Disconnection Rules are Complete for Chemical Reactions

Towards functorial chemistry

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21st International Colloquium on Theoretical Aspects of Computing, Bangkok, Thailand

27 November 2024

Outline

- Two perspectives on chemical processes:

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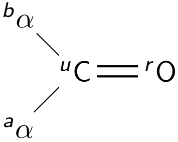
  2. **Disc** – local graph rewrites of chemical bonds
- There is a functor R : **Disc** $\rightarrow$ **React** which is faithful, and full up to an isomorphism

Chemical graphs

Molecular entities are represented by labelled graphs:

A



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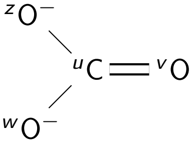

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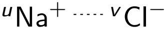
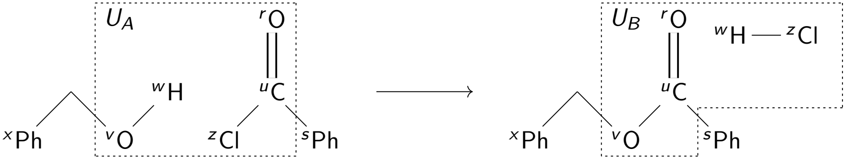
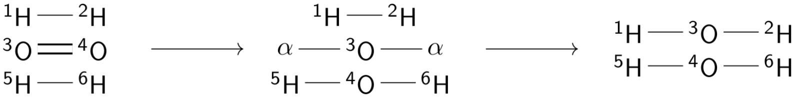


Reactions: Example

Formation of benzyl benzoate from benzoyl chloride and benzyl alcohol



Composition in **React**



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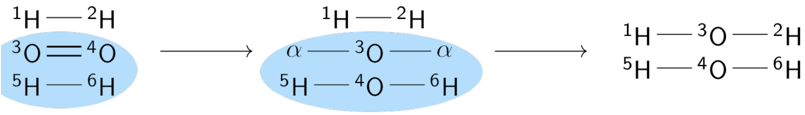

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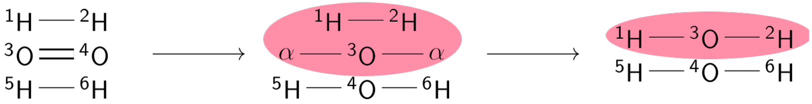

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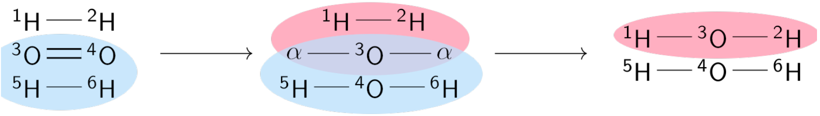

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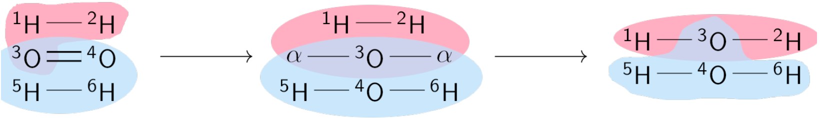

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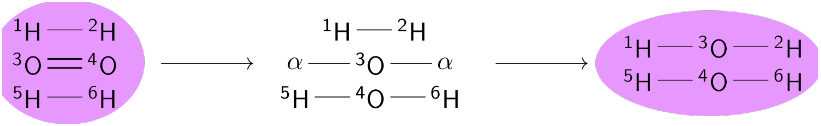
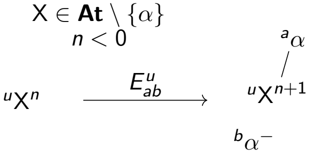
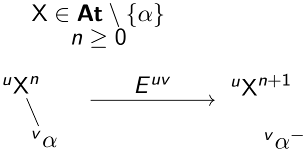


Disconnection rules

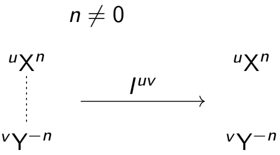
Motto: Chemical processes are movements of electrons



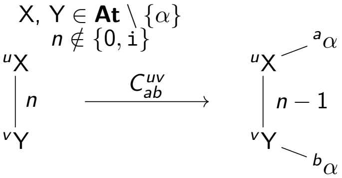
Electron detachment (negative charge)



Electron detachment (nonnegative charge)



Ionic bond breaking



Covalent bond breaking

Disconnection category: Terms

We define the set of terms with types:

- $\mathrm{id} : A \to A$,
- if $u \in V_A$, let $S^u : A \to A$,
- if $u \in \alpha(A)$ and $v \notin V_A \setminus \{u\}$, let $R^{u \mapsto v} : A \to A[v/u]$,
- $d^{uv}_{ab} : A \to d^{uv}_{ab}(A)$ and $\bar{d}^{uv}_{ab} : d^{uv}_{ab}(A) \to A$,
- if $\mathtt{t} : A \to B$ and $\mathtt{s} : B \to C$, then $\mathtt{t};\mathtt{s} : A \to C$.

Disconnection category: Equations

$$R^{u\mapsto z}; R^{z\mapsto w} \lesssim R^{u\mapsto w} \tag{1}$$
$$R^{u\mapsto z}; R^{v\mapsto w} \approx R^{v\mapsto w}; R^{u\mapsto z} \tag{2}$$
$$R^{u\mapsto u} \lesssim S^{u} \tag{3}$$
$$R^{b\mapsto z}; R^{a\mapsto b} \approx S^{b}; R^{a\mapsto z} \tag{4}$$
$$R^{u\mapsto v}; S^{w} \approx S^{w}; R^{u\mapsto v} \tag{5}$$
$$R^{u\mapsto v}; S^{v} \simeq S^{u}; R^{u\mapsto v} \simeq R^{u\mapsto v} \tag{6}$$

$$R^{u\mapsto v}; d_D^U \approx d_D^U; R^{u\mapsto v} \tag{7}$$
$$R^{u\mapsto v}; E^{wv} \simeq E^{wu}; R^{u\mapsto v} \tag{8}$$
$$d^U_{D[u]}; R^{u\mapsto v} \simeq d^U_{D[v/u]} \tag{9}$$
$$d^{U'}_{ij}; \bar{h}^U_{ab}; R^{i\mapsto c}; R^{j\mapsto d} \lesssim \bar{h}^U_{ab}; d^{U'}_{cd} \tag{10}$$

$$d^U_{ab}; \bar{d}^U_{cd} \approx S^U; R^{c\mapsto a}; R^{d\mapsto b} \tag{11}$$
$$d^U_{ab}; \bar{d}^U_{cb} \approx S^U; R^{c\mapsto a} \tag{12}$$
$$d^U_{ab}; \bar{d}^U_{ad} \approx S^U; R^{d\mapsto b} \tag{13}$$
$$d^U_D; \bar{d}^U_D \lesssim S^U \tag{14}$$
$$\bar{d}^U_D; d^U_D \lesssim S^U; S^D \tag{15}$$
$$E^{ua}; \bar{E}^{ub} \approx S^u; R^{a\mapsto z}; R^{b\mapsto a}; R^{z\mapsto b} \tag{16}$$
$$\bar{d}^{uv}; d^{wz} \approx d^{wz}; \bar{d}^{uv} \tag{17}$$

$$S^u; S^v \simeq S^v; S^u \tag{18}$$
$$S^u; S^u \simeq S^u \tag{19}$$
$$S^u; d^U_D \lesssim d^U_D; S^u \tag{20}$$
$$d^{U[v]}_D; S^v \simeq d^{U[v]}_D \tag{21}$$
$$C^{uv}_{ab} \simeq C^{vu}_{ba} \tag{22}$$

$$d^U_D; d^{U'}_{D'} \simeq d^{U'}_{D'}; d^U_D \tag{23}$$
$$C^{uv}_{ab}; I^{wz} \simeq I^{wz}; C^{uv}_{ab} \tag{24}$$
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$$\bar{E}^{uv}; I^{wz} \lesssim I^{wz}; \bar{E}^{uv} \tag{27}$$
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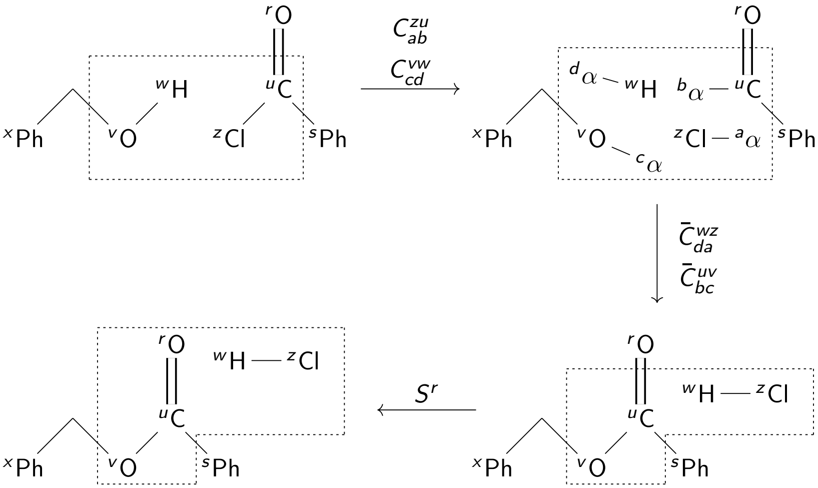
$$E^u_{ab}; C^{wz}_{cd} \simeq C^{wz}_{cd}; E^u_{ab} \tag{30}$$
$$E^{uv}; C^{wz}_{cd} \lesssim C^{wz}_{cd}; E^{uv} \tag{31}$$
$$\bar{E}^{uv}; C^{wz}_{cd} \simeq C^{wz}_{cd}; \bar{E}^{uv} \tag{32}$$
$$E^{uv}; E^w_{cd} \lesssim E^w_{cd}; E^{uv} \tag{33}$$
$$\bar{E}^{uv}; E^w_{cd} \simeq E^w_{cd}; \bar{E}^{uv} \tag{34}$$

From disconnections to reactions

Define the translation $R : \textbf{Disc} \to \textbf{React}$ by

- $R(\mathrm{id}_A) := (\varnothing, \varnothing)$,
- $R\left(S^u\right) := (\{u\}, \{u\})$,
- $R\left(R^{u \mapsto v}\right) := (\{u\}, \{v\})$,
- $R(d^U_D) := (U, U \cup D)$,
- $R\left(\bar{d}^{uv}_{ab}\right) := \overline{R\left(d^{uv}_{ab}\right)}$,
- $R(\mathtt{t}; \mathtt{s}) := R(\mathtt{t}); R(\mathtt{s})$.

From disconnections to reactions: Example



Soundness, completeness, universality

Proposition (Soundness)

R : **Disc** $\to$ **React** *is a dagger functor.*

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Theorem (Completeness)

*R : **Disc** $\to$ **React** is faithful: for any terms $\mathtt{t}, \mathtt{s}$ we have $R(\mathtt{t}) = R(\mathtt{s})$ in **React** if and only if $\mathtt{t} = \mathtt{s}$ in **Disc**.*

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Theorem (Universality)

*Given a reaction $r : A \to C$ in **React**, there is a term $\mathtt{t} : A \to B$ in **Disc** and an isomorphism $\iota : B \xrightarrow{\sim} C$ in **React** such that $R(\mathtt{t}); \iota = r$.*

Example

The reaction we saw (formation of benzyl benzoate from benzoyl chloride and benzyl alcohol) decomposes into:

$$C^{zu}_{ab}; C^{vw}_{cd}; C^{ru}_{ij}; C^{ru}_{nm}; E^{vc}; E^{wd}; E^{za}; E^{ub}; E^{ri}; E^{uj}; E^{rn}; E^{um};$$
$$\bar{E}^{vc}; \bar{E}^{wd}; \bar{E}^{za}; \bar{E}^{ub}; \bar{E}^{ri}; \bar{E}^{uj}; \bar{E}^{rn}; \bar{E}^{um}; \bar{C}^{ru}_{ij}; \bar{C}^{ru}_{nm}; \bar{C}^{wz}_{da}; \bar{C}^{uv}_{bc};$$
$$S^{z}; S^{u}; S^{v}; S^{w}; S^{r},$$

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$$S^{z}; S^{u}; S^{v}; S^{w}; S^{r},$$

which is equal to:

$$C^{zu}_{ab}; C^{vw}_{cd}; \bar{C}^{wz}_{da}; \bar{C}^{uv}_{bc}; S^{r}.$$

Future work

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Mathematical questions:

- What is the categorical structure of **React** and **Disc**?
- Monoidal structure?

References

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Thank you for your attention!

Reactions

The category **React** is defined as:

- objects: chemical graphs
- morphisms $A \to B$: tuples (U_A, U_B, b, i), where
  - $U_A \subseteq V_A$ and $U_B \subseteq V_B$ with $\mathtt{Net}\,(U_A) = \mathtt{Net}\,(U_B)$
  - $b : \mathtt{Chem}\,(U_A) \to \mathtt{Chem}\,(U_B)$ is a bijection preserving the atoms
  - $i : V_A \setminus U_A \to V_B \setminus U_B$ is an isomorphism

  such that for all $u \in \mathtt{Chem}\,(U_A)$ and $a \in V_A \setminus U_A$ we have

$$m_A(u, a) = m_B(bu, ia)$$

- the composition of $(U_A, U_B, b, i) : A \to B$ and $(W_B, W_C, c, j) : B \to C$ is

$$(Z_A, Z_C, (c + j)(b + i), ji) : A \to C$$

  where $Z_A := U_A \cup i^{-1}(W_B \setminus U_B)$ and $Z_C := W_C \cup j(U_B \setminus W_B)$
- the identity on A: $(\varnothing, \varnothing, !, \mathrm{id}_A)$

Proof ideas

Completeness

1. Show that every term is equal to the form

$$\mathtt{I}; \mathtt{C}; \mathtt{E}^{<0}; \mathtt{E}^{\geq 0}; \bar{\mathtt{E}}^{\geq 0}; \bar{\mathtt{E}}^{<0}; \bar{\mathtt{C}}; \bar{\mathtt{I}}; \mathtt{R}; \mathtt{S}$$

2. Under certain conditions, such normal form is unique
3. Show that if $R(\mathtt{t}) = R(\mathtt{s})$, then $\mathtt{t}$ and $\mathtt{s}$ have the same normal form

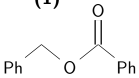
Universality

1. Every reaction $r : A \to B$ factorises as $(\varnothing, \varnothing, !, \iota) \circ (A, B, \mathrm{id}, \mathrm{id})$
2. Keep applying disconnections to A until there is nothing to disconnect
3. Apply connections to obtain B: preservation of atoms and charge guarantees that this can always be done

Retrosynthetic analysis

(1) Start with the target molecule(s)

(1)



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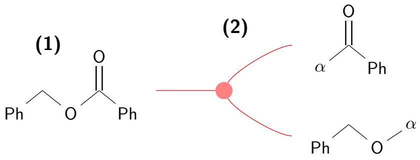

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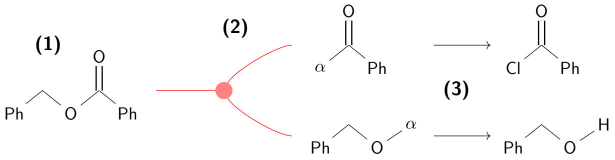

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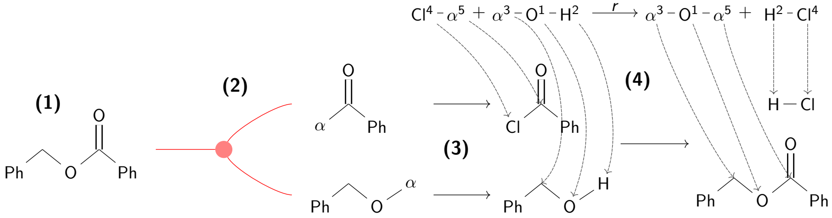

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(5) Check whether the synthetic equivalents are known molecules: if yes, terminate, if no, return to **(1)** taking them as the target