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Comparing reactions in reaction systems

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ABSTRACT

Originally, reaction systems were introduced to describe in a formal way the interactions between biochemical reactions taking place in living cells. They are also investigated as an abstract model of interactive computation. A reaction system is determined by a finite background set of entities and a finite set of reactions. Each reaction specifies the entities that it needs to be able to occur, the entities which block its execution, and the entities that it produces if it occurs. Based on the entities available in a state of the system, all reactions of the system that are enabled take place and together produce the entities that form the next state. In this paper we compare reactions in terms of their enabledness and results. We investigate three partial orders on reactions that build on two definitions of equivalence of (sets of) reactions. It is demonstrated how each partial order defines a lattice (with greatest lower bounds and least upper bounds) for all nontrivial reactions. Together, these orders provide an insight in possible redundancies and (re)combinations of the reactions of a reaction system.

1. Introduction

Reaction systems were introduced in [12] with the aim to formalize the interactions between biochemical reactions that take place in living cells. The mechanisms behind such interactions are *facilitation* and *inhibition*. In the framework of reaction systems these are captured in the definition of a reaction. Each reaction a specifies a set R_a of entities (*reactants*) that must be present in order for it to be able to take place, as well as a set I_a of entities (*inhibitors*) that cannot be present as they block its execution. If a reaction is enabled (*i.e.* facilitated, but not inhibited), it produces new entities specified as a set P_a of (*products*). Thus a is enabled by a set of entities (a *state*) T if $R_a \subseteq T$ and $I_a \cap T = \varnothing$ and in that case $\mathrm{res}_a(T)$, the *result of a on T* is P_a (otherwise $\mathrm{res}_a(T) = \varnothing$). Reaction systems are determined by a finite (background) set S of entities and a set A of reactions with reactants, inhibitors, and products from S. Based on the entities available in a state of the system (a subset of S), all reactions in A that are enabled take place and together produce the entities that form the next state. So, an important aspect of reaction systems is non-permanency: entities that are not produced will not (no longer) be present in the next state. Another important feature, and most relevant to this paper, is the 'threshold assumption': either a reactant x is not present or it is present in a sufficient amount for all reactions that have x in their reactant sets, to use it. There is no 'conflict' of resources. Consequently, the basic reaction system model is qualitative rather than quantitative. This abstract model however, is well-suited to be extended with concrete features of the cellular biochemistry. Indeed, reaction systems currently form a broad and flexible framework comprising all kinds of extensions introduced to

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study computational aspects of biochemical processes taking place in the living cell (see, *e.g.* [1,2,4,8,10,12,13]). Apart from biological considerations, reaction systems are also an interesting abstract model of computation and they have been studied extensively as such since their introduction (see, *e.g.* [3,6,7,14,15,20]).

Obviously, how a system behaves is one of its most important characteristics and, from a computational point of view, behavioural equivalence is an appropriate method to compare systems, once the relevant aspects of behaviour have been identified and formally defined. Already in [12], a notion of equivalence was introduced to compare reaction systems. This *functional equivalence* identifies two systems if their result functions are the same. Another equivalence (introduced in [8]) is *enabling equivalence* that compares the effect of two sets of reactions only for those states that enable all reactions involved. Here the motivation comes from reaction systems that may evolve, *i.e.* their sets of reactions may change over time provided such transformations are 'invisible'. As demonstrated in [8], enabling equivalence and functional equivalence are incomparable relations. Whereas these two relations are based on the effect of reactions on states, there are also equivalences that take into account the dynamic behaviour of reaction systems in terms of their transitioning from state to state with or without interaction with the environment. In [18], a framework is presented for considering various notions of behavioural equivalence for reaction systems. Some of these equivalences, are defined directly in terms of reactions and (interactive) processes, while others (*e.g.* bisimulation) are based on labelled transition systems and may involve a controlled environment. Also in [16], reaction systems are compared through their labelled transition systems. Now they are considered equivalent if their labelled transition systems are isomorphic. In [19], a reaction algebra is presented with two different types of compositional semantics and a behavioural equivalence that subsumes functional equivalence. When compared with functional equivalence, enabling equivalence is more subtle in the sense that it focuses on specific states namely those where all reactions under consideration are active. In fact, it treats a set of reactions as if it were a single reaction. This approach is discussed in [17] and applied to transition system representations of the behaviour of reaction systems.

Motivated by the idea that the external behaviour of a system is better understood, if the internal structure of the system has been identified, we investigate in this paper how reactions relate to each other in terms of enabledness and results. In particular, we are interested in how the effect of combining a reaction with another one may subsume the effect of the reaction on its own. The *cover relation*, a relation derived from functional equivalence, was introduced already in [12]. Reaction b is said to be covered by reaction a if $\{a, b\}$ is functional equivalent to a. In other words, the result of a and b together is always the same as that of a alone ($\mathrm{res}_a(T) \cup \mathrm{res}_b(T) = \mathrm{res}_a(T)$ for all states T). Thus b can be considered to be redundant in the context of a. The new *exact cover* relation introduced in this paper, refines the cover relation in the sense that for a to exactly cover b it is required that a and b have the same result $\mathrm{res}_a(T) = \mathrm{res}_b(T)$ whenever b is enabled by T. Finally, we introduce the *enabling cover relation* that is derived from enabling equivalence in the same way as the cover relation is derived from functional equivalence, formally $\mathrm{res}_a(T) \cup \mathrm{res}_b(T) = \mathrm{res}_a(T)$ for all states T that enable both a and b. In fact we consider a and b together as a single, combined reaction $r_{\{a,b\}}$. As our main results, we describe the landscape of reactions over a given background set in the form of lattices defined by the three relations. We compare these lattices and we prove how the difference between cover and exact cover is captured by the enabling cover relation.

The paper is organized as follows. In the preliminary Section 2, we set the terminology and notation for partially ordered sets and lattices used in the body of the paper. In Section 2, we also recall the definitions of reactions and reaction systems and explicitly identify trivial reactions as reactions that are never enabled. We discuss functional and enabling equivalence of sets of reactions in Section 3 as well as consistency of reactions which guarantees that reactions can be combined into a single nontrivial reaction. Sections 4 and 5 explore the cover relation and its associated lattice of reactions. The concept of exact cover is introduced in Section 6 and compared with the cover relation. In Section 7, we invoke enabling equivalence and demonstrate how it fills the gap between the cover and exact cover relations. The concluding Section 8 wraps up the results and draws conclusions with pointers to future work.

2. Preliminaries

After a brief discussion of partial orders and lattices, we formally introduce reactions and reaction systems.

2.1. Partial orders and lattices

In this section, we recall some basic notions and results on partially ordered sets and lattices to set the notation and terminology for the results we present about the relations between reactions discussed in the body of the paper. For more details, we refer the reader to [5].

Ordered sets. Let V be a set. A *partial order* on V is a binary relation $\leqslant$ on V with the following properties for all $x, y, z \in V$: (i) $x \leqslant x$ (*reflexivity*), (ii) $x \leqslant y$ and $y \leqslant x$ imply $x = y$ (*anti-symmetry*), and (iii) $x \leqslant y$ and $y \leqslant z$ imply $x \leqslant z$ (*transitivity*). We refer to V, equipped with a partial order, as a *partially ordered set*, or simply as an *ordered set*. Clearly, $\leqslant$ is a partial order on V if and only if the inverse relation $\geqslant$ is a partial order (where $x \geqslant y$ if and only if $y \leqslant x$). Given a set X, set-inclusion (the subset relation) $\subseteq$ and its inverse (the superset relation) $\supseteq$ are partial orders on the powerset, $\mathcal{P}(X)$, of X.

Let $(V_1, \leqslant_1), \ldots, (V_n, \leqslant_n)$ be ordered sets. Then, the *cartesian product*, $V_1 \times \cdots \times V_n$, is an ordered set with the componentwise *product order* $\leqslant$, defined by $(x_1, \ldots, x_n) \leqslant (y_1, \ldots, y_n)$, if $x_i \leqslant_i y_i$ for every $1 \leq i \leq n$.

Let V be an ordered set[1] and let $W \subseteq V$. Then, $a \in W$ is a *maximal* element of W, if for every $x \in W$, $a \leqslant x \in W$ implies $a = x$. Also, $a \in W$ is the *greatest* (*maximum*) element of W, if $x \leqslant a$ for every $x \in W$. Dually, $a \in W$ is a *minimal* element of W, if for every $x \in W$, $x \leqslant a \in W$ implies $a = x$. It is the *least* (*minimum*) element of W, if $a \leqslant x$ for every $x \in W$. The greatest element of V (if it exists) is called the *top* element of V and, usually, denoted by $\top$. Similarly, *bottom* $\bot$ denotes the least element of V, if it exists.

Given an ordered set V (with or without $\bot$), we form $V_\bot$, V *lifted*, by taking a new element $\mathbf{0} \notin V$ and extending $\leqslant$ to $V \cup \{\mathbf{0}\}$ by: $x \leqslant y$ if $x = \mathbf{0}$ or $x \leqslant y$ in V.

Lattices. Let V be an ordered set and let $W \subseteq V$. An element $x \in V$ is an *upper bound* of W, if $w \leqslant x$ for every $w \in W$. Moreover, x is the *least upper bound* of W, if: (i) x is an upper bound of W, and (ii) $x \leqslant y$ for every upper bound y of W. Dually, we have a (*greatest*) *lower bound*. It is convenient to consider the binary case separately. Then, we write $x \vee y$ for the least upper bound of $\{x, y\}$, called the *join* of x and y (when it exists) and $x \wedge y$ for the greatest lower bound of $\{x, y\}$, called the *meet* of x and y (when it exists). An ordered set, in which every pair of elements has a join, is called a *join-semilattice* and, dually, if every pair of elements has a meet, the ordered set is called a *meet-semilattice*. A *lattice* is an ordered set, in which the meet and the join exist for every pair of elements, *i.e.* if it is both a join-semilattice and a meet-semilattice. Note that, $(V, \leqslant)$ is a lattice if and only if $(V, \geqslant)$ is. Usually, we do not distinguish between the two and define upper bounds and lower bounds in relation to $\leqslant$.

It follows immediately that, a finite nonempty lattice always has a top element and a bottom element.

Example 2.1. Given a set X, its powerset, $V = \mathcal{P}(X)$, is a lattice under set-inclusion $\subseteq$. The join of any two subsets $A, B \subseteq X$ equals their union $A \cup B$, whereas their meet equals their intersection $A \cap B$. Hence, $\mathcal{P}(X)$ is a lattice. If X is finite, then X is the top element of $\mathcal{P}(X)$ and $\varnothing$ its bottom element. $\Diamond$

Let $(V, \leqslant)$ be a lattice. Then it is immediate that $\vee$ and $\wedge$ are associative, commutative, idempotent ($x \vee x = x$ and $x \wedge x = x$), and satisfy the absorption laws $x \vee (x \wedge y) = x$ and $x \wedge (x \vee y) = x$.

We conclude with stating an observation used throughout the paper; it also follows easily from the definitions.

Fact 2.2. If $V_1, \ldots, V_n$ are lattices, then the product order on $V_1 \times \cdots \times V_n$ is a lattice when join and meet are taken componentwise: $(x_1, \ldots, x_n) \vee (y_1, \ldots, y_n) = (x_1 \vee y_1, \ldots, x_n \vee y_n)$ and $(x_1, \ldots, x_n) \wedge (y_1, \ldots, y_n) = (x_1 \wedge y_1, \ldots, x_n \wedge y_n)$.

2.2. Reactions and reaction systems

We build upon the definitions for reactions, reaction systems, and related notions from [12].

Let S be a *background set*, *i.e.* a finite, nonempty set. The elements of a background set are called *entities*. A *reaction (over S)* is a triple $a = (R_a, I_a, P_a)$ of nonempty subsets of S, where R_a is the *reactant set of* a, I_a is the *inhibitor set of* a, and P_a is the *product set of* a, respectively. Sometimes (see, *e.g.* [9]) the elements of $R_a \cup I_a$ are referred to as the *resources of* a. Throughout the paper, we assume that two distinct symbols $\mathtt{r}$ and $\mathtt{i}$ are present in every background set. Moreover, every reaction (R_a, I_a, P_a) satisfies: $\mathtt{r} \in R_a \setminus I_a$, $\mathtt{i} \in I_a \setminus R_a$, and $\mathtt{r} \in P_a$. We refer to $\mathtt{r}$ and $\mathtt{i}$ as *universal entities* as they are assumed to be always present as reactant and product, and as inhibitor, respectively. This guarantees that R_a, I_a, and P_a are never empty. Note that, in [12], each of R_a, I_a, and P_a may be empty. In later papers on reaction systems however, *e.g.* [8], reactions a are required to have nonempty R_a, I_a, and P_a; in other words, every reaction needs reactants in order to occur and will always produce something; moreover there always exists an entity that – when present – inhibits the occurrence of a reaction. Furthermore, $R_a \cap I_a = \varnothing$ is required in these papers to exclude reactions that are never enabled. As we want to be able to distinguish between different types of trivial situations (when reactions can never occur or will not produce anything), we have chosen to be more explicit, and therefore, assume the existence of universal entities. Moreover, the assumption that $\mathtt{r}$ and $\mathtt{i}$ are the same elements for all reactions, guarantees that they are maintained in combinations of reactions defined using unions and intersections of the reactant, inhibitor, or product sets as a means to describe upper and lower bounds. In the sequel, we will point out explicitly, where our assumptions could lead to observations different from those presented in the papers we cite.

The set of all reactions over S is denoted by $\mathrm{rac}(S)$.

For the rest of the paper, assume that S is an arbitrary, but fixed background set, unless stated otherwise.

For a reaction $a = (R_a, I_a, P_a) \in \mathrm{rac}(S)$ and a finite set $T \subseteq S$, we say that a is *enabled by* T, denoted by $en_a(T)$, if $R_a \subseteq T$ and $I_a \cap T = \varnothing$. Thus, a reaction a is enabled by T, if T separates R_a from I_a. The *result of a on T*, denoted by $\mathrm{res}_a(T)$, is defined by $\mathrm{res}_a(T) = P_a$ if a is enabled by T and $\mathrm{res}_a(T) = \varnothing$, otherwise. This has led, in [12], to the following natural idea to compare two reactions.

[1] If the order is not explicitly given, we use $\leqslant$ as a default.

Definition 2.3. Let $a, b \in \mathrm{rac}(S)$. Then a and b are *functionally equivalent in* S, denoted by $a \sim_S b$, if $\mathrm{res}_a(T) = \mathrm{res}_b(T)$ for every $T \subseteq S$.

Clearly, functional equivalence is an equivalence relation.

A reaction $a \in \mathrm{rac}(S)$ is called *trivial* if $\mathrm{res}_a(T) = \varnothing$ for all $T \subseteq S$. A reaction that is not trivial, is *nontrivial*. We use $\mathrm{Rac}(S)$ to denote all nontrivial reactions in $\mathrm{rac}(S)$. Note that, if $a \sim b$ for two reactions a and b and one of them is trivial, then the other one is trivial, as well. Moreover, all trivial reactions are functionally equivalent to one another. So they form a single functional equivalence class. As every enabled reaction produces at least $\mathtt{r}$, it must be that a trivial reaction is never enabled. Observe that, if a reaction a is never enabled, then necessarily, $R_a \cap I_a \neq \varnothing$ for, otherwise, a will be enabled by $T = R_a$. Thus, we arrive at the following characterization.

Lemma 2.4. *Let $a \in \mathrm{rac}(S)$. Then a is trivial if and only if $R_a \cap I_a \neq \varnothing$.*

In [12], a reaction a is said to be trivial if it is functionally equivalent to $\Phi = (\varnothing, \varnothing, \varnothing)$, *i.e.* if and only if $P_a = \varnothing$ (nothing is produced) or $R_a \cap I_a \neq \varnothing$ (nothing can be produced). In both cases, $\mathrm{res}_a(T) = \varnothing$. Having $\mathtt{r} \in P_a$ for every a, makes it possible to distinguish between these two trivial situations. On the other hand, as proved in [12] and also in our setting, for nontrivial reactions a and b, $a \sim b$ if and only if $R_a = R_b$, $I_a = I_b$ and $P_a = P_b$. So, whenever $a \sim_S b$ and a is not trivial, then $a = b$.

Reaction systems are specified as a background set of entities together with a set of reactions over that background set. The states of the system are subsets of the entities from the background set and states change when (all enabled) reactions take place.

For a set of reactions A and a finite set T, the *result of A on T*, denoted by $\mathrm{res}_A(T)$, is defined by: $\mathrm{res}_A(T) = \bigcup_{a \in A} \mathrm{res}_a(T)$. Hence, the result of A on T is the accumulation of the results of all individual reactions $a \in A$.

A *reaction system* is an ordered pair $\mathcal{A} = (S, A)$, where S is a background set and $A \subseteq \mathrm{rac}(S)$. The function $\mathrm{res}_{\mathcal{A}}$ is defined by $\mathrm{res}_{\mathcal{A}}(T) = \mathrm{res}_A(T)$ for all $T \subseteq S$. Thus, $\mathrm{res}_{\mathcal{A}}$ is a function from $\mathcal{P}(S)$ to $\mathcal{P}(S)$. It has the property that both $\mathrm{res}_{\mathcal{A}}(\varnothing) = \varnothing$ and $\mathrm{res}_{\mathcal{A}}(S) = \varnothing$. Moreover, as a consequence of our assumptions, $\mathtt{r} \in \mathrm{res}_{\mathcal{A}}(T)$ whenever there is at least one reaction in A enabled by T.

3. Equivalence and consistency of sets of reactions

In this section we focus on sets of reactions. First, we lift functional equivalence to the level of sets of reactions (using the same notation as before).

Definition 3.1. Let $A, B \subseteq \mathrm{rac}(S)$. Then A and B are *functionally equivalent in* S, denoted by $A \sim_S B$, if $\mathrm{res}_A(T) = \mathrm{res}_B(T)$ for every $T \subseteq S$.

Note that if A and B consist of trivial reactions only, then $\mathrm{res}_A(T) = \mathrm{res}_B(T) = \varnothing$ for all $T \subseteq S$. On the other hand, if A contains at least one nontrivial reaction, then there exists a $T \subseteq S$ such that $\mathrm{res}_A(T) \neq \varnothing$. Consequently, all subsets of $\mathrm{rac}(S) \setminus \mathrm{Rac}(S)$ are a single equivalence class of $\sim_S \subseteq \mathcal{P}(S) \times \mathcal{P}(S)$.

Extending functional equivalence further to reaction systems, we can say that two reaction systems $\mathcal{A} = (S, A)$ and $\mathcal{B} = (S, B)$ with the same background set S, are functionally equivalent, denoted as $\mathcal{A} \sim \mathcal{B}$, whenever $A \sim_S B$, *i.e.* if $\mathrm{res}_{\mathcal{A}} = \mathrm{res}_{\mathcal{B}}$. In contrast to the situation for single reactions, determining whether two sets of reactions (and hence in particular two reaction systems) are functionally equivalent is not trivial. As shown in [12], this problem is Co-NP-complete.

We now turn to a second equivalence, introduced in [8], which is based not only on the result of reactions but also on their enabledness. When considering the application of a set A of reactions to a set T of entities, then it may be that none, some, or all of the reactions in A are enabled by T. For the next equivalence, we interpret A acting as a "block" of reactions, all taking place at the same time, *i.e.* we handle it as a single reaction. Let $A \subseteq \mathrm{rac}(S)$ be a nonempty set of reactions. Then $r_A = (R_A, I_A, P_A)$ is *the reaction defined by* A, where $R_A = \bigcup_{a \in A} R_a$, $I_A = \bigcup_{a \in A} I_a$, and $P_A = \bigcup_{a \in A} P_a$. Hence, if $A = \{a\}$ for some $a \in \mathrm{rac}(S)$, then $r_A = a$. In general, $(R_A, I_A, P_A) \in \mathrm{rac}(S)$ as $\mathtt{r} \in R_A \setminus I_A$, $\mathtt{i} \in I_A \setminus R_A$, and $\mathtt{r} \in P_A$. Thus, r_A is enabled by T if $R_A \subseteq T$ and $I_A \cap T = \varnothing$, *i.e.* if T separates R_A from I_A. Consequently, we arrive at the following result.

Lemma 3.2. *Let $A \subseteq \mathrm{rac}(S)$ be nonempty. Then $en_{r_A}(T)$ if and only if $en_a(T)$ for all $a \in A$.*

Here we should remark that $en_{r_A}(T)$ has the same meaning as $en_A(T)$ used in [8]; actually the concept also occurs in [12], but is left there without notation. We chose this new notation to avoid confusion, since in general, the result of a set of reactions applied when combined in one reaction is not the same as the result of that same set of reactions, when they are applied independently: the result of r_A on T is $\mathrm{res}_{r_A}(T) = P_{r_A} = \bigcup_{a \in A} P_a$ if r_A is enabled by T, meaning that *every* $a \in A$ is enabled by T; otherwise, $\mathrm{res}_{r_A}(T) = \varnothing$. The result of applying the set A on T is $\mathrm{res}_A(T) = \bigcup_{a \in A} \mathrm{res}_a(T)$, meaning the union of those P_a for which a is enabled by T. Hence, in general, $\mathrm{res}_{r_A}(T) \neq \mathrm{res}_A(T)$ for a set of reactions $A \subseteq \mathrm{rac}(S)$ and a subset $T \subseteq S$. Consider for example, a set of reactions $A = \{a, b\} \subseteq \mathrm{rac}(S)$ and $T \subseteq S$, such that a is enabled by T,

but b is not. Thus, we have $en_a(T)$ but not $en_b(T)$ and, hence, also not $en_{r_A}(T)$. Consequently, $\mathrm{res}_A(T) = \mathrm{res}_a(T) = P_a \neq \varnothing$, while $\mathrm{res}_{r_A}(T) = \varnothing$.

We are now ready to introduce the enabling equivalence from [8].

Definition 3.3. Let $A, B \subseteq rac(S)$. Then A and B are *enabling equivalent* (in S), denoted by $A \approx_S B$, if for each $T \subseteq S$:

1. $en_{r_A}(T)$ if and only if $en_{r_B}(T)$;
2. if $en_{r_A}(T)$, then $\mathrm{res}_A(T) = \mathrm{res}_B(T)$.

So, two sets of reactions are enabling equivalent when they have the same result on every set T that enables all of their reactions. Clearly, $\approx_S$ is an equivalence relation. Extending this equivalence to reaction systems as we did for functional equivalence, we have that reaction systems $\mathcal{A} = (S, A)$ and $\mathcal{B} = (S, B)$, are enabling equivalent if $A \approx B$.

It may happen that the reaction defined by a set of reactions is trivial (and hence never enabled) even if each reaction individually is nontrivial. Let $A = \{a, b\}$ and assume that a is a nontrivial reaction and $R_a \cap I_b \neq \varnothing$. Then, $R_A \cap I_A \neq \varnothing$. Thus, r_A is trivial and $\mathrm{res}_{r_A}(T) = \varnothing$ for all $T \subseteq S$, even though there exists a subset T such that $\mathrm{res}_A(T) \supseteq P_a \neq \varnothing$. Thus, when combining reactions into a single reaction, the following notion is crucial.

Definition 3.4. Let $A \subseteq \mathrm{rac}(S)$ be a nonempty set of reactions. Then A is *consistent* if r_A is nontrivial.

In [8], consistency of a set of reactions A is defined by $R_A \cap I_A = \varnothing$. By Lemma 2.4, this is the same as the requirement that r_A is nontrivial. Hence, the two definitions are equivalent. If a set of reactions is not consistent, it is called *inconsistent*. The following observation is easily proved. It demonstrates that inconsistent sets of reactions form a single enabling equivalence class.

Lemma 3.5. *Let $A, B \subseteq rac(S)$.*

1. *If A and B are inconsistent, then $A \approx_S B$.*
2. *If $A \approx_S B$ and A is consistent, then so is B.*

Like Lemma 3.5, the following result is from [8]. Its proof here would be the same as given there since it does not depend on the presence or absence of `r` and `i` in the reactant, inhibitor, and product sets of reactions.

Theorem 3.6. *Let $A, B \subseteq rac(S)$ be two consistent sets of reactions. Then $A \approx_S B$ if and only if $R_A = R_B$, $I_A = I_B$, and $P_A = P_B$.*

In other words, if A and B are consistent set of reactions, then $A \approx_S B$ if and only if $r_A = r_B$.

Example 3.7. Let $A = \{a\}$ with $a = (\{\mathtt{r}, 1, 2\}, \{\mathtt{i}, 3, 4\}, \{\mathtt{r}, 1, 3\})$, and let $B = \{b_1, b_2\}$ with $b_1 = (\{\mathtt{r}, 1\}, \{\mathtt{i}, 3\}, \{\mathtt{r}, 1, 3\})$ and $b_2 = (\{\mathtt{r}, 2\}, \{\mathtt{i}, 4\}, \{\mathtt{r}, 1, 3\})$. Then $A \approx_S B$, because $R_A = R_B = \{\mathtt{r}, 1, 2\}$, $I_A = I_B = \{\mathtt{i}, 3, 4\}$, and $P_A = P_B = \{\mathtt{r}, 1, 3\}$. ♢

By Theorem 3.6 and Lemma 3.5, we can omit the subscript S from $\approx_S$.

Note that, for a reaction $a \in \mathrm{rac}(S)$, we have that a is nontrivial if and only if $\{a\}$ is consistent. In general, if a nonempty set A of reactions is consistent, then every $a \in A$ is nontrivial, but not necessarily vice versa (as exemplified above).

Theorem 3.8. *Let $A \subseteq \mathrm{rac}(S)$ be a nonempty set. Then A is consistent if and only if every pair of not necessarily distinct reactions $a, b \in A$ forms a consistent set $\{a, b\}$.*

Proof. By Definition 3.4 and Lemma 2.4, A is inconsistent if and only if $\bigcup_{a \in A} R_a \cap \bigcup_{b \in A} I_b \neq \varnothing$. This latter intersection is nonempty if and only if there exist, not necessarily distinct, reactions $a, b \in A$ such that $R_a \cap I_b \neq \varnothing$. Hence equivalently, either there is a single reaction $a = b \in A$ that is trivial ($\{a\}$ is inconsistent) or there are two distinct reactions a and b such that $\{a, b\}$ is inconsistent. □

As a corollary to this result, we observe that every nonempty subset of a consistent set is consistent and, in particular, also that every reaction in a consistent set is nontrivial.

Since by Theorem 3.6 for consistent sets of reactions, $A \approx B$ if and only if $r_A = r_B$, we have that, in particular, for nontrivial reactions a and b, $\{a\} \approx \{b\}$ if and only if $a = b$. Hence, it follows that functional equivalence $\sim_S$ and enabling equivalence $\approx$ are the same for all pairs of reactions $a, b \in \mathrm{rac}(S)$ (*cf.* the observations in Subsection 2.2). Thus, also $A \approx B$ if and only if $r_A \sim_S r_B$. However, as shown in [8], in general, enabling equivalence and functional equivalence are incomparable. Moreover, as mentioned above, deciding whether two sets of reactions are functionally equivalent, is Co-NP-complete,

whereas deciding enabling equivalence is no more than a simple syntactic check. Consequently, when comparing the results of sets of reactions, the requirement that all reactions in the sets are enabled is an essential restriction.

By definition, a set A of reactions is consistent, if r_A is not trivial, *i.e.* if there exists a $T \subseteq S$ such that $\mathrm{res}_{r_A}(T)$ is nonempty and, in that case, $\mathrm{res}_{r_A}(T) = \mathrm{res}_A(T)$. We characterize the sets T, for which this occurs.

Theorem 3.9. *Let $A \subseteq \mathrm{rac}(S)$ be nonempty, and let $T \subseteq S$. Then, $\mathrm{res}_{r_A}(T)$ and $\mathrm{res}_A(T)$ are equal and nonempty if and only if $en_a(T)$ for all $a \in A$.*

Proof. If $\mathrm{res}_{r_A}(T)$ is nonempty, then r_A is enabled by T. By Lemma 3.2, all $a \in A$ are enabled by T. Conversely, suppose all $a \in A$ are enabled by T. By Lemma 3.2, r_A is enabled. Then $\mathrm{res}_A(T)$ and $\mathrm{res}_{r_A}(T)$ both consist of the union of all P_a, $a \in A$. □

4. The cover relation

In this section, we investigate a binary relation on $\mathrm{rac}(S)$ that expresses redundancy of a reaction when combined with another one. It was first defined in [12] (and denoted there by $\geq$).

Definition 4.1. Let $a, b \in \mathrm{rac}(S)$. Then *a covers b (in S)*, denoted by $a \gtrsim_S b$, if $\mathrm{res}_{\{a,b\}}(T) = \mathrm{res}_a(T)$ for all $T \subseteq S$.

If a reaction a covers reaction b in background set S, then we also say that *b is covered by a in S*, denoted by $b \lesssim_S a$. As usual, we can switch between $\gtrsim_S$ and $\lesssim_S$ and we will consider b to be the "smaller" reaction when $a \gtrsim_S b$.

The cover relation can be characterized in terms of functional equivalence as formulated in Definition 3.1. It explicitly demonstrates the redundancy of a reaction in the context of a reaction that covers it.

Lemma 4.2. *Let $a, b \in \mathrm{rac}(S)$. Then $a \gtrsim_S b$ if and only if $\{a, b\} \sim_S \{a\}$.*

The result of a set of reactions is defined as the union of the results of the individual reactions. Hence, the requirement in Definition 4.1 can be rephrased as the inclusion between the individual result sets.

Lemma 4.3. *Let $a, b \in \mathrm{rac}(S)$. Then $a \gtrsim_S b$ if and only if $\mathrm{res}_b(T) \subseteq \mathrm{res}_a(T)$ for all $T \subseteq S$.*

Proof. Let $T \subseteq S$. By definition, $\mathrm{res}_{\{a,b\}}(T) = \mathrm{res}_a(T) \cup \mathrm{res}_b(T)$. Hence, $\mathrm{res}_{\{a,b\}}(T) = res_a(T)$ if and only if $\mathrm{res}_a(T) \cup \mathrm{res}_b(T) = \mathrm{res}_a(T)$ if and only if $\mathrm{res}_b(T) \subseteq \mathrm{res}_a(T)$. □

Consequently, if b is trivial ($\mathrm{res}_b(T) = \varnothing$), then it is covered by every reaction $a \in \mathrm{rac}(S)$. If b is nontrivial, then we have the following characterization similar to [12, Theorem 2].

Theorem 4.4. *Let $a, b \in \mathrm{rac}(S)$ with b nontrivial. Then $a \gtrsim_S b$ if and only if $R_a \subseteq R_b$, $I_a \subseteq I_b$ and $P_a \supseteq P_b$.*

Proof. By Lemma 4.3, $a \gtrsim_S b$ if and only if $\mathrm{res}_b(T) \subseteq \mathrm{res}_a(T)$ for all $T \subseteq S$. In other words, $a \gtrsim_S b$ if and only if (i) whenever b is enabled by some $T \subseteq S$, then so is a; and (ii) $P_b \subseteq P_a$ because b is nontrivial and hence enabled by some subset T of S. Point (i) is equivalent to $R_a \subseteq R_b$ and $I_a \subseteq I_b$. □

From Theorem 4.4 it follows that the subscript S can be omitted from $a \gtrsim_S b$ if b is not trivial. Moreover, if b is trivial all reactions in $\mathrm{rac}(S)$ cover b. Since b is trivial if and only if $R_b \cap I_b \neq \varnothing$, it follows that also in this case, the subscript S is not relevant in $a \gtrsim_S b$ and can be omitted.

In addition to Lemma 4.2, it can now be seen that in a reaction system, reactions that are covered by one or more other reactions of the system, are indeed redundant in the sense that they can be removed from the system without changing its functioning. As trivial reactions can always be deleted from a reaction system $\mathcal{A}$ without changing its function $\mathrm{res}_{\mathcal{A}}$, we thus have:

Corollary 4.5. *Let (S, A) be a reaction system. Let $a, b \in A$ be such that $a \neq b$ and $a \gtrsim b$. Then, $(S, A) \sim (S, A \setminus \{b\})$.*

Furthermore note that, by Theorem 4.4, $a \gtrsim b$ with b nontrivial is equivalent to $r_{\{a,b\}} = (R_b, I_b, P_a)$. Thus if $a \gtrsim b$ and b is nontrivial, then both a and $r_{\{a,b\}}$ are nontrivial. Conversely, by Theorem 3.8, if $a \gtrsim b$ and $\{a, b\}$ is consistent, *i.e.* $r_{\{a,b\}}$ is nontrivial, then b is nontrivial. Summarizing:

Corollary 4.6. *Let $a, b \in \mathrm{rac}(S)$ such that $a \gtrsim b$. Then*

1. $r_{\{a,b\}} = (R_b, I_b, P_a)$ *if* b *is nontrivial.*
2. a *is nontrivial if* b *is nontrivial.*
3. $r_{\{a,b\}}$ *is nontrivial if and only if* $\{a, b\}$ *is consistent if and only if* b *is nontrivial.*

As demonstrated next, consistency of two reactions does not imply that one covers the other.

Example 4.7. If $a = (\{\mathtt{r}, 1\}, \{\mathtt{i}, 2\}, \{\mathtt{r}, 1\})$ and $b = (\{\mathtt{r}, 3\}, \{\mathtt{i}, 4\}, \{\mathtt{r}, 2\})$, then the set $\{a, b\}$ is consistent, but none of a and b covers the other, as *e.g.* $\{\mathtt{r}, 1\} \not\subseteq \{\mathtt{r}, 3\}$ and $\{\mathtt{r}, 3\} \not\subseteq \{\mathtt{r}, 1\}$. $\Diamond$

Finally, it also follows from Theorem 4.4, that whenever two reactions a and b form a consistent pair, we can characterize how their combined reaction $r_{\{a,b\}} = (R_a \cup R_b, I_a \cup I_b, P_a \cup P_b)$ is related to a and b.

Corollary 4.8. *Let* $a, b \in \mathrm{rac}(S)$ *be such that* $\{a, b\}$ *is consistent. Then*

1. $r_{\{a,b\}} \gtrsim b$ *if and only if* $R_a \subseteq R_b$ *and* $I_a \subseteq I_b$.
2. $a \gtrsim r_{\{a,b\}}$ *if and only if* $P_b \subseteq P_a$.
3. $a \gtrsim r_{\{a,b\}} \gtrsim b$ *if and only if* $a \gtrsim b$.

Theorem 4.4 strongly resembles [12, Theorem 2]. The only difference is that the latter has the additional assumption that also a is not trivial. However, as both Corollary 4.6(2) and the proof of [12, Theorem 2] show, this assumption can be left implicit.

Let us now investigate the statements of Lemma 4.3 and Theorem 4.4.

First of all, the lemma deals with all reactions while the theorem concerns only nontrivial reactions. Then, an important difference between the two seems to be that the lemma considers the *semantics* (the effect or the result) of reactions, whereas the theorem is concerned with their *syntax* (their form). In general, one would prefer a structural (syntax) check to compare reactions a and b to establish whether $a \gtrsim b$ holds. However, whether or not a reaction b is trivial, can be checked syntactically (by checking whether $R_b \cap I_b = \varnothing$), and since all trivial reactions are covered by all other reactions, there is no need to explicitly verify that the relation $a \gtrsim b$ holds.

In addition, Lemma 4.3 shows that $\gtrsim$ is a preorder (*i.e.* it is reflexive and transitive) on the set of all reactions. It is not anti-symmetric as all trivial reactions cover each other. However, as is immediate from Theorem 4.4, $\gtrsim$ is anti-symmetric when restricted to nontrivial reactions. Hence, $\gtrsim$ is a partial order on $\mathrm{Rac}(S)$, the set of all nontrivial reactions in $\mathrm{rac}(S)$.

Finally, the characterization in Theorem 4.4 invites to explicitly consider the *product order* $\sqsupseteq$ on $\mathrm{rac}(S)$. This order relates the three sets constituting reactions componentwise using set inclusion. We define $a \sqsupseteq b$ if and only if $R_a \subseteq R_b$, $I_a \subseteq I_b$, $P_a \supseteq P_b$. Thus, $\sqsupseteq$ is a partial order, also when restricted to $\mathrm{Rac}(S)$.

Remark 4.9. Informally, each of the three components of $\sqsupseteq$ is the powerset $\mathcal{P}(S)$ ordered by set inclusion (or its reverse). Recall, however, that the components are assumed to contain or not to contain a specific universal element (either $\mathtt{r}$ or $\mathtt{i}$), so formally, only a quarter of the elements of the power set occur in the first two components, and half of the elements of $\mathcal{P}(S)$ occur in the third element. This does not, essentially, change the order theoretic properties of the components.

To conclude this section, we summarize the relationship between cover and product order. As illustrated by the following example, the product order and the cover relation are not the same.

Example 4.10. Let $b = (\{\mathtt{r}, 1\}, \{\mathtt{i}, 1\}, \{\mathtt{r}\})$. Then, b is trivial, so $a \gtrsim b$, for every $a \in \mathrm{rac}(S)$. Take however, $a = (\{\mathtt{r}, 2\}, \{\mathtt{i}\}, \{\mathtt{r}\})$, then a is nontrivial and $a \not\sqsupseteq b$. $\Diamond$

The following observation follows from Theorem 4.4, together with the observation that $a \gtrsim b$ whenever b is trivial.

Corollary 4.11. *Let* $a, b \in \mathrm{rac}(S)$. *Then,* $a \gtrsim b$ *if and only if either* b *is trivial or* $a \sqsupseteq b$.

When restricted to nontrivial reactions, the two relations are the same. This follows from Corollary 4.11 and the observations just before Remark 4.9

Corollary 4.12. *Both* $\gtrsim$ *and* $\sqsupseteq$ *are partial orders on* $\mathrm{Rac}(S)$ *and they coincide on that domain.*

5. A lattice of reactions

We now introduce two operations on pairs of reactions with the aim to identify a least common covering reaction and a greatest common covered reaction. These operations are tentatively called ‘meet’ and ‘join’, as they are those operations

for the (inverted) product order $\sqsubseteq$. We first investigate their role for the cover relation (actually, to be more precise, for its inversion $\lesssim$). Next, to interpret $\mathrm{Rac}(S)$ with the cover relation as a lattice, we identify a top and a bottom element with the latter representing the (functional equivalence class of) trivial reactions.

Definition 5.1. Let $a, b \in \mathrm{rac}(S)$.
Then $a \sqcup b = (R_a \cap R_b, I_a \cap I_b, P_a \cup P_b)$ is the *join of a and b* and $a \sqcap b = (R_a \cup R_b, I_a \cup I_b, P_a \cap P_b)$ is the *meet of a and b*.

Clearly, $a \sqcap b$ and $a \sqcup b$ are reactions in S if a and b are. And, as join and meet for the product order on $\mathrm{rac}(S)$, the operations are commutative, associative, and idempotent. Furthermore, $a \sqcap b$ and $a \sqcup b$ are a lower bound and an upper bound respectively, for a and b under the cover relation.

Lemma 5.2. *Let $a, b \in \mathrm{rac}(S)$. Then $a \sqcup b \gtrsim a$ and $a \gtrsim a \sqcap b$.*

Proof. The proposed relations hold as join and meet for the product order $\sqsubseteq$. By Corollary 4.11, $\sqsupseteq$ implies $\gtrsim$ and the statement of the lemma follows. □

Remark 5.3. Recall that $r_{\{a,b\}} = (R_a \cup R_b, I_a \cup I_b, P_a \cup P_b)$. Hence $r_{\{a,b\}} = a \sqcap b$ if and only if $P_a = P_b$. Indeed, by Corollary 4.8(2), if $\{a, b\}$ is consistent, then $P_a = P_b$ if and only if $r_{\{a,b\}}$ is a lower bound for a and b. Note that in case $\{a, b\}$ is not consistent, both $a \sqcap b$ and $r_{\{a,b\}}$ are trivial reactions. □

We cannot conclude that $\mathrm{rac}(S)$ with the cover relation forms a lattice since as observed in Section 4, $\lesssim$ is not even a partial order on $\mathrm{rac}(S)$. On the other hand, $\lesssim$ is a partial order on $\mathrm{Rac}(S)$, but it may be that the meet of two nontrivial reactions is a trivial reaction. Moreover, the join of two trivial reactions is in some cases trivial and in other cases nontrivial.

Example 5.4. Let $a = (\{\mathtt{r}, 1\}, \{\mathtt{i}\}, \{\mathtt{r}\})$ and $b = (\{\mathtt{r}, 2\}, \{\mathtt{i}, 1\}, \{\mathtt{r}, 2\})$ be two nontrivial reactions. Then the meet of these $a \sqcap b = (\{\mathtt{r}, 1, 2\}, \{\mathtt{i}, 1\}, \{\mathtt{r}\})$ is a trivial reaction. On the other hand, the join of the two trivial reactions $a' = (\{\mathtt{r}, 1\}, \{\mathtt{i}, 1\}, \{\mathtt{r}, 1\})$ and $b' = (\{\mathtt{r}, 2\}, \{\mathtt{i}, 2\}, \{\mathtt{r}, 2\})$ is the nontrivial reaction $a' \sqcup b' = (\{\mathtt{r}\}, \{\mathtt{i}\}, \{\mathtt{r}, 1, 2\})$. However, the join of the two trivial reactions a' and b'', for $b'' = (\{\mathtt{r}, 1, 2\}, \{\mathtt{i}, 1, 2\}, \{\mathtt{r}, 2\})$, is the trivial reaction $a' \sqcup b'' = (\{\mathtt{r}, 1\}, \{\mathtt{i}, 1\}, \{\mathtt{r}, 1, 2\})$. Finally, note that the join of a trivial reaction and a nontrivial one may be nontrivial, e.g., $a \sqcup b' = (\{\mathtt{r}\}, \{\mathtt{i}\}, \{\mathtt{r}, 2\})$. ◊

The following lemma states that the join of a trivial reaction and a nontrivial one is always nontrivial. It moreover relates the meet operation to the consistency of reactions. Note that, as a consequence of this and in contrast with the situation for the join, the meet of two reactions is necessarily trivial if at least one of these reactions is trivial.

Lemma 5.5. *Let $a, b \in \mathrm{rac}(S)$. Then*

1. *$a \sqcup b$ is a nontrivial reaction in S if a or b is nontrivial.*
2. *$a \sqcap b$ is a nontrivial reaction in S if and only if $\{a, b\}$ is consistent.*

Proof. (1) The join $a \sqcup b$ is nontrivial if and only if $R_{a \sqcup b} \cap I_{a \sqcup b} = \varnothing$, *i.e.* if and only if $(R_a \cap R_b) \cap (I_a \cap I_b) = \varnothing$. Given the fact that a or b is nontrivial, we know that $R_a \cap I_a = \varnothing$ or $R_b \cap I_b = \varnothing$, and so is their intersection.
(2) The meet $a \sqcap b$ is nontrivial if and only if $R_{a \sqcap b} \cap I_{a \sqcap b} = \varnothing$. Observe that $R_{a \sqcap b} = R_a \cup R_b = R_{\{a,b\}}$ and $I_{a \sqcap b} = I_a \cup I_b = I_{\{a,b\}}$, and we see that this requirement is equivalent to the consistency of $\{a, b\}$. □

As argued next, the operation meet yields the greatest lower bound of any two reactions, not only for the product order, but also for the cover relation.

Lemma 5.6. *Let $a, b, c \in \mathrm{rac}(S)$. Then $a \sqcap b \gtrsim c$ whenever $a \gtrsim c$ and $b \gtrsim c$.*

Proof. If c is trivial then we are done. Otherwise, when c is nontrivial, we use Theorem 4.4. Since $a \gtrsim c$ and $b \gtrsim c$, we have $R_a, R_b \subseteq R_c$, $I_a, I_b \subseteq I_c$, and $P_c \subseteq P_a, P_b$. Hence, $R_a \cup R_b \subseteq R_c$, $I_a \cup I_b \subseteq I_c$, and $P_c \subseteq P_a \cap P_b$, by which $a \sqcap b \gtrsim c$. □

It follows that the meet of two (nontrivial) reactions is nontrivial if there exists a nontrivial reaction covered by both. Note that for the reactions a and b in Example 5.4, there exists no nontrivial reaction that is covered by both.

We would want to obtain a result like Lemma 5.6 for the join $\sqcup$ as the least upper bound for the cover relation, ($c \gtrsim a \sqcup b$ whenever $c \gtrsim a$ and $c \gtrsim b$), but unfortunately this cannot be proved in a similar way. In fact, the result cannot be proved at all.

Example 5.7. Consider $a = (\{\mathtt{r}, 1\}, \{\mathtt{i}\}, \{\mathtt{r}\})$ and $b' = (\{\mathtt{r}, 2\}, \{\mathtt{i}, 2\}, \{\mathtt{r}, 2\})$ from Example 5.4 and their join $a \sqcup b' = (\{\mathtt{r}\}, \{\mathtt{i}\}, \{\mathtt{r}, 2\})$. Let $c' = (\{\mathtt{r}\}, \{\mathtt{i}\}, \{\mathtt{r}\})$. Then $c' \gtrsim a$ (by Theorem 4.4) and $c' \gtrsim b'$ (as b' is trivial). However, $\mathrm{res}_{c'}(\{\mathtt{r}\}) = \{\mathtt{r}\}$, whereas $\mathrm{res}_{a \sqcup b'}(\{\mathtt{r}\}) = \{\mathtt{r}, 2\}$. Hence, by Lemma 4.3, $c' \not\gtrsim a \sqcup b'$. ◊

However, when restricted to nontrivial reactions cover and product order coincide, so the join satisfies its requirements for both orders.

Lemma 5.8. *Let $a, b \in \mathrm{Rac}(S)$ and $c \in rac(S)$. Then $c \gtrsim a \sqcup b$ whenever $c \gtrsim a$ and $c \gtrsim b$.*

Proof. Assume a and b are two nontrivial reactions. By Lemma 5.5, $a \sqcup b$ is nontrivial, as well. Suppose $c \gtrsim a$ and $c \gtrsim b$. Then, it follows by Theorem 4.4 that $R_c \subseteq R_a, R_b$, $I_c \subseteq I_a, I_b$ and $P_a, P_b \subseteq P_c$. This implies $R_c \subseteq R_a \cap R_b = R_{a \sqcup b}$, $I_c \subseteq I_a \cap I_b = I_{a \sqcup b}$, and $P_a \cup P_b = P_{a \sqcup b} \subseteq P_c$. Then, again by Theorem 4.4, since $a \sqcup b$ is nontrivial, we conclude that $c \gtrsim a \sqcup b$. □

There are two extremal objects in the set $\mathrm{rac}(S)$ of all reactions: *top* $\top_S = (\{\mathtt{r}\}, \{\mathtt{i}\}, S)$, and *bottom* $\bot_S = (S \setminus \{\mathtt{i}\}, S \setminus \{\mathtt{r}\}, \{\mathtt{r}\})$. That these are indeed the greatest and the least element, respectively, in $\mathrm{rac}(S)$ follows directly from the definitions.

Theorem 5.9. *Let $a \in \mathrm{rac}(S)$. Then $\top_S \gtrsim a$ and $a \gtrsim \bot_S$. Moreover, $a \sqcap \top_S = a$, $a \sqcup \top_S = \top_S$, $a \sqcap \bot_S = \bot_S$, and $a \sqcup \bot_S = a$.*

Note that $\top_S$ and $\bot_S$ differ, even when S just consists of the universal entities $\mathtt{r}$ and $\mathtt{i}$ (and in that case $\mathrm{rac}(S) = \{\top_S, \bot_S\}$). Clearly, $\top_S$ is always nontrivial, while $\bot_S$ is trivial if S has three or more elements.

From here on, we assume that S has at least one entity apart from $\mathtt{r}$ and $\mathtt{i}$.

Moreover, to simplify the notation and since S is fixed, we omit the subscript S and simply write $\top$ and $\bot$.

Recall that, as stated in Corollary 4.12, $\gtrsim$ is a partial order on $\mathrm{Rac}(S)$. There is a greatest element in $\mathrm{Rac}(S)$ (namely $\top$, see Theorem 5.9), but $\mathrm{Rac}(S)$ has no smallest element, as all reactions of the form $(X, S \setminus X, S)$ are minimal. Reactions with such complementary R and I are called *maximally inhibited* in [21]. Consequently, $(\mathrm{Rac}(S), \gtrsim)$ is not a lattice, but it is a join-semilattice. We can extend it into a lattice by lifting it (see Subsection 2.1). Thus, we add a new element, smaller than any existing element from the domain. Rather than choosing a new abstract element, we can use $\bot$ as the new, added minimal element, since $\bot \notin \mathrm{Rac}(S)$ and $a \gtrsim \bot$ for every $a \in \mathrm{Rac}(S)$. Alternatively, adding $\bot$ as a bottom element, can be seen as a quotient construction (with $\bot$ representing the functional equivalence class comprising all trivial reactions), a common tool to change a preorder into an partial order.

Theorem 5.10. *The set $\mathrm{Rac}_\bot(S)$, with the cover relation $\gtrsim$, forms a lattice.*

Proof. We already know that $\gtrsim$ is a partial order on $\mathrm{Rac}_\bot(S)$. Thus, we only have to show that every pair of elements in $\mathrm{Rac}_\bot(S)$ has a greatest lower bound and a least upper bound.

As in the case with only nontrivial reactions, we can use the join $a \sqcup b$ as the least upper bound of a and b. By Lemma 5.5, $a \sqcup b$ is a nontrivial reaction in S, if a or b is nontrivial. The only trivial element in $\mathrm{Rac}_\bot(S)$ is $\bot$ and since $a \sqcup \bot = a$ for all $a \in \mathrm{Rac}(S) \cup \{\bot\}$ by Theorem 5.9, we have a least upperbound for any reaction a and $\bot$.

For the greatest lower bound we have to adapt the existing meet operation. The reason is that ranging over nontrivial reactions a, b the meet $a \sqcap b$ can be various trivial reactions, whereas our current domain $\mathrm{Rac}_\bot(S)$ has only a single trivial reaction. We have to merge these trivial reactions into one. Define the new meet operation $\widehat{\sqcap}$ for $\mathrm{Rac}_\bot(S)$ by $a \mathbin{\widehat{\sqcap}} b = a \sqcap b$ when $\{a, b\}$ is consistent, and let $a \mathbin{\widehat{\sqcap}} b = \bot$ when $\{a, b\}$ is not consistent. By Lemma 5.5 this is well-defined: $\{a, b\}$ consistent implies that $a \sqcap b$ is nontrivial. This operation produces the greatest lower bound indeed. This follows from the fact that the original meet is a greatest lower bound. If $\{a, b\}$ is consistent, then there can be no reaction ordered below a, b and above $a \sqcap b$. Otherwise, if $\{a, b\}$ is inconsistent, then there can be no nontrivial reaction below both a, b (as otherwise that would be $a \sqcap b$). Hence the greatest lower bound is $\bot$. □

The lattice formed by $\mathrm{Rac}_\bot(S)$ and $\gtrsim$ is sketched in Fig. 1.

6. The exact cover relation

The cover relation is based on functional equivalence, *cf.* Definitions 2.3 and 4.1. That is, if a covers b, then the combined result function $\mathrm{res}_{\{a,b\}}$ of a and b coincides with the result function res_a of a. In this section, we study a new relation which compares a and b directly, rather than $\{a, b\}$ and a.

Definition 6.1. Let $a, b \in \mathrm{rac}(S)$. Then a *exactly covers b (in S)*, for short a *e-covers* b (in S), denoted by $a \geq_{e,S} b$ if, for all $T \subseteq S$, $en_b(T)$ implies that $\mathrm{res}_a(T) = \mathrm{res}_b(T)$.

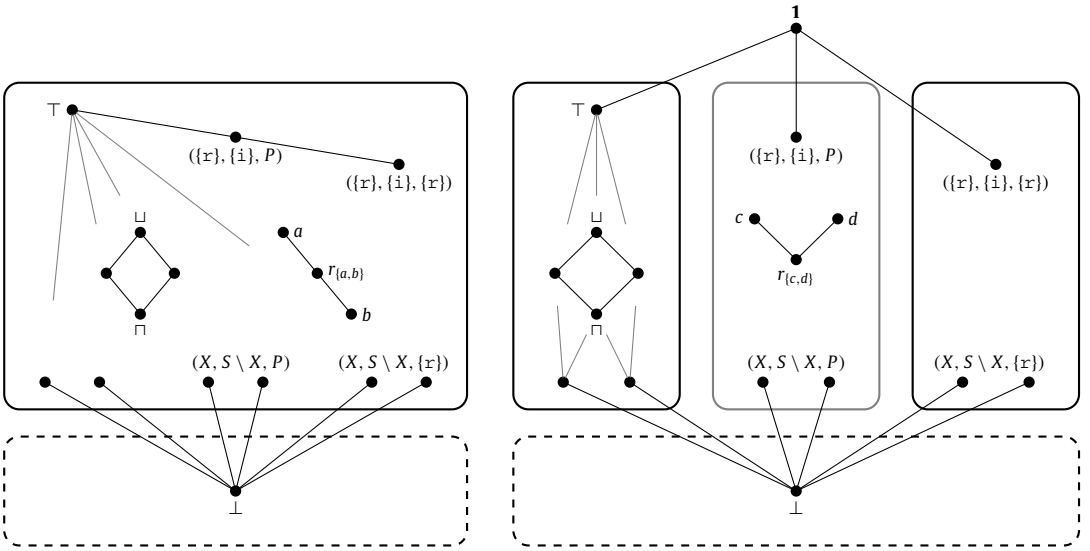

Fig. 1. A sketch of the lattices based on $\lesssim$ (*left*) and on $\preceq_e$ (*right*). The dotted box stands for the functional equivalence class of all trivial reactions. For $\lesssim$, the solid box comprises $\mathrm{Rac}(S)$. For $\preceq_e$, there is a solid box for each product set P.

The requirement that the results of a and b are compared only when b is enabled, expresses that b indeed is seen as the 'lesser' reaction. It also implies that if b is a trivial reaction, then it is e-covered by all reactions in $\mathrm{rac}(S)$. Note furthermore that, if b is enabled by a state $T \subseteq S$, then $\mathrm{res}_b(T) \neq \varnothing$. Hence if $a \geq_{e,S} b$ and $en_b(T)$ then $\mathrm{res}_a(T) \neq \varnothing$, which implies that a is enabled by T as well.

The following example demonstrates that the cover relation $\gtrsim$ does not imply $\geq_{e,S}$.

Example 6.2. Consider $a = (\{\mathtt{r}\}, \{\mathtt{i}\}, \{r, 1\})$ and $b = (\{r, 1\}, \{\mathtt{i}, 2\}, \{\mathtt{r}\})$. Since b is nontrivial we can use Theorem 4.4 and, thus, we have that $a \gtrsim b$. Consider now $T \subseteq S$. If b is enabled by T, then $\{r, 1\} \subseteq T$ and $\{\mathtt{i}, 2\} \cap T = \varnothing$. Consequently, also a is enabled by T. However $\mathrm{res}_a(T) = \{r, 1\} \neq \{\mathtt{r}\} = \mathrm{res}_b(T)$. Hence $a \geq_{e,S} b$ does not hold. ♢

If $a \geq_{e,S} b$, then res_b is the restriction[2] of res_a to the states that enable b. This is different from the cover relation which requires for $a \gtrsim b$ to hold that res_a and $\mathrm{res}_{\{a,b\}}$ are the same function. Moreover, by Lemma 4.3, this requirement (*i.e.* $\mathrm{res}_a(T) = \mathrm{res}_{\{a,b\}}(T)$, for all T) is equivalent to $\mathrm{res}_b(T) \subseteq res_a(T)$ for all T, an inclusion rather than an equality. This crucial difference is reflected in the next result, which should be compared with Theorem 4.4.

Theorem 6.3. *Let $a, b \in \mathrm{rac}(S)$ with b nontrivial. Then $a \geq_{e,S} b$ if and only if $R_a \subseteq R_b$, $I_a \subseteq I_b$ and $P_a = P_b$.*

Proof. If $R_a \subseteq R_b$ and $I_a \subseteq I_b$, then it is immediate that, for all $T \subseteq S$, $en_b(T)$ implies $en_a(T)$. If moreover, $P_a = P_b$, then $\mathrm{res}_a(T) = \mathrm{res}_b(T)$ whenever $en_b(T)$ holds. Hence $a \geq_{e,S} b$.

Conversely, let us consider $T = R_b$. Since b is nontrivial, we have $R_b \cap I_b = \varnothing$ and so $en_b(T)$. Since $en_b(T)$ implies $en_a(T)$, it follows that $R_a \subseteq T = R_b$. Moreover, $P_a = \mathrm{res}_a(T) = \mathrm{res}_b(T) = P_b$. Now let $T = S \setminus I_b$. Again, $en_b(T)$ and because $en_b(T)$ implies $en_a(T)$, it follows that $I_a \cap S \setminus I_b = \varnothing$. So, $I_a \subseteq I_b$ and we are done. □

From Theorem 6.3, it follows that the subscript S can be omitted from $a \geq_{e,S} b$, if b is not trivial. If b is trivial, then $a \geq_{e,S} b$ holds for all reactions a and, thus, also in this case, the subscript S is not relevant. Another consequence of Theorem 6.3 and Theorem 4.4 is that $a \geq_e b$ implies $a \gtrsim b$.

Corollary 6.4. *Let $a, b \in \mathrm{rac}(S)$. Then $a \geq_e b$ implies $a \gtrsim b$.*

However, as shown in Example 6.2, the converse does not hold.

Since $\geq_e$ is contained in $\gtrsim$, the statements of Corollary 4.6 also hold for exact cover. More specifically, if $a \geq_e b$, then $r_{\{a,b\}} = (R_b, I_b, P_a)$ if b is nontrivial. By Theorem 6.3, $a \geq_e b$ with b nontrivial implies that $P_a = P_b$ and so $r_{\{a,b\}} = (R_b, I_b, P_b) = b$. As a result, the following observation holds for exact cover, but not for cover (*cf.* Corollary 4.8 (1) and (3)).

[2] Here res_b is considered as a partial function, undefined for those states T that do not enable b, *i.e.* $\mathrm{res}_b(T) = \varnothing$.

Corollary 6.5. *Let $a, b \in \mathrm{rac}(S)$ such that $a \geq_e b$. Then $r_{\{a,b\}} = b$ if b is nontrivial.*

Given the above observations, the structure imposed on $\mathrm{rac}(S)$ by $\geq_e$ is rather straightforward. It follows immediately from Definition 6.1 that $\geq_e$ is a preorder. Also, every trivial reaction is e-covered by any other reaction, while Theorem 6.3 implies that $\geq_e$ is a partial order when restricted to $\mathrm{Rac}(S)$. Again by Theorem 6.3, nontrivial reactions with different product sets are always incomparable with respect to the exact cover relation (in contrast with the cover relation). In addition, for any pair of nontrivial reactions with the same product set, the exact cover relation is the product order of the superset relations for their reaction and inhibitor sets. Thus, for two nontrivial reactions a and b such that $P_a = P_b$, the join $a \sqcup b = (R_a \cap R_b, I_a \cap I_b, P_a \cup P_b)$ from Definition 5.1 is their least upper bound w.r.t. $\leq_e$, as it is nontrivial and also has $P_a = P_b$ as product set. If a and b are nontrivial reactions with different product sets, they do not have any common upper bound in $\mathrm{Rac}(S)$. Similarly, every pair a, b of nontrivial reactions such that $P_a = P_b$, has the meet $a \sqcap b = (R_a \cup R_b, I_a \cup I_b, P_a \cap P_b)$ from Definition 5.1 as their greatest lower bound, provided $\{a, b\}$ is consistent. It is worthwhile to note that in this case $a \sqcap b = r_{\{a,b\}}$ (see also Remark 5.3). If a and b are nontrivial reactions with different product sets, they do not have a lower bound in $\mathrm{Rac}(S)$ w.r.t. the exact cover relation.

Using a technique similar to the one employed in Theorem 5.10 for the cover relation, it is possible to turn $\mathrm{Rac}(S)$ with the e-cover relation into a lattice. This time, we have to extend the domain not only with a bottom element $\bot$ (representing all trivial reactions), but also with a new (artificial) top element **1**. This top element cannot be taken to be $\top = (\{\mathtt{r}\}, \{\mathtt{i}\}, S)$, as $\top$ itself is a nontrivial reaction in $\mathrm{Rac}(S)$, incomparable to reactions with other product sets. In $\mathrm{Rac}(S)$, extended with $\bot$ and **1**, the join of any pair of incomparable reactions will be defined as **1**. We summarize the above.

Theorem 6.6. *The set $\mathrm{Rac}(S) \cup \{\bot, \mathbf{1}\}$, with the exact cover relation $\geq_e$, forms a lattice.*

The two lattices based on $\mathrm{Rac}(S)$ as discussed in this and the previous section are illustrated in Fig. 1. The lattice defined by the cover relation $\lesssim$ is depicted on the left of the figure, while the one based on the exact cover $\leq_e$ is presented on the right. For $\lesssim$, we have $\top = (\{\mathtt{r}\}, \{\mathtt{i}\}, S)$ as the maximum element. The maximally inhibited reactions $(X, S \setminus X, P)$ where $\{\mathtt{r}\} \subseteq X \subseteq S \setminus \{\mathtt{i}\}$ and $\{\mathtt{r}\} \subseteq P \subseteq S$ are the minimal reactions w.r.t. $\lesssim$ in $\mathrm{Rac}(S)$. Adding $\bot$ (which can be seen as representing the equivalence class of trivial reactions) yields the lattice. For the second lattice, defined by $\leq_e$, recall that by Corollary 6.4 we know that $\leq_e$ is contained in $\lesssim$. There are, however, components (solid boxes), one for each $P \subseteq S$ with $\mathtt{r} \in P$, consisting of all nontrivial reactions with P as their product set. Reactions in different components are not related by $\leq_e$. Each subset of $\mathrm{Rac}(S)$ determined by a product set P has its own maximum element $(\{\mathtt{r}\}, \{\mathtt{i}\}, P)$, and the maximally inhibited nontrivial reactions $(X, S \setminus X, P)$ are minimal elements in this subset. By adding $\bot$ and the artificial top **1** we, again, obtain a lattice.

Finally, consider $r_{\{a,b\}}$, the reaction defined by a and b. First, recall that if $\{a, b\}$ is not consistent, then both $r_{\{a,b\}}$ and $a \sqcap b$ are trivial reactions. In the case, however, that $\{a, b\}$ is consistent, we know from Corollary 4.8, that $a \gtrsim r_{\{a,b\}} \gtrsim b$ if and only if $a \gtrsim b$; moreover in this case, $a \sqcap b = r_{\{a,b\}}$ for all consistent pairs a, b with $P_a = P_b$ (see the right side of Fig. 1).

7. Cover, exact cover, and enabling cover

In this section, we propose and investigate a third relationship, next to cover and exact cover, between reactions a and b now based on the equality of the functions $\mathrm{res}_{\{a,b\}}$ and res_a when restricted to those T for which a and b are both enabled. We provide in Theorem 7.5, a characterization of each of the three relations in terms of reactant, inhibitor, and product sets. Then, as a corollary, we can capture the precise difference between the cover and the exact cover relations.

As stated in Lemma 4.2, the cover relation $a \gtrsim b$ can be expressed as the functional equivalence $\{a, b\} \sim_S \{a\}$ and as such reflects the equality of the functions $\mathrm{res}_{\{a,b\}}$ and res_a on $\mathcal{P}(S)$. In other words, $\mathrm{res}_a(T) \cup \mathrm{res}_b(T) = \mathrm{res}_a(T)$ should hold for all states T that enable either a or b which means that b never contributes additional products in addition to those produced by a. The new relation is defined using enabling equivalence.

Definition 7.1. Let $a, b \in \mathrm{rac}(S)$. Then *a covers b when enabled (in S)*, for short *a en-covers b* (in S), denoted by $a \gtrapprox_S b$, if $\{a, b\} \approx \{a\}$.

In other words, by Definition 3.3, $a \gtrapprox_S b$ holds if and only if, for each $T \subseteq S$, (i) $en_{r_{\{a,b\}}}(T)$ if and only if $en_a(T)$ and (ii) $\mathrm{res}_{r_{\{a,b\}}}(T) = \mathrm{res}_a(T)$ whenever $en_{r_{\{a,b\}}}(T)$. So, intuitively, the en-cover relation expresses that reaction b has no additional products to contribute when both a and b are enabled. Note that, by (i), b is enabled whenever a is enabled. The next lemma gives different formulations for the same condition.

Lemma 7.2. *Let $a, b \in \mathrm{rac}(S)$. Then the following are equivalent:*

1. *$en_a(T)$ implies $en_b(T)$.*
2. *$en_a(T)$ implies $en_{r_{\{a,b\}}}(T)$.*
3. *$en_a(T)$ if and only if $en_{r_{\{a,b\}}}(T)$.*

Proof. Since by Lemma 3.2, $en_{r_{\{a,b\}}}(T)$ if and only if both $en_a(T)$ and $en_b(T)$, the three propositions are easily seen to be logically equivalent. □

Note that by Lemma 7.2(1), the above condition (i) for $a \gtrapprox_S b$ can be replaced by the condition that b is enabled whenever a is enabled. This is the opposite of the situation for $a \geq_e b$ where the result of a and b should be the same if b is enabled (see Definition 6.1) and hence a should be enabled whenever b is. Another relevant observation is that for trivial reactions a, we have that $\{a, b\} \approx \{a\}$ and $a \gtrapprox_S b$ hold for all reactions b. Moreover, by the next result, every reaction that is en-covered by a nontrivial one, is itself nontrivial. It is interesting to compare this observation with Corollary 4.6(2).

Lemma 7.3. *Let $a, b \in \mathrm{rac}(S)$ such that $a \gtrapprox_S b$. Then b is nontrivial if a is nontrivial.*

Proof. Since a is nontrivial, $R_a \cap I_b \neq \varnothing$ and so there exists a $T \subseteq S$ that enables a. Since $a \gtrapprox_S b$ we have $\{a, b\} \approx \{a\}$ and hence by Definition 3.3, T also enables $r_{\{a,b\}}$. Consequently, by Lemma 3.2, T enables b. Thus $R_b \cap I_b = \varnothing$ and b is not trivial. □

For any trivial reaction b we have $b \gtrapprox_S a$, $a \geq_e b$ and $a \gtrsim b$ for all reactions a. Furthermore, if b is not trivial and any of $b \gtrapprox_S a$, $a \geq_e b$, and $a \geq b$ holds, the set $\{a, b\}$ is consistent by Lemma 3.5, Corollary 6.5, and Corollary 4.6(3), respectively.

The following theorem is a consequence of Theorem 3.6.

Theorem 7.4. *Let $a, b \in \mathrm{rac}(S)$ with a nontrivial. Then $a \gtrapprox_S b$ if and only if $R_b \subseteq R_a$, $I_b \subseteq I_a$, and $P_b \subseteq P_a$.*

Proof. Suppose first that $a \gtrapprox_S b$. Thus we have $\{a, b\} \approx \{a\}$. Since a is nontrivial, $\{a\}$ is consistent. Hence $\{a, b\} \approx \{a\}$ implies that $\{a, b\}$ is consistent. Now we can apply Theorem 3.6 to conclude that $R_a \cup R_b = R_a$, $I_a \cup I_b = I_a$, and $P_a \cup P_b = P_a$. Consequently, $R_b \subseteq R_a$, $I_b \subseteq I_a$, and $P_b \subseteq P_a$.

Conversely, if a is nontrivial, then $R_a \cap I_a = \varnothing$. It then follows from $R_b \subseteq R_a$ and $I_b \subseteq I_a$ that also $(R_a \cup R_b) \cap (I_a \cup I_b) = \varnothing$ and hence $\{a, b\}$ is consistent. Moreover $R_a \cup R_b = R_a$, $I_a \cup I_b = I_a$, and $P_a \cup P_b = P_a$. Thus, we can apply Theorem 3.6 and it follows that $\{a, b\} \approx \{a\}$, *i.e.* $a \gtrapprox_S b$. □

By this theorem and our earlier observation on trivial reactions it follows that we can safely omit the subscript S from $\gtrapprox_S$ as we did before for $\approx$.

Theorem 7.4 resembles Theorem 4.4 for $\gtrsim$ and Theorem 6.3 for $\geq_e$. However, the set inclusion relations for reactant sets and for inhibitor sets are now reversed. In particular, if $a \gtrsim b$, then $R_a \subseteq R_b$ and $I_a \subseteq I_b$ and, similarly, for $a \geq_e b$. To summarize, the cover, exact cover, and enabling cover can be characterized as follows.

Theorem 7.5. *Let $a, b \in \mathrm{rac}(S)$ with b nontrivial. Then*

1. *$b \gtrapprox a$ if and only if $R_a \subseteq R_b$, $I_a \subseteq I_b$, and $P_a \subseteq P_b$;*
2. *$a \geq_e b$ if and only if $R_a \subseteq R_b$, $I_a \subseteq I_b$, and $P_a = P_b$;*
3. *$a \gtrsim b$ if and only if $R_a \subseteq R_b$, $I_a \subseteq I_b$, and $P_a \supseteq P_b$.*

Moreover, we have a characterization of the difference between the cover and the exact cover relations.

Corollary 7.6. *Let $a, b \in \mathrm{rac}(S)$ with b nontrivial. Then*

1. *$a \geq_e b$ if and only if $a \gtrsim b$ and $b \gtrapprox a$.*
2. *$a \geq_e b$ if and only if $\{a, b\} \sim \{a\}$ and $\{a, b\} \approx \{b\}$.*

Functional equivalence of $\{a, b\}$ and $\{a\}$ (in other words, $a \gtrsim b$) means that b is redundant and can be dropped (*cf.* Corollary 4.5) because whenever b is enabled and can contribute its products, a will produce the same (and possibly more). On the other hand, enabling equivalence of $\{a, b\}$ and $\{b\}$ (in other words, $b \gtrapprox a$) means that a is redundant in those states by which b is enabled (and hence a). So, whenever b is enabled, b will produce at least the products of a, but it doesn't say anything about the states that do not enable b, but perhaps enable a. When combined, $a \gtrsim b$ and $b \gtrapprox a$ say that if b is enabled by a state T, then also a and, moreover, $\mathrm{res}_a(T) = \mathrm{res}_b(T)$. In other words, $a \geq_e b$ holds.

Obviously $\gtrapprox$ is a reflexive relation. By Lemma 7.3 and Theorem 7.4 and because trivial reactions en-cover all reactions, it is also transitive. Hence it is a preorder on $\mathrm{rac}(S)$. It is not anti-symmetric as all trivial reactions en-cover each other. However, through the product order as given in Theorem 7.4, $\gtrapprox$ is a partial order on $\mathrm{Rac}(S)$.

As with the cover relation, we can construct a lattice based on en-cover $\gtrapprox$ by representing the trivial reactions by a single element. This time $a \gtrapprox_S b$ holds if each of the three components of reaction a are a superset of the respective components of reaction b. The minimal element w.r.t. $\gtrapprox_S$ in $\mathrm{rac}(S)$ is $(\{\mathtt{r}\}, \{\mathtt{i}\}, \{\mathtt{r}\})$ and as the maximal element we choose the trivial

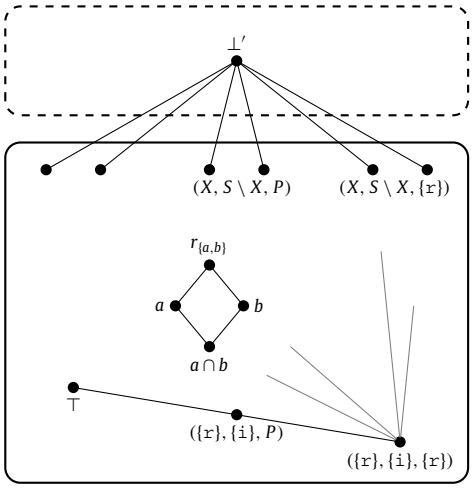

Fig. 2. A sketch of the lattice based on $\lessapprox$. The dotted box stands for the class of all trivial reactions. The solid box comprises $\mathrm{Rac}(S)$.

reaction $\bot'_S = (S \setminus \{\mathtt{i}\}, S \setminus \{\mathtt{r}\}, S)$ rather than $\bot = (S \setminus \{\mathtt{i}\}, S \setminus \{\mathtt{r}\}, \{\mathtt{r}\})$. Note that $\top = (\{\mathtt{r}\}, \{\mathtt{i}\}, S)$ is neither minimal nor maximal with S having at least three elements. Consistent with the product order, the greatest lower bound of reactions a and b equals the componentwise intersection $a \cap b = (R_a \cap R_b, I_a \cap I_b, P_a \cap P_b)$, even when either a or b (or both) are trivial (*i.e.* equals $\bot'_S$). Note that $a \cap b$ is nontrivial if either a or b is nontrivial, *cf.* Lemma 5.5. Dually, the least upper bound of a and b equals their componentwise union $a \cup b = (R_a \cup R_b, I_a \cup I_b, P_a \cup P_b) = r_{\{a,b\}}$, provided the pair $\{a, b\}$ is consistent. Otherwise the least upper bound equals $\bot'_S$. We summarize. (See Fig. 2.)

Theorem 7.7. *The set* $\mathrm{Rac}(S) \cup \{\bot'_S\}$*, with the en-cover relation* $\gtrapprox$*, forms a lattice.*

8. Discussion

In this paper we have been concerned with comparing the reactions of a reaction system in terms of resources and results. Next to the cover relation from [12], we have introduced two new order relations, *viz.* exact cover and enabling cover. The cover relation expresses the redundancy of one reaction in the context of another one, *i.e.* the covered reaction needs more resources (more reactants and more inhibitors) and produces nothing that the other reaction cannot produce as well. Exact cover expresses that the two reactions involved have the same products, but the covering reaction needs fewer resources (less reactants and less inhibitors) than the other one. Enabling cover on the other hand is based on the enabling equivalence from [8] and only compares two reactions when both are enabled. This implies in particular, that if a nontrivial reaction en-covers another nontrivial one, they form a consistent pair and hence can be combined into a nontrivial reaction. Moreover, the en-covered reaction needs less resources and produces nothing the other reaction cannot produce as well. Our investigations have led to a map of the landscape of nontrivial reactions over a given background set S. Each relation has been shown to be a partial order on $\mathrm{Rac}(S)$, the nontrivial reactions over S, that could be extended to a lattice by appropriate notions of meet and join, and adding top or bottom elements. Here having a concept of trivial reactions and universal elements has turned out to be convenient. The lattices show how $r_{\{a,b\}}$ the (nontrivial) reaction defined by a consistent set $\{a, b\}$ can be identified as both the greatest lower bound for a and b with respect to $\geq_e$ and the least upper bound for a and b with respect to $\gtrapprox_e$. With respect to the cover relation however, $r_{\{a,b\}}$ is in general incomparable with a and b (see Corollary 4.8).

Recall that in [8], it has been shown that functional equivalence and enabling equivalence are incomparable relations. Our results shed some additional light on the nature of their difference. It has been demonstrated how the enabling cover relation fills the gap between the cover relation and the exact cover relation. Furthermore, as discussed above and expressed in Theorem 3.9, the difference between $\{a, b\} \sim \{a\}$ ('a covers b') and $\{a, b\} \approx \{a\}$ ('a en-covers b') comes to light only in those states that do not enable both a and b. More precisely, by Theorem 7.5, $\{a, b\} \sim \{a\}$ and $\{a, b\} \approx \{a\}$ both hold if and only if a and b have the same enabling conditions ($R_a = R_b$ and $I_a = I_b$), and in addition $P_a \supseteq P_b$ holds. Thus, one could say that in case of the same enabling conditions of reactions a and b, functional equivalence of $\{a, b\}$ and a is a special case of (implies) enabling equivalence of $\{a, b\}$ and a.

The cover relation was introduced in [12] to determine the redundancy of reactions in reaction systems. In [9] this is taken further. There, it is investigated how reaction systems can be reduced to functional equivalent reaction systems that are minimal with respect to the number of resources per reaction. In [11] on the other hand, the relevance of entities is investigated. For this the concept of a *reduced* reaction system is introduced in which all reactions add something new to the results produced by other reactions in the system and no reaction is (strictly) covered by another reaction. It is

proved that for each reaction system, there exists a functionally equivalent reduced reaction system. In the proof of this result, the set of reactions of the reaction system under consideration is first extended with all reactions that can be added without affecting the system's result function. Next, all reactions that are not 'maximal' with respect to the cover relation are removed (*cf.* Corollary 4.5). In our future work, the partial orders studied in this paper could be useful to guide such processes of reducing or otherwise optimizing and modifying reaction systems by deleting or adding, splitting or combining reactions thus lowering or increasing the number of resources and/or the number of products. Clearly, deciding when and how to remove reactions that do not meet some optimization requirement, will depend on the goal, *e.g.* whether the aim is to obtain a new functionally equivalent or enabling equivalent set of reactions (or equivalent in a sense as discussed in the Introduction). Consistency and perhaps a dual relation (intersection consistency) may be interesting notions to further investigate in this context. Also, lifting the cover, exact cover and enabling cover relations from reactions to sets might prove useful.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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