends that of atoms. In this extension, two elementary species may be  
51 distinct and yet have identical composition. We obtain several results. A  
52 notable one is Theorem 3.6 on canonical bases for the stoichiometric space  
53 and its orthogonal, the conservation space. The basis of the conservation  
54 space consists of vectors that are linear combinations of species with non-  
55 negative integer coefficients. This basis describes in a comprehensive and  
56 minimal fashion the conservativeness of the network. In the literature, this  
57 basis is usually found by visual inspection of networks used to illustrate theo-  
58 rems. That it is a basis of the conservation space is typically a tacit property.

59  
60 We believe that incorporating the idea of species composition in theoretical  
61 investigations could yield more results on classes of networks that model ac-  
62 tual biochemical interactions. Instances of such approaches include our work  
63 in Gnacadja [5] on the existence, uniqueness and global asymptotic stability  
64 of equilibria in networks of reversible binding reactions, and the work of Shi-  
65 nar, Alon and Feinberg [6] on the sensitivity of equilibrium concentrations  
66 with respect to total concentrations of elementary species. In this paper, we

67 obtain a sufficient condition for vacuous persistence as follows.

68 **Theorem 1.1 (Theorem 6.9).** *Suppose that a mass-action reaction net-*  
69 *work is explicitly-reversibly constructive. If there is no isomerism among*  
70 *the elementary species, then the network is vacuously persistent.*  $\square$

71 Isomeric species are species that have the same composition. Basically, a net-  
72 work is constructive if species have compositions which are consistent across  
73 reactions and can be inferred completely from them, and all required ele-  
74 mentary species are actually in the network, possibly with isomerism among  
75 them. A network is explicitly-reversibly constructive if in addition, every  
76 non-elementary species occurs as the target of a binding reaction and also  
77 as the source of a dissociation reaction, and every elementary species occurs  
78 in the source of a binding reaction and also in the target of a dissociation  
79 reaction. Explicitly-reversibly constructive networks are frequent in phar-  
80 macology and biochemistry, e.g. in models of receptor-ligand interactions  
81 and enzyme-catalyzed conversions.

82

83 We have observed that instances of non-persistence and of non-obvious per-  
84 sistence in the literature always involve networks with isomerism among the  
85 building blocks. Theorem 1.1 shows that this is not accidental. However,  
86 the absence of isomerism among the elementary species is not an absolute  
87 requirement for vacuous persistence. Such isomerism occurs among sub-  
88 strates and products in enzymatic networks and yet, they can be vacuously  
89 persistent. We show this in Gnacadja [4], the third and final paper in this  
90 series of articles.

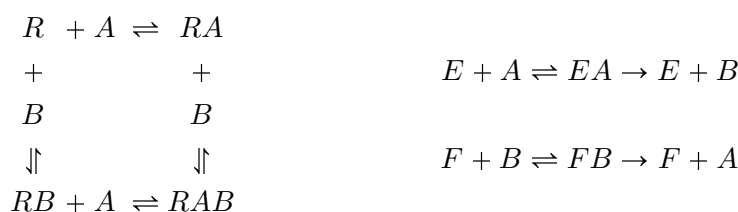
91

92 The remaining content of the paper covers five sections. In Section 2, we de-  
93 fine and study species compositions, constructive networks and several con-  
94 nected concepts. In Section 3, we describe canonical bases for the stoichio-  
95 metric space and its orthogonal, the conservation space. Section 4 presents  
96 results on how to prove that a reaction network is constructive. Section 5  
97 describes the stoichiometry compatibility classes of constructive networks.  
98 Finally, in Section 6, we discuss topics related to the reachability approach  
99 to persistence (Gnacadja [3]) in the context of construction networks. This  
100 culminates with Theorem 6.9 already noted in this introduction as Theorem  
101 1.1.

102 **2 Species Composition and Constructive Networks**

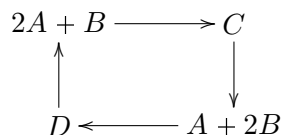
103 We propose and develop a formal notion of species composition to account  
 104 for the idea that species are composed of elementary units or building blocks.  
 105 As this article is the second in a series of three, we rely on Section 3 of  
 106 Gnacadja [3], the first article, for general background material on reaction  
 107 networks. Figure 2.1 shows examples of reaction networks.

108



(a) The allosteric ternary complex model of pharmacology. The interaction is allosteric, i.e. not orthosteric, because the receptor  $R$  has different binding sites for the ligands  $A$  and  $B$ .

(b) Two enzymes  $E$  and  $F$  catalyzing the interconversion of two substrates  $A$  and  $B$ . This is a futile cycle because each enzyme reverses the action of the other.



(c) This network does not model a biochemical interaction we know of, but it serves as an illustrative example in a number of instances.

Figure 2.1: Examples of chemical reaction networks.

109 To begin, we set some notations to be used throughout the paper.

110 **Notation 2.1.** For  $m, n \in \mathbb{Z}$ ,  $[m..n] = \{k \in \mathbb{Z} : m \leq k \leq n\}$ . For  $n \in \mathbb{Z}_{\geq 1}$ ,  
 111  $0_n$  denotes the  $n$ -tuples whose components all equal 0, and for  $i \in [1..n]$ ,  $e_{n,i}$   
 112 denotes the  $n$ -tuple having 1 in position  $i$  and 0 in the other  $n - 1$  positions.  
 113 For  $x = (x_1, \dots, x_n) \in \mathbb{R}^n$ , the length of  $x$  is  $|x| = |x_1| + \dots + |x_n| = \|x\|_{\ell^1}$ .  
 114 For  $x, y \in \mathbb{R}^n$ , we write  $x \leq y$  or  $y \geq x$  (resp.  $x < y$  or  $y > x$ ) to mean that  
 115  $x_i \leq y_i$  (resp.  $x_i < y_i$ ) for all  $i \in [1..n]$ . For a finite set  $E$ , we denote  $|E|$  the  
 116 cardinality of  $E$ ; and when addition makes sense, we write  $\text{sum}(E)$  for the  
 117 sum of its elements.  $\square$

118 A reaction network  $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$  is fixed throughout this section and  $S$   
 119 denotes its stoichiometric space.

120 **Definition 2.2.**

- 121 • A *binding* or *association reaction* is a reaction  $Q' \rightarrow Q''$   
 122 such that  $|Q'| \geq 2$  and  $|Q''| = 1$ . ( $Q''$  is a species,  $Q'$  is not.)
- 123 • An *unbinding* or *dissociation reaction* is a reaction  $Q' \rightarrow Q''$  such that  
 124  $|Q'| = 1$  and  $|Q''| \geq 2$ . ( $Q'$  is a species,  $Q''$  is not.)
- 125 • An *isomerization reaction* is a reaction  $Q' \rightarrow Q''$  such that  
 126  $|Q'| = |Q''| = 1$ . (Both  $Q'$  and  $Q''$  are species.)
- 127 • Two species  $X'$  and  $X''$  are *stoichiometrically isomeric* if  $X' - X'' \in S$ .
- 128 • A *bound species* is a species that is the target of a binding reaction or  
 129 the source of a dissociation reaction (or both).  $\square$

130 The notion of stoichiometric isomerism is intended to account for combina-  
 131 tions of reactions whose net effect is to transform one species into another,  
 132 as is the case for instance in enzymatic reactions. Stoichiometric isomerism  
 133 gives rise to an equivalence relation on the set  $\mathcal{S}$  of species.

134

135 For illustration of Definition 2.2, the network of Figure 2.1(a) consists of  
 136 four reversible binding reactions (four pairs each consisting of a binding  
 137 reaction and the reverse dissociation reaction). The bound species are  $RA$ ,  
 138  $RB$  and  $RAB$  (not because they are denoted with expressions of more than  
 139 one letter). The network of Figure 2.1(b) consists of two binding reactions  
 140 and four dissociation reactions. The bound species are  $EA$  and  $FB$ . The  
 141 species  $A$  and  $B$  are stoichiometrically isomeric because

$$142 \quad A - B = ((F + A) - FB) + (FB - (F + B)) \in S.$$

143 The network of Figure 2.1(c) consists of two binding reactions and two  
 144 dissociation reactions. The bound species are  $C$  and  $D$ . The species  $A$  and  
 145  $B$  are stoichiometrically isomeric, and so are the species  $C$  and  $D$ , because

$$146 \quad A - B = ((2A + B) - D) + (D - (A + 2B)) \in S \text{ and}$$

$$147 \quad C - D = (C - (2A + B)) + ((A + 2B) - D) \in S.$$

148 **Definition 2.3.** A *species composition map*, or simply a *composition* of  $\mathcal{N}$   
 149 is a map  $\mathcal{C} : \mathcal{S} \rightarrow \mathbb{Z}_{\geq 0}^n \setminus \{0_n\}$ , where  $n$  is a positive integer.  $\square$

150 A composition map  $\mathcal{E} = (\mathcal{E}_1, \dots, \mathcal{E}_n) : \mathcal{S} \rightarrow \mathbb{Z}_{\geq 0}^n \setminus \{0_n\}$  for the network  $\mathcal{N}$  is  
 151 fixed for the rest of this section. The idea of a composition map will become  
 152 more precise as we develop it, but the basic intuition is that the composition  
 153  $\mathcal{E}(X)$  of a species  $X$  indicates how many instances of the species of reference  
 154 are present in  $X$ . There could be species of reference that are not in the  
 155 network  $\mathcal{N}$ .

156 **Definition 2.4.**

- 157 • A species  $X \in \mathcal{S}$  is  $\mathcal{E}$ -*elementary* if  $|\mathcal{E}(X)| = 1$ ,  
 158 i.e. if  $\mathcal{E}(X) \in \{e_{n,1}, \dots, e_{n,n}\}$ .
- 159 • A species  $X \in \mathcal{S}$  is  $\mathcal{E}$ -*composite* if  $|\mathcal{E}(X)| \geq 2$ ,  
 160 i.e. if  $\mathcal{E}(X) \in \mathbb{Z}_{\geq 0}^n \setminus \{0_n, e_{n,1}, \dots, e_{n,n}\}$ .
- 161 • Two species  $X', X'' \in \mathcal{S}$  are  $\mathcal{E}$ -*isomeric* if  $\mathcal{E}(X') = \mathcal{E}(X'')$ . □

162  $\mathcal{E}$ -isomerism gives rise to an equivalence relation on the set  $\mathcal{S}$  of species.

163 Let  $\tilde{\mathcal{E}} = (\tilde{\mathcal{E}}_1, \dots, \tilde{\mathcal{E}}_n) : \mathbb{R}\mathcal{S} \rightarrow \mathbb{R}^n$  be the unique  $\mathbb{R}$ -linear extension of  $\mathcal{E}$ . The  
 164 map  $\tilde{\mathcal{E}}$  gives rise to a sensible notion of composition of complexes, which  
 165 leads to a concept of conservation of composition.  
 166

167 **Definition 2.5.**

- 168 • A reaction  $Q' \rightarrow Q''$  is  $\mathcal{E}$ -*conservative* if  $\tilde{\mathcal{E}}(Q') = \tilde{\mathcal{E}}(Q'')$ .
- 169 • The network  $\mathcal{N}$  is  $\mathcal{E}$ -*conservative*, or equivalently the composition  $\mathcal{E}$   
 170 is *conserved* in the network  $\mathcal{N}$ , if all reactions are  $\mathcal{E}$ -conservative. □

171 Figure 2.2 shows examples of conserved compositions for the networks of  
 172 Figure 2.1. These compositions are suggested by visual inspection of the  
 173 networks. The developments in this paper provide systematic means of as-  
 174 certaining the conservativeness features that are the reason why one usually  
 175 needs such compositions.  
 176

177 We record a few obvious results.

178 **Proposition 2.6.** *(The network  $\mathcal{N}$  is  $\mathcal{E}$ -conservative)  $\Leftrightarrow (\text{Ker } \tilde{\mathcal{E}} \supseteq S)$ .* □

179 **Proposition 2.7.** *If the network  $\mathcal{N}$  is  $\mathcal{E}$ -conservative, then stoichiometric  
 180 isomerism implies  $\mathcal{E}$ -isomerism; i.e. if two species are stoichiometrically  
 181 isomeric, then they are  $\mathcal{E}$ -isomeric.* □

| $X$   | $\mathcal{E}(X)$ | $X$  | $\mathcal{E}(X)$ | $X$ | $\mathcal{E}(X)$ |
|-------|------------------|------|------------------|-----|------------------|
| $R$   | (1, 0, 0)        | $E$  | (1, 0, 0)        | $A$ | 1                |
| $A$   | (0, 1, 0)        | $F$  | (0, 1, 0)        | $B$ | 1                |
| $B$   | (0, 0, 1)        | $A$  | (0, 0, 1)        | $C$ | 3                |
| $RA$  | (1, 1, 0)        | $B$  | (0, 0, 1)        | $D$ | 3                |
| $RB$  | (1, 0, 1)        | $EA$ | (1, 0, 1)        |     |                  |
| $RAB$ | (1, 1, 1)        | $FB$ | (0, 1, 1)        |     |                  |

(a)  $\mathcal{E}$  for network 2.1(a).(b)  $\mathcal{E}$  for network 2.1(b).(c)  $\mathcal{E}$  for network 2.1(c).

Figure 2.2: Examples of conserved compositions  $\mathcal{E}$  for the networks of Figure 2.1. The upper and lower parts of the tables show the  $\mathcal{E}$ -elementary and the  $\mathcal{E}$ -composite species respectively. In the network of Figure 2.1(b), the species  $A$  and  $B$  form the only non-singleton  $\mathcal{E}$ -isomerism class. In the network of Figure 2.1(c), the sets  $\{A, B\}$  and  $\{C, D\}$  are the  $\mathcal{E}$ -isomerism classes. These three compositions are core compositions (Definition 2.10) of their respective networks and the three networks are explicitly-reversibly constructive (Definitions 2.13 and 2.14).

182 **Lemma 2.8.** For a nonzero nonsingleton complex  $Q \in \mathcal{C}$ , and for a species  
 183  $X \in \text{Supp}(Q)$ , we have  $\mathcal{E}(X) \leq \tilde{\mathcal{E}}(Q)$  and  $\mathcal{E}(X) \neq \tilde{\mathcal{E}}(Q)$ .  $\square$

184 **Proposition 2.9.** Suppose the network  $\mathcal{N}$  is  $\mathcal{E}$ -conservative. Then every  
 185 bound species is  $\mathcal{E}$ -composite.  $\square$

186 The canonical example of a composition is of course the atomic composition  
 187 of molecules. In this case,  $n$  could be the number of entries in the Periodic  
 188 Table of the Elements and positions in composition  $n$ -tuples could represent  
 189 atomic numbers. However, this example is cumbersome and impractical,  
 190 especially if the species under consideration are macromolecules. For the  
 191 network of Figure 2.1(a) for instance, and as illustrated on Figure 2.2(a),  
 192 we have an intuition that species  $RAB$  is composed of species  $R$ ,  $A$  and  
 193  $B$ , which are elementary within the network, even though they may not be  
 194 atoms. We formalize this observation with the notion of core composition.

195 **Definition 2.10.** The composition  $\mathcal{E}$  is a *core composition* for  $\mathcal{N}$  provided

196 •  $e_{n,1}, \dots, e_{n,n} \in \mathcal{E}(\mathcal{S})$  and

197 •  $\text{Ker} \tilde{\mathcal{E}} = S$ .  $\square$

198 One can verify, either by direct calculations or by applying Theorems 4.2  
 199 and 4.3, that the three compositions of Figure 2.2 are core compositions.  
 200 This terminology is intended to express that a core composition  $\mathcal{E}$  is com-  
 201 plete, in that all  $n$   $\mathcal{E}$ -elementary compositions do occur in the network, and  
 202 is minimal, in that  $\mathcal{E}$ -conservativeness does not impose constraints beyond  
 203 those that stoichiometry already imposes. The following two theorems ar-  
 204 ticulate these in a formal algebraic way. Theorem 2.11 says that any core  
 205 composition is ‘at the core’ of any conserved composition. Theorem 2.12  
 206 essentially says that there can only be one core composition.

207 **Theorem 2.11.** *Any core composition of  $\mathcal{N}$  is universal among all con-*  
 208 *served compositions of  $\mathcal{N}$ . For elaboration, suppose that  $\mathcal{E} : \mathcal{S} \rightarrow \mathbb{Z}_{\geq 0}^n \setminus \{0_n\}$*   
 209 *is a core composition of  $\mathcal{N}$ , and let  $\mathcal{F} : \mathcal{S} \rightarrow \mathbb{Z}_{\geq 0}^N \setminus \{0_N\}$  be a conserved com-*  
 210 *position of  $\mathcal{N}$ . Then there exists a unique  $\mathbb{Z}$ -linear map  $\Phi : \mathbb{Z}^n \rightarrow \mathbb{Z}^N$  that*  
 211 *makes the following diagram commute, and  $\Phi$  maps  $\mathbb{Z}_{\geq 0}^n$  into  $\mathbb{Z}_{\geq 0}^N$ .*

212

$$\begin{array}{ccc} \mathcal{S} & \xrightarrow{\mathcal{F}} & \mathbb{Z}^N \\ \mathcal{E} \downarrow & \nearrow \Phi & \\ \mathbb{Z}^n & & \end{array}$$

213 *Proof.* Let  $\tilde{\mathcal{F}} : \mathbb{R}\mathcal{S} \rightarrow \mathbb{R}^N$  be the linear extension of  $\mathcal{F}$ . The map  
 214  $\tilde{\mathcal{E}} : \mathbb{R}\mathcal{S} \rightarrow \mathbb{R}^n$  is surjective and  $\text{Ker}\tilde{\mathcal{F}} \supseteq S = \text{Ker}\tilde{\mathcal{E}}$ . Therefore, there exists  
 215 a unique  $\mathbb{R}$ -linear map  $\tilde{\Phi} : \mathbb{R}^n \rightarrow \mathbb{R}^N$  such that  $\tilde{\mathcal{F}} = \tilde{\Phi} \circ \tilde{\mathcal{E}}$ . Then, by restric-  
 216 tion to  $\mathcal{S}$ , we have  $\mathcal{F} = \tilde{\Phi} \circ \mathcal{E}$ . As a result,  $\tilde{\Phi}$  maps  $e_{n,1}, \dots, e_{n,n}$  into  $\mathbb{Z}_{\geq 0}^N$ .  
 217 Therefore,  $\tilde{\Phi}$  is the extension of a  $\mathbb{Z}$ -linear map  $\Phi : \mathbb{Z}^n \rightarrow \mathbb{Z}^N$  which maps  
 218  $e_{n,1}, \dots, e_{n,n}$  into  $\mathbb{Z}_{\geq 0}^N$ . The map  $\Phi$  satisfies  $\mathcal{F} = \Phi \circ \mathcal{E}$ . The uniqueness of  
 219  $\tilde{\Phi}$  implies the uniqueness of  $\Phi$ .  $\square$

220 **Theorem 2.12.** *If a reaction network has a core composition, then all core*  
 221 *compositions are equivalent up to indexing permutations in composition tu-*  
 222 *ples. For elaboration, suppose  $\mathcal{E} : \mathcal{S} \rightarrow \mathbb{Z}_{\geq 0}^n \setminus \{0_n\}$  and  $\mathcal{E}' : \mathcal{S} \rightarrow \mathbb{Z}_{\geq 0}^{n'} \setminus \{0_{n'}\}$*   
 223 *are core compositions of the network  $\mathcal{N}$ . Then  $n = n'$  and the  $\mathbb{Z}$ -linear*  
 224 *map  $\Phi$  such that  $\mathcal{E}' = \Phi \circ \mathcal{E}$  is an automorphism of  $\mathbb{Z}^n$  that permutes the*  
 225 *canonical basis vectors  $e_{n,1}, \dots, e_{n,n}$ .*

226 *Proof.* Let  $\Phi : \mathbb{Z}^n \rightarrow \mathbb{Z}^{n'}$  (resp.  $\Phi' : \mathbb{Z}^{n'} \rightarrow \mathbb{Z}^n$ ) be the  $\mathbb{Z}$ -linear map such that  
 227  $\mathcal{E}' = \Phi \circ \mathcal{E}$  (resp.  $\mathcal{E} = \Phi' \circ \mathcal{E}'$ ). Then we have  $\mathcal{E} = \varphi \circ \mathcal{E}$  (resp.  $\mathcal{E}' = \varphi' \circ \mathcal{E}'$ )  
 228 both if  $\varphi = \Phi' \circ \Phi$  and  $\varphi = \text{Id}_{\mathbb{Z}^n}$  (resp.  $\varphi' = \Phi \circ \Phi'$  and  $\varphi' = \text{Id}_{\mathbb{Z}^{n'}}$ ). There-  
 229 fore  $\Phi' \circ \Phi = \text{Id}_{\mathbb{Z}^n}$  and  $\Phi \circ \Phi' = \text{Id}_{\mathbb{Z}^{n'}}$ . It follows that  $n = n'$  and  $\Phi$  is a  $\mathbb{Z}$ -  
 230 linear automorphism of  $\mathbb{Z}^n$  with inverse  $\Phi^{-1} = \Phi'$ . Because  $\Phi$  maps  $\mathbb{Z}_{\geq 0}^n$  into



231 itself, we have  $|\Phi(x)| \geq |x|$  for all  $x \in \mathbb{Z}_{\geq 0}^n$ . Likewise, we have  $|\Phi^{-1}(x)| \geq |x|$   
 232 for all  $x \in \mathbb{Z}_{\geq 0}^n$ , whence  $|x| \geq |\Phi(x)|$  for all  $x \in \mathbb{Z}_{\geq 0}^n$ . So  $|\Phi(x)| = |x|$  for all  
 233  $x \in \mathbb{Z}_{\geq 0}^n$ , and it follows that  $\Phi(\{e_{n,1}, \dots, e_{n,n}\}) = \{e_{n,1}, \dots, e_{n,n}\}$ .  $\square$

234 As a result of Theorem 2.12, if  $\mathcal{E}$  is a core composition of  $\mathcal{N}$ , then the no-  
 235 tions of  $\mathcal{E}$ -elementary,  $\mathcal{E}$ -composite, and  $\mathcal{E}$ -isomeric species are independent  
 236 of the choice of  $\mathcal{E}$  among core compositions, and we simply use the termi-  
 237 nology of *elementary*, *composite*, and *isomeric* species. Also, stoichiometric  
 238 isomerism and  $\mathcal{E}$ -isomerism coincide and we simply call isomerism classes  
 239 the equivalence classes with respect to the two relations.

240 **Definition 2.13.** A reaction network is *constructive* if it admits a core  
 241 composition.  $\square$

242 This terminology is from Shinar, Alon and Feinberg [6, Definition 8.1]. The  
 243 two usages are consistent because of Theorem 3.6. The notions of elements  
 244 and compounds in this prior work correspond to our elementary and com-  
 245 posite species respectively. We note however that if an element is one of  
 246 many isomers, then the isomers other than the element are compounds.

247 **Definition 2.14.** Consider a reaction network.

- 248 • A species  $Y$  is *explicitly constructible* (resp. *explicitly destructible*) if  
 249 there are isomerization reactions  $Y_0 \rightarrow \dots \rightarrow Y_\ell$  (resp.  $Y_\ell \rightarrow \dots \rightarrow Y_0$ ),  
 250 where  $\ell \in \mathbb{Z}_{\geq 0}$ , such that  $Y_0$  is the target of a binding reaction (resp.  
 251 the source of a dissociation reaction) and  $Y_\ell = Y$ .
- 252 • A species  $X$  is *explicitly constructive* (resp. *explicitly destructive*)  
 253 if there is a binding reaction  $Q \rightarrow Y$  (resp. a dissociation reaction  
 254  $Y \rightarrow Q$ ) such that  $X \in \text{Supp}(Q)$ .
- 255 • The reaction network is *explicitly constructive* provided
  - 256 – The network is constructive;
  - 257 – Each composite species is explicitly constructible or explicitly  
 258 destructible or both; and
  - 259 – Each elementary species is explicitly constructive or explicitly  
 260 destructive or both.
- 261 • The reaction network is *explicitly-reversibly constructive* provided
  - 262 – The network is constructive;

- 263           – Each composite species is both explicitly constructible and ex-  
 264           plicitly destructible; and
- 265           – Each elementary species is both explicitly constructive and ex-  
 266           plicitly destructive.  $\square$

267 The pre-complete networks of reversible binding reactions we introduced  
 268 in Gnacadja [5] are explicitly-reversibly constructive; the network of Fig-  
 269 ure 2.1(a) is of that class. More generally, if a reaction network consisting  
 270 of binding and dissociation reactions is constructive and weakly reversible,  
 271 then it is explicitly-reversibly constructive; the networks of Figures 2.1(a)  
 272 and 2.1(c) are of that class. The futile enzymatic cycle of Figure 2.1(b)  
 273 is an example of an explicitly-reversibly constructive network that is not  
 274 weakly reversible. More generally, futile binary enzymatic networks (see  
 275 Gnacadja [4]) are explicitly-reversibly constructive networks that are usu-  
 276 ally not weakly reversible.

### 277 3 Canonical Bases

278 A reaction network  $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$  with stoichiometric space  $S$  is fixed  
 279 for this section. The results presented here show that in the presence of a  
 280 core composition, one has explicit, fairly canonical information about the  
 281 stoichiometric space  $S$  and the conservation space  $S^\perp$ . Most of these pro-  
 282 perties do not require that the composition conservativeness of the network  
 283 be minimal, whence the following definition.

284 **Definition 3.1.** A composition  $\mathcal{E} : \mathcal{S} \rightarrow \mathbb{Z}_{\geq 0}^n \setminus \{0_n\}$  is a *near-core composi-*  
 285 *tion* of the network  $\mathcal{N}$  if

- 286           •  $e_{n,1}, \dots, e_{n,n} \in \mathcal{E}(\mathcal{S})$ , i.e. all  $\mathcal{E}$ -elementary compositions occur, and
- 287           •  $\text{Ker} \tilde{\mathcal{E}} \supseteq S$ , i.e.  $\mathcal{N}$  is  $\mathcal{E}$ -conservative.  $\square$

288 Figure 3.1 shows an example of a near-core non-core composition.

289

290 A near-core composition  $\mathcal{E} = (e_1, \dots, e_n) : \mathcal{S} \rightarrow \mathbb{Z}_{\geq 0}^n \setminus \{0_n\}$  for the network  
 291  $\mathcal{N}$  is fixed for the rest of this section. We set the following notations.

292 **Notation 3.2.**

- 293           • For  $i \in [1..n]$ ,  $\mathcal{X}_i := \mathcal{E}^{-1}(e_{n,i})$  is the  $\mathcal{E}$ -isomerism class of  $\mathcal{E}$ -elementary  
 294           species with  $\mathcal{E}$ -composition  $e_{n,i}$ , and  $p_i := |\mathcal{X}_i|$  is the number of these  
 295           species.



(a) A hypothetical network with species in usual chemistry notation.

| $X$    | $\mathcal{E}'(X)$ | $X$    | $\mathcal{E}''(X)$ |
|--------|-------------------|--------|--------------------|
| $H$    | (1, 0, 0)         | $H$    | (1, 0, 0, 0)       |
| $C$    | (0, 1, 0)         | $C$    | (0, 1, 0, 0)       |
| $O$    | (0, 0, 1)         | $O$    | (0, 0, 1, 0)       |
| $OH$   | (1, 0, 1)         | $OH$   | (0, 0, 0, 1)       |
| $H_2O$ | (2, 0, 1)         | $H_2O$ | (1, 0, 0, 1)       |
| $CO_2$ | (0, 1, 2)         | $CO_2$ | (0, 1, 2, 0)       |

(b)  $\mathcal{E}'$ , a near-core non-core composition.

(c)  $\mathcal{E}''$ , a core composition.

Figure 3.1: A near-core non-core composition  $\mathcal{E}'$  and a core composition  $\mathcal{E}''$  for the network shown. The upper and lower parts of the tables show the elementary and the composite species relative to each composition. The composition  $\mathcal{E}'(OH) = (1, 0, 1)$  is suggested by known information not represented in the network. Within the scope of the network, the species  $OH$  is elementary as shown by the core composition  $\mathcal{E}''$ . This reveals that the network may not have all the reactions that were intended.

- 296 •  $I := \mathcal{E}(\mathcal{S}) \setminus \{e_{n,1}, \dots, e_{n,n}\}$  is the set of  $n$ -tuples that occur as  $\mathcal{E}$ -  
 297 composition of  $\mathcal{E}$ -composite species;  $I \subset \mathbb{Z}_{\geq 0}^n \setminus \{0_n, e_{n,1}, \dots, e_{n,n}\}$ .
- 298 • For  $\alpha \in I$ ,  $\mathcal{Y}_\alpha := \mathcal{E}^{-1}(\alpha)$  is the  $\mathcal{E}$ -isomerism class of  $\mathcal{E}$ -composite  
 299 species with  $\mathcal{E}$ -composition  $\alpha$ , and  $q_\alpha := |\mathcal{Y}_\alpha|$  is the number of these  
 300 species.
- 301 •  $\mathcal{S}_e$  is the set of  $\mathcal{E}$ -elementary species;  $\mathcal{S}_e = \bigsqcup_{i \in [1..n]} \mathcal{X}_i$ .  
 302  $\mathcal{S}_c$  is the set of  $\mathcal{E}$ -composite species;  $\mathcal{S}_c = \bigsqcup_{\alpha \in I} \mathcal{Y}_\alpha$ .  
 303  $\mathcal{S}_e^1$  is the set of  $\mathcal{E}$ -elementary species whose  $\mathcal{E}$ -isomerism classes are  
 304 singletons;  $\mathcal{S}_e^1 = \bigsqcup_{i \in [1..n], |p_i|=1} \mathcal{X}_i$ .  
 305 For  $i \in [1..n]$ ,  $\mathcal{S}_{c,i}$  is the set of composite species whose  $\mathcal{E}$ -composition  
 306 has a positive term of index  $i$ ;  $\mathcal{S}_{c,i} := \{Y \in \mathcal{S}_c : \mathcal{E}_i(Y) \geq 1\}$ .
- 307 •  $p := |\mathcal{S}_e| = \sum_{i=1}^n p_i$  is the total number of  $\mathcal{E}$ -elementary species.  
 308  $q := |\mathcal{S}_c| = \sum_{\alpha \in I} q_\alpha$  is the total number of  $\mathcal{E}$ -composite species.  
 309  $r := |\mathcal{S}| = p + q$  is the total number of species.  
 310  $n$  already denotes the number of  $\mathcal{E}$ -isomerism classes of elementary

311 species.

312  $m := |I|$  is the number of  $\mathcal{E}$ -isomerism classes of composite species.  $\square$

313 Here is, for illustration, what these notations evaluate to for the futile en-  
314 zymatic cycle of Figure 2.1(b) with the core composition of Figure 2.2(b):

$$\begin{aligned}
 315 \quad & \mathcal{X}_1 = \{E\}, \mathcal{X}_2 = \{F\}, \mathcal{X}_3 = \{A, B\}, p_1 = 1, p_2 = 1, p_3 = 2, \\
 316 \quad & I = \{(1, 0, 1), (0, 1, 1)\}, \\
 317 \quad & \mathcal{Y}_{(1,0,1)} = \{EA\}, \mathcal{Y}_{(0,1,1)} = \{FB\}, q_{(1,0,1)} = 1, q_{(0,1,1)} = 1, \\
 318 \quad & \mathcal{S}_e = \{E, F, A, B\}, \mathcal{S}_c = \{EA, FB\}, \\
 319 \quad & \mathcal{S}_e^1 = \{E, F\}, \mathcal{S}_{c,1} = \{EA\}, \mathcal{S}_{c,2} = \{FB\}, \mathcal{S}_{c,3} = \{EA, FB\}, \\
 320 \quad & p = 4, q = 2, r = 6, n = 3, m = 2.
 \end{aligned}$$

322 By the Rank-Nullity Theorem, we have:

**Theorem 3.3.**

$$323 \quad \text{nullity} \left( \tilde{\mathcal{E}} \right) = \dim \text{Ker} \tilde{\mathcal{E}} = r - n = p + q - n = q + \sum_{i=1}^n (p_i - 1).$$

324 *In particular, if (and only if) there is no  $\mathcal{E}$ -isomerism among the  $\mathcal{E}$ -elementary*  
325 *species (i.e.  $\mathcal{S}_e^1 = \mathcal{S}_e$ ), then the nullity of  $\tilde{\mathcal{E}}$  equals the number of  $\mathcal{E}$ -*  
326 *composite species. Note that if  $\mathcal{E}$  is a core composition, then the nullity*  
327 *of  $\tilde{\mathcal{E}}$  equals the rank of the network.  $\square$*

328 Using Theorem 3.3 on the networks of Figures 2.1(a), 2.1(b), 2.1(c) and  
329 3.1(a), and their core compositions of Figures 2.2(a), 2.2(b), 2.2(c) and  
330 3.1(c), we readily obtain that they have rank 3, 3, 3 and 2 respectively.  
331 Thus, this can be helpful in calculating the deficiency, an integer attribute  
332 of a reaction network of importance in Chemical Reaction Network Theory.  
333 See for instance Feinberg [2] for the definition and some implications of the  
334 deficiency. The rank of a network is the one ingredient that is usually the  
335 least readily available. The other ingredients, the number of complexes and  
336 the number of linkages classes, are usually obtained by visual inspection. Of  
337 course, for this remark to be pertinent, we must have convenient ways to  
338 find core compositions. Section 4 addresses this matter.

339  
340 We continue in this section with results on canonical bases. Theorem 3.4  
341 provides a canonical basis for  $\text{Ker} \tilde{\mathcal{E}}$ . Theorem 3.5 provides for the orthogonal

342  $(\text{Ker}\tilde{\mathcal{E}})^\perp$  of  $\text{Ker}\tilde{\mathcal{E}}$  a canonical basis consisting of vectors that are linear com-  
 343 binations of species with nonnegative integer coefficients. Finally, Theorem  
 344 3.6 combines these two results with canonical bases for the stoichiometric  
 345 and conservation spaces  $S$  and  $S^\perp$  in the case where  $\mathcal{E}$  is a core composition.

346

347 We define the linear map  $\rho : \mathbb{R}\mathcal{S} \rightarrow \mathbb{R}\mathcal{S}$  by

$$348 \quad \rho(Z) = Z - \sum_{i=1}^n \frac{\mathcal{E}_i(Z)}{p_i} \text{sum}(\mathcal{X}_i) \quad \text{for } Z \in \mathcal{S}. \quad (3.1)$$

349 In particular,

$$350 \quad \rho(X) = X - \frac{1}{p_i} \text{sum}(\mathcal{X}_i) \quad \text{if } X \in \mathcal{X}_i, \text{ and} \quad (3.2)$$

$$351 \quad \rho(Y) = Y - \sum_{i=1}^n \frac{\alpha_i}{p_i} \text{sum}(\mathcal{X}_i) \quad \text{if } Y \in \mathcal{Y}_\alpha. \quad (3.3)$$

352

353 **Theorem 3.4.** For each  $i \in [1..n]$ , let  $\mathcal{B}_i$  be one of the  $p_i$  sets of  $(p_i - 1)$   
 354 elements obtained by excising one element from the set  $\{\rho(X) : X \in \mathcal{X}_i\}$ .  
 355 Then let

$$356 \quad \mathcal{B} = \{\rho(Y) : Y \in \mathcal{S}_c\} \sqcup \bigsqcup_{i=1}^n \mathcal{B}_i = \{\rho(Y) : Y \in \mathcal{S}_c\} \sqcup \bigsqcup_{\substack{1 \leq i \leq n \\ p_i > 1}} \mathcal{B}_i.$$

357 The set  $\mathcal{B}$  is a basis of  $\text{Ker}\tilde{\mathcal{E}}$ .

358 *Proof.*

359 We see from Equations (3.2) and (3.3) that the vectors  $\rho(Z)$  for  $Z \in \mathcal{S} \setminus \mathcal{S}_c^1$   
 360 are pairwise distinct. So the disjoint unions in the expression of  $\mathcal{B}$  are justi-  
 361 fied and the cardinality of  $\mathcal{B}$  is equal to the dimension of  $\text{Ker}\tilde{\mathcal{E}}$  as provided  
 362 by Theorem 3.3.

363 From Equation (3.1), we get that  $\tilde{\mathcal{E}}(\rho(Z)) = 0_n$  for all  $Z \in \mathcal{S}$ . Hence,  
 364  $\mathcal{B} \subset \text{Ker}\tilde{\mathcal{E}}$ .

365 One can verify that the set  $\{\rho(Y) : Y \in \mathcal{S}_c\}$  is linearly independent, and that  
 366 so is the set  $\mathcal{B}_i$  for each  $i \in [1..n]$  with  $p_i > 1$ . Furthermore, the sets  $\mathcal{B}_i$  are  
 367 pairwise orthogonal because  $\mathcal{B}_i \subset \mathbb{R}\mathcal{X}_i$ . So the set  $\bigsqcup_{i=1}^n \mathcal{B}_i$  is linearly inde-  
 368 pendent. Now, intersecting the subspaces spanned by  $\{\rho(Y) : Y \in \mathcal{S}_c\}$  and  
 369 by  $\bigsqcup_{i=1}^n \mathcal{B}_i$  yields the zero space. So the set  $\mathcal{B}$  is linearly independent.  $\square$

370 Let the linear map  $\tau : \mathbb{R}^n \rightarrow \mathbb{R}\mathcal{S}$  be defined by  $\tau(e_{n,i}) = T_i$  for  $i \in [1..n]$ ,  
 371 where

$$372 \quad T_i := \text{sum}(\mathcal{X}_i) + \sum_{\alpha \in I} \alpha_i \text{sum}(\mathcal{Y}_\alpha) = \text{sum}(\mathcal{X}_i) + \sum_{Y \in \mathcal{S}_c} \mathcal{E}_i(Y) Y. \quad (3.4)$$

373 **Theorem 3.5.** *We have  $(\text{Ker}\tilde{\mathcal{E}})^\perp = \text{Im}\tau$  and the set  $\mathcal{B}' = \{T_1, \dots, T_n\}$  is*  
 374 *a basis of  $(\text{Ker}\tilde{\mathcal{E}})^\perp$ . In particular,  $\mathcal{B}'$  is a linearly independent subset of*  
 375 *the conservation space  $S^\perp$ .*

376 *Proof.* We obtain the adjunction property

$$377 \quad \langle \tau(x), Q \rangle = \langle x, \tilde{\mathcal{E}}(Q) \rangle, \quad \forall x \in \mathbb{R}^n, \forall Q \in \mathbb{R}\mathcal{S} \quad (3.5)$$

378 by verifying that each side of the equality equals  $\mathcal{E}_i(Q)$  when  $x \in \{e_{n,1}, \dots, e_{n,n}\}$   
 379 and  $Q \in \mathcal{S}_e$  or  $Q \in \mathcal{S}_c$ . As a result, we have  $(\text{Im}\tau)^\perp = \text{Ker}\tilde{\mathcal{E}}$ . Hence,  
 380  $(\text{Ker}\tilde{\mathcal{E}})^\perp = \text{Im}\tau$ , and the set  $\{T_1, \dots, T_n\}$  spans  $(\text{Ker}\tilde{\mathcal{E}})^\perp$ . From Theo-  
 381 rem 3.3,  $(\text{Ker}\tilde{\mathcal{E}})^\perp$  has dimension  $n$ , so the set  $\{T_1, \dots, T_n\}$  is a basis of  
 382  $(\text{Ker}\tilde{\mathcal{E}})^\perp$ . □

383 We combine in Theorem 3.6 what Theorems 3.4 and 3.5 say when  $\mathcal{E}$  is a  
 384 core composition.

385 **Theorem 3.6.** *Suppose that  $\mathcal{E}$  is a core composition of  $\mathcal{N}$ . Then:*

- 386 • *The set  $\mathcal{B}$  from Theorem 3.4 is a basis of the stoichiometric space  $S$ .*
- 387 • *The set  $\mathcal{B}'$  from Theorem 3.5 is a basis of the conservation space  $S^\perp$ .*  
 388 *Each vector in  $\mathcal{B}'$  is a linear combination of species with nonnegative*  
 389 *integer coefficients.* □

390 The basis  $\mathcal{B}'$  provides a canonical, comprehensive and minimal description  
 391 of the conservativeness of the network. Because of Theorem 2.12, the basis  
 392  $\mathcal{B}'$  is independent of the choice of a core composition for the (constructive)  
 393 network  $\mathcal{N}$ . This result and its proof are rigorous statement and justifi-  
 394 cation for the common practice of cataloging conservation laws by visual  
 395 inspection of reaction networks. Section 4 provides means of finding core  
 396 compositions, thereby turning Theorem 3.6 into a useful tool for applica-  
 397 tions. To illustrate this theorem, we use the futile enzymatic cycle of Figure

398 2.1(b), its core composition of Figure 2.2(b), and the related values of the  
 399 notations of Notation 3.2 listed earlier in this section. We have

$$\begin{aligned}
 400 \quad & \rho(E) = 0, \rho(F) = 0, \rho(A) = \frac{1}{2}(A - B), \rho(B) = \frac{1}{2}(B - A), \\
 401 \quad & \rho(EA) = EA - E - \frac{1}{2}(A + B), \rho(FB) = FB - F - \frac{1}{2}(A + B), \\
 402 \quad & T_1 = E + EA, T_2 = F + FB, T_3 = A + B + EA + FB.
 \end{aligned}$$

404 Below are one of the two possible bases  $\mathcal{B}$  and the basis  $\mathcal{B}'$ .

$$\begin{aligned}
 405 \quad & \mathcal{B} = \left\{ \frac{1}{2}(A - B), EA - E - \frac{1}{2}(A + B), FB - F - \frac{1}{2}(A + B) \right\} \\
 406 \quad & \mathcal{B}' = \{E + EA, F + FB, A + B + EA + FB\}
 \end{aligned}$$

#### 408 4 Finding Core Compositions

409 Let  $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$  be a reaction network and let  $\mathcal{E} : \mathcal{S} \rightarrow \mathbb{Z}_{\geq 0}^n \setminus \{0_n\}$  be  
 410 a composition of  $\mathcal{N}$ . We devote this section to ways to prove that  $\mathcal{E}$  is a  
 411 core composition of  $\mathcal{N}$  when it is known that  $\mathcal{E}$  is a near-core composition.  
 412 We adopted this approach because the common practice of cataloging con-  
 413 servation laws by visual inspection produces near-core compositions. The  
 414 difficulty lies in the minimality aspect of a core composition, i.e. the fact  
 415 that  $\text{Ker} \tilde{\mathcal{E}} \subseteq S$ . Because of Theorem 3.4, this containment relationship is  
 416 equivalent to the property that  $\rho(Z) \in S$  for all  $Z \in \mathcal{S}$ . But proving this  
 417 from the expressions of Equations (3.1), (3.2) and (3.3) may not be obvious.  
 418 The following result provides other useful expressions for these vectors.

419 **Lemma 4.1.** *Suppose that  $\mathcal{E}$  is a near-core composition of  $\mathcal{N}$  and refer to*  
 420 *Notation 3.2.*

421 • For  $i \in [1..n]$  and  $X \in \mathcal{X}_i$ , we have

$$422 \quad \rho(X) = \frac{1}{p_i} \sum_{W \in \mathcal{X}_i} (X - W). \quad (4.1)$$

423 • For  $\alpha \in I$  and  $Y \in \mathcal{Y}_\alpha$ , we have

$$424 \quad \rho(Y) = \frac{1}{p_1 \cdots p_n} \sum_{(W_1, \dots, W_n) \in \mathcal{X}_1 \times \cdots \times \mathcal{X}_n} \left( Y - \sum_{i=1}^n \alpha_i W_i \right). \quad (4.2)$$

425 *Proof.* Equation (4.1) is an obvious reformulation of Equation (3.2). We  
 426 prove Equation (4.2). We have:

$$\begin{aligned}
 427 \quad & \sum_{(W_1, \dots, W_n) \in \mathcal{X}_1 \times \dots \times \mathcal{X}_n} \left( \sum_{i=1}^n \alpha_i W_i \right) \\
 428 \quad &= \sum_{i=1}^n \left( \sum_{(W_1, \dots, W_n) \in \mathcal{X}_1 \times \dots \times \mathcal{X}_n} \alpha_i W_i \right) \\
 429 \quad &= \sum_{i=1}^n \alpha_i \left( \sum_{(W_1, \dots, W_n) \in \mathcal{X}_1 \times \dots \times \mathcal{X}_n} W_i \right) \\
 430 \quad &= \sum_{i=1}^n \alpha_i \left( \sum_{(W_1, \dots, W_{i-1}, W_{i+1}, \dots, W_n) \in \mathcal{X}_1 \times \dots \times \mathcal{X}_{i-1} \times \mathcal{X}_{i+1} \times \dots \times \mathcal{X}_n} \left( \sum_{W_i \in \mathcal{X}_i} W_i \right) \right) \\
 431 \quad &= \sum_{i=1}^n \alpha_i \left( \sum_{(W_1, \dots, W_{i-1}, W_{i+1}, \dots, W_n) \in \mathcal{X}_1 \times \dots \times \mathcal{X}_{i-1} \times \mathcal{X}_{i+1} \times \dots \times \mathcal{X}_n} \text{sum}(\mathcal{X}_i) \right) \\
 432 \quad &= \sum_{i=1}^n \alpha_i p_1 \cdots p_{i-1} p_{i+1} \cdots p_n \text{sum}(\mathcal{X}_i) \\
 433 \quad &= p_1 \cdots p_n \sum_{i=1}^n \frac{\alpha_i}{p_i} \text{sum}(\mathcal{X}_i) \\
 434 \quad &= p_1 \cdots p_n (Y - \rho(Y)) . \\
 435
 \end{aligned}$$

436 It follows that:

$$\begin{aligned}
 437 \quad p_1 \cdots p_n \rho(Y) &= p_1 \cdots p_n Y - \sum_{(W_1, \dots, W_n) \in \mathcal{X}_1 \times \dots \times \mathcal{X}_n} \left( \sum_{i=1}^n \alpha_i W_i \right) \\
 438 \quad &= \sum_{(W_1, \dots, W_n) \in \mathcal{X}_1 \times \dots \times \mathcal{X}_n} \left( Y - \sum_{i=1}^n \alpha_i W_i \right) . \quad \square
 \end{aligned}$$

439 Following is one of the two main results of this section.

440 **Theorem 4.2.** *Refer to Notation 3.2 and suppose that:*

- 441 (1)  $\mathcal{E}$  is a near-core composition of  $\mathcal{N}$ ;
- 442 (2) For every  $i \in [1..n]$ , all ( $\mathcal{E}$ -elementary) species of composition  $e_{n,i}$  are  
 443 stoichiometrically isomeric, i.e.  $(X, W \in \mathcal{X}_i) \Rightarrow (X - W \in S)$ ; and



444 (3) For every  $\alpha \in I$  and  $Y \in \mathcal{Y}_\alpha$ , there exist  $W_1 \in \mathcal{X}_1, \dots, W_n \in \mathcal{X}_n$  such  
 445 that  $Y - \sum_{i=1}^n \alpha_i W_i \in S$ .

446 Then  $\mathcal{E}$  is a core composition of  $\mathcal{N}$ .

447 *Proof.* We just need to show that  $\rho(Z) \in S$  for all  $Z \in \mathcal{S}$ .

448 Condition (2) of the theorem along with Equation (4.1) of Lemma 4.1 imply  
 449 that  $\rho(X) \in S$  if  $X \in \mathcal{X}_i$  for some  $i \in [1..n]$ .

450 Let  $\alpha \in I$  and  $Y \in \mathcal{Y}_\alpha$ . With Condition (3), we have  $W_1^0 \in \mathcal{X}_1, \dots, W_n^0 \in \mathcal{X}_n$   
 451 such that  $Y - \sum_{i=1}^n \alpha_i W_i^0 \in S$ . Let  $W_1 \in \mathcal{X}_1, \dots, W_n \in \mathcal{X}_n$ . For every  $i \in [1..n]$ ,  
 452 both  $W_i^0$  and  $W_i$  are in  $\mathcal{X}_i$ , and so  $W_i^0 - W_i \in S$  by Condition (2). Hence,

$$453 \quad Y - \sum_{i=1}^n \alpha_i W_i = Y - \sum_{i=1}^n \alpha_i W_i^0 + \sum_{i=1}^n \alpha_i (W_i^0 - W_i) \in S.$$

454 Then, Equation (4.2) of Lemma 4.1 implies that  $\rho(Y) \in S$ . □

455 Theorem 4.2 is directly applicable if each composite species is explicitly con-  
 456 structible or explicitly destructible from a non-singleton complex in which  
 457 all species are elementary. This is the case for the networks of Figures 2.1(b)  
 458 and 2.1(c). Theorem 4.2 does readily show that the compositions of Figures  
 459 2.2(b) and 2.2(c) are core compositions. But this is not the case for the  
 460 allosteric ternary complex model of Figure 2.1(a). To show that the com-  
 461 position of Figure 2.2(a) is a core composition, or in other such cases, one  
 462 can ascertain Condition (3) of Theorem 4.2 by induction, or one can use the  
 463 following theorem.

464 **Theorem 4.3.** *Suppose that:*

- 465 (1)  $\mathcal{E}$  is a near-core composition of  $\mathcal{N}$ ;  
 466 (2)  $\mathcal{E}$ -isomerism implies stoichiometric isomerism; and  
 467 (3) Every  $\mathcal{E}$ -composite species is stoichiometrically isomeric to a bound  
 468 species.

469 Then  $\mathcal{E}$  is a core composition of  $\mathcal{N}$ .

470 We state and prove a technical result, which we then use to prove Theorem  
 471 4.3. For  $\alpha \in I$ , let  $I_\alpha = \{\beta \in I : \beta \leq \alpha \text{ and } \beta \neq \alpha\}$ .

472 **Lemma 4.4.** Assume the hypotheses of Theorem 4.3 and refer to Notation  
 473 3.2. Let  $Y \in \mathcal{S}_C$  and  $\alpha = \mathcal{E}(Y)$ . There exist  $\sigma_i \in \mathbb{Z}_{\geq 0}$  for  $i \in [1..n]$  and  
 474  $\sigma_\beta \in \mathbb{Z}_{\geq 0}$  for  $\beta \in I_\alpha$  such that, for all  $i \in [1..n]$  and  $X_i \in \mathcal{X}_i$ , and all  $\beta \in I_\alpha$   
 475 and  $Y_\beta \in \mathcal{Y}_\beta$ , we have

$$476 \quad Y - \left( \sum_{i=1}^n \sigma_i X_i + \sum_{\beta \in I_\alpha} \sigma_\beta Y_\beta \right) \in S.$$

477 We have the conservation relation  $\alpha = (\sigma_1, \dots, \sigma_n) + \sum_{\beta \in I_\alpha} \sigma_\beta \beta$ .

478 *Proof.* Condition (3) of Theorem 4.3 implies the existence of a complex  
 479  $Q = \sum_{Z \in \mathcal{S}} Q_Z Z \in \mathcal{C}$  of length  $|Q| \geq 2$  such that  $Y - Q \in S$ . For each  $i \in [1..n]$ ,

480 let  $\sigma_i = \sum_{Z \in \mathcal{X}_i} Q_Z$  and  $X_i \in \mathcal{X}_i$ . For each  $\beta \in I$ , let  $\sigma_\beta = \sum_{Z \in \mathcal{Y}_\beta} Q_Z$  and  $Y_\beta \in \mathcal{Y}_\beta$ .

481 One can verify that

$$482 \quad -Q = - \left( \sum_{i=1}^n \sigma_i X_i + \sum_{\beta \in I} \sigma_\beta Y_\beta \right) \\ 483 \quad + \sum_{i=1}^n \sum_{Z \in \mathcal{X}_i} Q_Z (X_i - Z) + \sum_{\beta \in I} \sum_{Z \in \mathcal{Y}_\beta} Q_Z (Y_\beta - Z).$$

484 With Condition (2) of Theorem 4.3, we get that  $X_i - Z \in S$  for  $i \in [1..n]$   
 485 and  $Z \in \mathcal{X}_i$ , and  $Y_\beta - Z \in S$  for  $\beta \in I$  and  $Z \in \mathcal{Y}_\beta$ . Plus we already have  
 486  $Y - Q \in S$ . Therefore

$$487 \quad Y - \left( \sum_{i=1}^n \sigma_i X_i + \sum_{\beta \in I} \sigma_\beta Y_\beta \right) \in S.$$

488 And because  $S \subseteq \text{Ker } \tilde{\mathcal{E}}$ , it follows that  $\alpha = (\sigma_1, \dots, \sigma_n) + \sum_{\beta \in I} \sigma_\beta \beta$ .

489 It remains to show that  $\sigma_\beta = 0$  for  $\beta \in I \setminus I_\alpha$ . Let  $\beta \in I$ . We have  $\sigma_\beta \beta \leq \alpha$ , so  
 490 if  $\sigma_\beta \geq 1$ , then  $\beta \leq \alpha$ . By contraposition, if  $\beta \notin I_\alpha$  and  $\beta \neq \alpha$ , then  $\sigma_\beta = 0$ .

491 We now need to show that  $\sigma_\alpha = 0$ . We in particular have  $\sigma_\alpha \alpha \leq \alpha$ , so  
 492  $\sigma_\alpha \leq 1$ . Suppose  $\sigma_\alpha = 1$ . Then we successively have

$$493 \quad 0_n = -\alpha + (\sigma_1, \dots, \sigma_n) + \sum_{\beta \in I} \sigma_\beta \beta = (\sigma_1, \dots, \sigma_n) + \sum_{\beta \in I \setminus \{\alpha\}} \sigma_\beta \beta;$$

494  $\sigma_i = 0$  for  $i \in [1..n]$  and  $\sigma_\beta = 0$  for  $\beta \in I \setminus \{\alpha\}$ ; and

495  $|Q| = \sum_{Z \in \mathcal{S}} Q_Z = \sum_{i=1}^n \sigma_i + \sum_{\beta \in I} \sigma_\beta = \sigma_\alpha = 1$ . But  $|Q| \geq 2$ . So  $\sigma_\alpha = 0$ .  $\square$

496 *Proof (Theorem 4.3).* Refer to Notation 3.2. Just as for Theorem 4.2, we  
 497 only need to prove that  $\rho(Z) \in S$  for all  $Z \in \mathcal{S}$ . Condition (2) of Theorem  
 498 4.3 along with Equation (4.1) of Lemma 4.1 imply that  $\rho(X) \in S$  if  $X \in \mathcal{X}_i$   
 499 for some  $i \in [1..n]$ . For a species  $Y$  with  $\mathcal{E}(Y) = \alpha \in I$ , we show that

$$500 \quad \forall X_1 \in \mathcal{X}_1, \dots, \forall X_n \in \mathcal{X}_n, Y - \sum_{i=1}^n \alpha_i X_i \in S. \quad (4.3)$$

501 This together with Equation (4.2) of Lemma 4.1 will imply that  $\rho(Y) \in S$ .  
 502 We proceed by induction on the length  $|\alpha|$  of  $\alpha$  to prove Property (4.3).

503 If  $|\alpha| = 2$ , then  $I_\alpha = \emptyset$  and Property (4.3) holds by Lemma 4.4.

504 Let  $\ell \geq 3$  and assume for induction that Property (4.3) holds if  $|\alpha| < \ell$ .  
 505 Suppose  $|\alpha| = \ell$  and let  $Y \in \mathcal{Y}_\alpha$ . Let  $\sigma_i$  for  $i \in [1..n]$  and  $\sigma_\beta$  for  $\beta \in I_\alpha$  be as  
 506 in Lemma 4.4. Then let  $X_i \in \mathcal{X}_i$  for  $i \in [1..n]$  and  $Y_\beta \in \mathcal{Y}_\beta$  for  $\beta \in I_\alpha$ . For  
 507 each  $\beta \in I_\alpha$ , we have  $|\beta| < \ell$ , and so by the induction hypothesis, we have  
 508  $Y_\beta - \sum_{i=1}^n \beta_i X_i \in S$ . Then:

$$509 \quad \begin{aligned} S &\ni Y - \sum_{i=1}^n \sigma_i X_i - \sum_{\beta \in I_\alpha} \sigma_\beta Y_\beta \\ 510 &= Y - \sum_{i=1}^n \sigma_i X_i - \sum_{i=1}^n \sum_{\beta \in I_\alpha} \sigma_\beta \beta_i X_i + \sum_{\beta \in I_\alpha} \sum_{i=1}^n \sigma_\beta \beta_i X_i - \sum_{\beta \in I_\alpha} \sigma_\beta Y_\beta \\ 511 &= Y - \sum_{i=1}^n \left( \sigma_i + \sum_{\beta \in I_\alpha} \sigma_\beta \beta_i \right) X_i - \sum_{\beta \in I_\alpha} \sigma_\beta \left( Y_\beta - \sum_{i=1}^n \beta_i X_i \right) \\ 512 &= Y - \sum_{i=1}^n \alpha_i X_i - \sum_{\beta \in I_\alpha} \sigma_\beta \left( Y_\beta - \sum_{i=1}^n \beta_i X_i \right). \end{aligned}$$

513 It follows that  $Y - \sum_{i=1}^n \alpha_i X_i \in S$ . Property (4.3) is thus proved.  $\square$

## 514 5 Stoichiometry Compatibility Classes of Constructive Networks

515 Stoichiometric compatibility classes are canonical invariants in the dynamics  
 516 of reaction networks. General background material may be found in Section  
 517 2 of Gnacadja [3], the first article in this series of three papers. Here we elab-  
 518 orate on the stoichiometric compatibility classes of constructive networks.

519 Let  $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$  be a constructive network, let  $S$  be the stoichiometric  
 520 space of  $\mathcal{N}$ , and let  $\mathcal{E} : \mathcal{S} \rightarrow \mathbb{Z}_{\geq 0}^n \setminus \{0_n\}$  be a core composition of  $\mathcal{N}$ . Notation  
 521 3.2 is in effect.

522

523 For  $b \in \mathbb{R}^n$ , let

$$524 \quad P(b) := \tilde{\mathcal{E}}^{-1}(b) \cap (\mathbb{R}_{\geq 0}^{\mathcal{S}}). \quad (5.1)$$

525 More explicitly,  $P(b)$  consists of the points  $u = (u_Z)_{Z \in \mathcal{S}} \in \mathbb{R}_{\geq 0}^{\mathcal{S}}$  that satisfy:  
 526

$$527 \quad \forall i \in [1..n], \quad \sum_{X \in \mathcal{X}_i} u_X + \sum_{\alpha \in I} \alpha_i \sum_{Y \in \mathcal{Y}_\alpha} u_Y = b_i. \quad (5.2)$$

528 **Theorem 5.1.** *The correspondence  $b \mapsto P(b)$  in which  $b$  ranges over  $\mathbb{R}_{\geq 0}^n$   
 529 establishes a bijective parameterization of the stoichiometric compatibility  
 530 classes of the network  $\mathcal{N}$ .*

531 *Proof.* The stoichiometric compatibility classes are the nonempty traces on  
 532  $\mathbb{R}_{\geq 0}^{\mathcal{S}}$  of the affine subspaces of  $\mathbb{R}^{\mathcal{S}}$  parallel to  $S$ . Because  $\mathcal{E}$  is a core  
 533 composition, the linear map  $\tilde{\mathcal{E}} : \mathbb{R}^{\mathcal{S}} \rightarrow \mathbb{R}^n$  is surjective with kernel  $S$ . As a  
 534 result, the affine spaces parallel to  $S$  are  $\tilde{\mathcal{E}}^{-1}(b)$  for  $b \in \mathbb{R}^n$ . Therefore, the  
 535 stoichiometric compatibility classes are the sets  $P(b)$  for  $b \in \mathbb{R}^n$  such that  
 536  $P(b) \neq \emptyset$ . One can verify that  $P(b) \neq \emptyset$  if and only if  $b \in \mathbb{R}_{\geq 0}^n$ , and that if  
 537  $b, b' \in \mathbb{R}_{\geq 0}^n$  and  $P(b) = P(b')$ , then  $b = b'$ .  $\square$

538 Let  $b \in \mathbb{R}_{\geq 0}^n$ . We consider the interior  $P_{>0}(b) = P(b) \cap \mathbb{R}_{>0}^{\mathcal{S}}$  and the bound-  
 539 ary  $P_{\neq 0}(b) = P(b) \setminus P_{>0}(b)$  of  $P(b)$ , both relative to the affine space parallel  
 540 to  $S$  that contains  $P(b)$ . The class  $P(b)$  is nondegenerate, i.e. its interior  
 541  $P_{>0}(b)$  is nonempty, if and only if  $b \in \mathbb{R}_{>0}^n$ . Consider also the subsets  $P_e(b)$   
 542 and  $P_e^1(b)$  of  $P(b)$  consisting of the points  $u = (u_Z)_{Z \in \mathcal{S}} \in P(b)$  that satisfy  
 543 the following properties.

$$544 \quad P_e(b) : \begin{cases} \forall i \in [1..n], \quad \sum_{X \in \mathcal{X}_i} u_X = b_i \\ \forall Y \in \mathcal{S}_u, \quad u_Y = 0. \end{cases}$$

$$545 \quad P_e^1(b) : \exists X_1 \in \mathcal{X}_1, \dots, \exists X_n \in \mathcal{X}_n : \begin{cases} (u_{X_1}, \dots, u_{X_n}) = b \\ \forall Z \in \mathcal{S} \setminus \{X_1, \dots, X_n\}, u_Z = 0. \end{cases}$$

547 One readily sees that  $P_e^1(b) \subseteq P_e(b) = P(b) \cap \mathbb{R}_{\mathcal{S}_e} \subseteq P_{\neq 0}(b)$ , and that

548  $P_e^1(b)$  is a finite set of cardinality  $|P_e^1(b)| = \prod_{i=1}^n p_i = \prod_{\substack{1 \leq i \leq n \\ p_i > 1}} p_i$ . If there is

549 no isomerism among the elementary species, i.e. if  $\mathcal{S}_e^1 = \mathcal{S}_e$ , then  
 550  $P_e^1(b) = P_e(b) = P(b) \cap \mathbb{R}\mathcal{S}_e = \{b\}$ .

551

552 The interpretation of the set  $P(b)$  is that it consists of all concentration  
 553 vectors such that for each  $i \in [1..n]$ ,  $b_i$  is the total concentration of all the  
 554 occurrences of the elementary composition  $e_{n,i}$ . The subset  $P_e(b)$  consists of  
 555 those concentration vectors for which only elementary species are present.  
 556 Further restricting by allowing only one elementary species in each isomerism  
 557 class yields  $P_e^1(b)$ . The stoichiometric compatibility class  $P(b)$  is a compact  
 558 convex polytope. The set  $P_e(b)$  is a face of  $P(b)$ , the maximal one lying in  
 559 the elementary species subspace  $\mathbb{R}\mathcal{S}_e$ . The points in  $P_e^1(b)$  are the vertices  
 560 of  $P_e(b)$ , or equivalently the vertices of  $P(b)$  lying in  $\mathbb{R}\mathcal{S}_e$ .

561

562 We illustrate this discussion by continuing with the example that closed Sec-  
 563 tion 3, i.e. the futile enzymatic cycle of Figure 2.1(b). For  $b = (b_1, b_2, b_3) \in \mathbb{R}_{\geq 0}^3$ ,  
 564 we describe the following sets by the condition that  $u = (u_E, u_F, u_A, u_B, u_{EA}, u_{FB}) \in \mathbb{R}_{\geq 0}\mathcal{S}$   
 565 must satisfy to be a member.

566  $P(b) : u_E + u_{EA} = b_1, u_F + u_{FB} = b_2, u_A + u_B + u_{EA} + u_{FB} = b_3$

567  $P_e(b) : u_E = b_1, u_F = b_2, u_A + u_B = b_3, u_{EA} = 0, u_{FB} = 0$

568  $P_e^1(b) : (u_E, u_F, u_A, u_B, u_{EA}, u_{FB}) = (b_1, b_2, b_3, 0, 0, 0)$  or  $(b_1, b_2, 0, b_3, 0, 0)$

570 The class  $P(b)$  is nondegenerate if and only if  $b_1, b_2, b_3 > 0$ . If  $b_3 > 0$ , then  
 571  $P_e(b)$  is a line segment and  $P_e^1(b)$  consists of its two vertices.

## 572 6 Persistence in Constructive Networks

573 This final section brings together the developments on species composition  
 574 is this paper and on reachability and persistence in the preceding paper  
 575 Gnacadja [3] to consider vacuous persistence in constructive networks. Va-  
 576 cuous persistence is the property that no species tend to extinction when-  
 577 ever all species are implicitly present at initial time. We will see that having  
 578 a core composition map can facilitate efforts to satisfy the necessary and  
 579 sufficient condition for vacuous persistence from that work. We begin by  
 580 recalling the result to be applied.

581 **Theorem 6.1 (Gnacadja [3, Theorem 5.5]).** *Consider a mass-action re-*  
 582 *action network for which that all trajectories are bounded. Then the follow-*  
 583 *ing are equivalent:*

- 584 • *The reaction network is vacuously persistent.*

- 585 • Among the subsets of the set of all species, only the full set is both  
 586 reach-closed and stoichiometrically admissible.  $\square$

587 All necessary explanations are in the paper. These include discussions on  
 588 stoichiometric admissibility, reachability and siphons. The next few prepara-  
 589 tory results are about understanding more about these concepts for con-  
 590 structive networks and lead to the main results of Theorems 6.8 and 6.9.  
 591 Let  $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$  be a constructive network and let  $\mathcal{E} : \mathcal{S} \rightarrow \mathbb{Z}_{\geq 0}^n \setminus \{0_n\}$   
 592 be a core composition of  $\mathcal{N}$ . Notation 3.2 is in effect.

593

594 The following result is a consequence of the characterization of stoichiometric  
 595 compatibility classes of Equation (5.2).

596 **Proposition 6.2.** *Let  $\mathcal{Z} \subseteq \mathcal{S}$ , let  $b \in \mathbb{R}_{\geq 0}^n$ , and let  $i \in [1..n]$ . Suppose that  
 597  $\mathcal{Z}$  is  $P(b)$ -admissible. We have  $\mathcal{Z} \cap (\mathcal{X}_i \sqcup \mathcal{S}_{c,i}) \neq \emptyset$ , i.e. the elementary  
 598 composition  $e_{n,i}$  occurs in  $\mathcal{Z}$ , either explicitly from an elementary species,  
 599 or implicitly from a composite species, or both, if and only if  $b_i > 0$ .  $\square$*

600 The next result is obtained by inductively applying Lemma 2.8.

601 **Lemma 6.3.** *Suppose that all composite species are explicitly destructible.  
 602 Consider a reach-closed set  $\mathcal{Z} \subseteq \mathcal{S}$  and let  $i \in [1..n]$ . If  $\mathcal{Z} \cap \mathcal{S}_{c,i} \neq \emptyset$ , then  
 603  $\mathcal{Z} \cap \mathcal{X}_i \neq \emptyset$ ; if the elementary composition  $e_{n,i}$  occurs implicitly (i.e. from  
 604 a composite species) in  $\mathcal{Z}$ , then it occurs explicitly (i.e. from an elementary  
 605 species) in  $\mathcal{Z}$ .  $\square$*

606 The combination of Proposition 6.2 and Lemma 6.3 immediately yields the  
 607 following result.

608 **Proposition 6.4.** *Suppose that all composite species are explicitly destruc-  
 609 tible. Let a set of species  $\mathcal{Z} \subseteq \mathcal{S}$  be both reach-closed and stoichiometrically  
 610 admissible. Then  $\mathcal{Z} \cap \mathcal{X}_i \neq \emptyset$  for all  $i \in [1..n]$ ; there is in  $\mathcal{Z}$  a species from  
 611 each isomerism class of elementary species. In particular, if there is no iso-  
 612 merism among the elementary species, then  $\mathcal{S}_e \subseteq \mathcal{Z}$ ; all elementary species  
 613 are in  $\mathcal{Z}$ .  $\square$*

614 **Lemma 6.5.** *Consider a siphon  $\mathcal{Z} \subseteq \mathcal{S}$ .*

- 615 (i) *Suppose that a species  $Y \in \mathcal{Z}$  is explicitly constructible. Then there  
 616 exists a species  $Z \in \mathcal{Z}$  such that  $\mathcal{E}(Z) \leq \mathcal{E}(Y)$  and  $\mathcal{E}(Z) \neq \mathcal{E}(Y)$ .*
- 617 (ii) *Suppose that a species  $X \in \mathcal{Z}$  is explicitly destructive. Then there  
 618 exists a species  $Z \in \mathcal{Z}$  such that  $\mathcal{E}(Z) \geq \mathcal{E}(X)$  and  $\mathcal{E}(Z) \neq \mathcal{E}(X)$ .*

619 *Proof.*

620 We prove statement (i). Let  $Y \in \mathcal{S}$  be explicitly constructible. Then let  $Q$   
 621 be a complex and  $Y_0, \dots, Y_\ell$  be species such that we have the binding re-  
 622 action  $Q \rightarrow Y_0$  and the isomerization reactions  $Y_0 \rightarrow \dots \rightarrow Y_\ell$ , and  $Y_\ell = Y$ .  
 623 By the conservation of composition, we have  $\tilde{\mathcal{E}}(Q) = \mathcal{E}(Y)$ . Then, because  
 624  $|Q| \geq 2$ , we have  $\mathcal{E}(Z) \leq \mathcal{E}(Y)$  and  $\mathcal{E}(Z) \neq \mathcal{E}(Y)$  for all  $Z \in \text{Supp}(Q)$  by  
 625 Lemma 2.8. Now suppose that  $Y \in \mathcal{Z}$ . Because  $\mathcal{Z}$  is a siphon we obtain  
 626  $Y_0 \in \mathcal{Z}$  by induction, and therefore  $Z \in \mathcal{Z}$  for some  $Z \in \text{Supp}(Q)$ .

627 We prove statement (ii). Let  $X \in \mathcal{S}$  be explicitly destructive. Then let  
 628  $Z \rightarrow Q$  be a dissociation reaction such that  $X \in \text{Supp}(Q)$ . By the conser-  
 629 vation of composition, we have  $\mathcal{E}(Z) = \tilde{\mathcal{E}}(Q)$ . Then, because  $|Q| \geq 2$  and  
 630  $X \in \text{Supp}(Q)$ , we have  $\mathcal{E}(Z) \geq \mathcal{E}(X)$  and  $\mathcal{E}(Z) \neq \mathcal{E}(X)$  by Lemma 2.8. Now  
 631 suppose that  $X \in \mathcal{Z}$ . Because  $\mathcal{Z}$  is a siphon, we have  $Z \in \mathcal{Z}$ .  $\square$

632 **Proposition 6.6.** *Consider a siphon  $\mathcal{Z} \subseteq \mathcal{S}$ .*

633 (i) *Suppose that all composite species are explicitly constructible.*  
 634 *If  $\mathcal{S}_c \cap \mathcal{Z} \neq \emptyset$ , then  $\mathcal{S}_e \cap \mathcal{Z} \neq \emptyset$ .*

635 (ii) *Suppose that all elementary species are explicitly destructive.*  
 636 *If  $\mathcal{S}_e \cap \mathcal{Z} \neq \emptyset$ , then  $\mathcal{S}_c \cap \mathcal{Z} \neq \emptyset$ .*

637 *Proof.* Statement (i) of Proposition 6.6 is proved by reasoning by induction  
 638 with Statement (i) of Lemma 6.5. Statement (ii) of Proposition 6.6 is a  
 639 direct consequence of Statement (ii) of Lemma 6.5.  $\square$

640 Since the reach-closed sets are the complements of siphons, we immediately  
 641 get the following result from Proposition 6.6.

642 **Theorem 6.7.** *Suppose that the reaction network  $\mathcal{N}$  is explicitly-reversibly*  
 643 *constructive and let  $\mathcal{Z} \subseteq \mathcal{S}$ . If  $\mathcal{Z}$  is reach-closed, and if  $\mathcal{S}_e \subseteq \mathcal{Z}$  or*  
 644  *$\mathcal{S}_c \subseteq \mathcal{Z}$ , then  $\mathcal{Z} = \mathcal{S}$ .*  $\square$

645 The next result is a direct consequence of the combination of Theorems  
 646 6.7 and 6.1. It characterizes vacuous persistence in mass-action explicitly-  
 647 reversibly constructive networks.

648 **Theorem 6.8.** *Suppose that the reaction network  $\mathcal{N}$  is explicitly-reversibly*  
 649 *constructive. Then the following are equivalent:*

- 650 • *If a subset  $\mathcal{Z} \subseteq \mathcal{S}$  is both reach-closed and stoichiometrically admis-*  
 651 *sible, then  $\mathcal{S}_e \subseteq \mathcal{Z}$  or  $\mathcal{S}_c \subseteq \mathcal{Z}$ .*

- 652 • Only  $\mathcal{S}$  is both reach-closed and stoichiometrically admissible.
- 653 • If the network is governed by mass-action kinetics, then it is vacuously
- 654 persistent. □

655 The particular case highlighted in Proposition 6.4 yields a means of satisfy-  
 656 ing the first of the three conditions in Theorem 6.8, whence the main result  
 657 that follows.

658 **Theorem 6.9.** *Suppose that the reaction network  $\mathcal{N}$  is explicitly-reversibly*  
 659 *constructive, that there is no isomerism among the elementary species, and*  
 660 *that the network is governed by mass-action kinetics. Then the network is*  
 661 *vacuously persistent.* □

662 It results from Siegel and MacLean [7, Theorem 3.2] that if a mass-action  
 663 reaction network is persistent and complex-balancing, then each nondegene-  
 664 rate stoichiometric compatibility class contains a unique equilibrium state  
 665 which is complex-balanced and is an attractor of the interior of the class.  
 666 Therefore, if the network  $\mathcal{N}$  satisfies the hypotheses of Theorem 6.9, and  
 667 if in addition  $\mathcal{N}$  is complex-balancing (in particular if  $\mathcal{N}$  is weakly re-  
 668 versible and has deficiency zero), then for every  $b \in \mathbb{R}_{>0}^n$ , the (unique, po-  
 669 sitive, complex-balanced) equilibrium state in  $P_{>0}(b)$  is an attractor of  $P(b)$ .  
 670

671 Theorem 6.9 shows that for a mass-action explicitly-reversibly construc-  
 672 tive network, the failure of vacuous persistence requires that there be iso-  
 673 merism among the elementary species. (Isomerism among composite species  
 674 does not affect this feature.) This explains the fact that instances of non-  
 675 persistence and of non-obvious persistence in the literature always involve  
 676 networks with isomerism among the building blocks. However, the absence  
 677 of isomerism among elementary species is not necessary for vacuous persis-  
 678 tence. This requirement is simply the easiest way to realize the implications  
 679

$$680 \quad (\mathcal{Z} \cap \mathcal{X}_i \neq \emptyset) \Rightarrow (\mathcal{X}_i \subseteq \mathcal{Z}) ; i = 1, \dots, n. \quad (6.1)$$

681 By Proposition 6.4, the implying clause in each of the  $n$  Implications (6.1)  
 682 is true for reach-closed, stoichiometrically admissible subsets  $\mathcal{Z} \subseteq \mathcal{S}$ . If  
 683 on another hand all  $n$  implied clauses are true for such sets  $\mathcal{Z}$ , we have  
 684  $\mathcal{S}_e \subseteq \mathcal{Z}$  and the first condition of Theorem 6.8 is satisfied. Therefore, that  
 685 the  $n$  Implications (6.1) are true is a sufficient condition for vacuous persis-  
 686 tence. (This is also tautologically necessary because both clauses of each  
 687 implication are trivially true when  $\mathcal{Z} = \mathcal{S}$ .) Realizing one of these implica-  
 688 tions amounts to seeking some kind of mutual reachability among isomeric



689 elementary species. For example, isomerism among elementary species can  
690 occur with substrates and products in enzymatic networks, and one could  
691 consider that a substrate reaches a product modulo a catalyzing enzyme. In  
692 Gnacadja [4], the third and final paper in this series of articles, we explore  
693 these ideas and arrive at a subclass of biochemically important enzymatic  
694 networks that have isomerism among elementary species and are vacuously  
695 persistent.

696

697 With Theorem 6.9, we obtain that the allosteric ternary complex model of  
698 Figure 2.1(a) is vacuously persistent. The theorem is not applicable to the  
699 networks of Figures 2.1(b) and 2.1(c) because both have isomerism among  
700 their elementary species. However, the futile enzymatic cycle of Figure  
701 2.1(b) is in the class of networks that are shown in Gnacadja [4] to be  
702 vacuously persistent. On another hand, we saw in Gnacadja [3, Section 5]  
703 that the network of Figure 2.1(c) is not vacuously persistent, and also that  
704 Angeli, De Leenheer and Sontag [1, Section 10] showed that it is persistent.

## 705 7 Conclusion

706 Motivated by the intuition that a reaction network should be persistent if  
707 it is constructed from building blocks that cannot be depleted, we devel-  
708 oped a formalism for species composition. This yielded the result that if a  
709 mass-action reaction network is explicitly-reversibly constructive, then the  
710 absence of isomerism among the elementary species implies that it is vac-  
711 uously persistent. The requirement that there be no isomerism among the  
712 elementary species is partially lifted with the work on binary enzymatic net-  
713 works in the third and last article in this series of three papers. We think  
714 that there is more to be discovered by incorporating the species composition  
715 formalism in theoretical investigations of reaction networks. For instance,  
716 there probably is within mass-action explicitly-reversibly constructive net-  
717 works a class of oscillation-free networks, and such class should contain a  
718 class of networks that are monostationary and globally asymptotically sta-  
719 ble. Just like we noticed that instances of non-persistence and of non-obvious  
720 persistence in the literature always involve networks with isomerism among  
721 the building blocks, we also observe that multistationarity seems to always  
722 be illustrated with networks that possess this same property, and cases of  
723 oscillations come with even more particular traits.

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