Autocatalysis

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What is autocatalysis?

Definition†: autocatalytic reaction

A chemical reaction in which a product (or a reaction intermediate) also **functions as a catalyst**. In such a reaction the observed rate of reaction is often found to increase with time from its initial value.

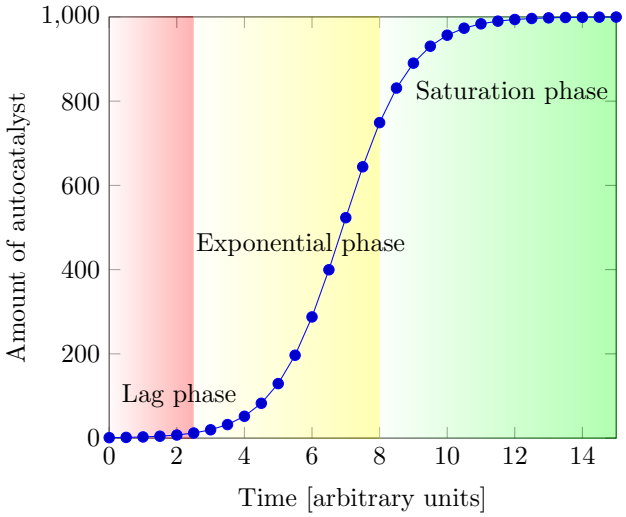
$$\mathrm{F} \xrightarrow{\mathrm{X}} \mathrm{X} \qquad \text{chemical equation}$$

$$\mathrm{F} \longrightarrow \mathrm{X} \qquad \text{uncatalyzed pathway}$$

$$\mathrm{X} + \mathrm{F} \longrightarrow 2{\cdot}\mathrm{X} \qquad \text{catalysed pathway}$$

$$\frac{\mathrm{d}[X]}{\mathrm{d}t} = f(X,F)\cdot[X]^n + g(F)$$

$$\underbrace{f(X,F)\cdot[X]^n}_{\text{catalyzed}} \gg \underbrace{g(F)}_{\text{uncatalysed}} \qquad n > 0$$



† taken from the IUPAC Gold Book

Formal Autocatalysis

Definition: formal autocatalysis

Every chemical process with an overall reaction

$$(\mathrm{F}) + \mathrm{m}\cdot\mathrm{X} \longrightarrow \mathrm{n}\cdot\mathrm{X} + (\mathrm{W})$$

with $n > m > 0$ is autocatalytic.

Counterexamples:

1. Paralell Pathways

$$\begin{array}{ll} (1)\ \mathrm{A} + \mathrm{X} \longrightarrow & \mathrm{X} + \mathrm{U} \\ (2)\ \mathrm{B} \longrightarrow & \mathrm{X} + \mathrm{V} \\ \hline (3)\ \mathrm{F} + \mathrm{X} \longrightarrow & 2\cdot\mathrm{X} + \mathrm{W} \end{array}$$

(1) does not contribute to the production of X
only sharing of X no feedback!

2. Degradation pathways

$$\begin{array}{ll} (4)\ \mathrm{A} \longrightarrow & 2\cdot\mathrm{X} + \mathrm{U} \\ (5)\ \mathrm{X} \longrightarrow & + \mathrm{V} \\ \hline (6)\ \mathrm{F} + \mathrm{X} \longrightarrow & 2\cdot\mathrm{X} + \mathrm{W} \end{array}$$

(5) does not contribute to the production of X
only sharing of X no feedback!

Formal autocatalysis is a very weak concept, and lacks a condition that ties the pathways more closely together!

Exclusive Autocatalysis

Can the notion of formal autocatalysis be fixed?

Definition: exclusive autocatalysis

A species X is exclusive autocatalytic if

1. X is formally autocatalytic.
2. X cannot be produced in a non-autocatalytic manner.

In other words, X cannot be produced from the food set F, unless a minute amount of X is already present at the outset.

Exclusice autocatalysis matches the intuition of autocatalysis.

Fixes the problems observed for formal autocatalysis.

Exclusive autocatalysis is a very strict concept, and discards cases which are consider to be autocatalytic.

Easy to find computationally.

2 boils down to a simple reachability question on a reaction network, $X \notin cl(F\backslash\{X\}, R)$ with R the set of reactions and F the set of food molecules; $cl()$ is the closure operation.

What is a catalyst?

Three reactions with the same net balance.

$$\mathrm{F} \rightleftharpoons \mathrm{X} \qquad \text{uncatalyzed}$$

$$\mathrm{E} + \mathrm{F} \rightleftharpoons \mathrm{X} + \mathrm{E} \qquad \text{catalysed (by E, amount constant)}$$

$$\mathrm{X} + \mathrm{F} \rightleftharpoons 2{\cdot}\mathrm{X} \qquad \text{catalysed (by X, amount increases)}$$

Criteria for a substance to qualify as catalyst:

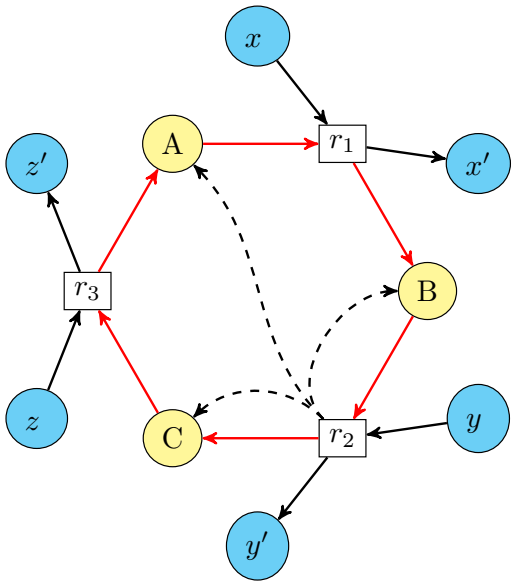
1. stoichiometric (reactant and product in catalysed reaction).
2. kinetic (rate acceleration, catalysed *vs* spontanious process).
3. thermodynamic (unaltered ΔG).

Criterium 1 is necessary but not sufficent to characterize (auto)catalysis (rate acceleration!), but may be used to find potential (auto)catalysts.

(Auto)Catalyst as Sets

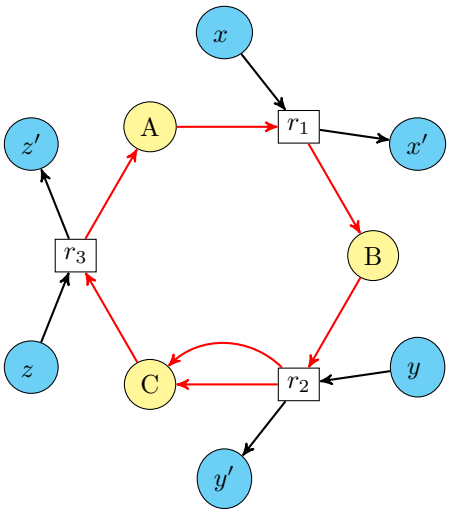
$$\mathrm{x} + \mathrm{y} + \mathrm{z} \overset{\{\mathrm{A,B,C}\}}{\rightleftharpoons} \mathrm{x}' + \mathrm{y}' + \mathrm{z}'$$

1. Rate acceleration: $r_1 - r_3$ must together proceed faster than the spontanious process.
2. Set of catalysts is conserved.
3. Each reaction involve:
   - catalysts.
   - at least 1 catalyst as reactant.
   - at least 1 catalysts as product.
4. The production of a species from the set of catalysts depends on the presence of another species from the set of catalysts.



In case of catalysis, pretend the dashed arrows are not there. 3 + 4 induce the presence of a cycle. Species ● show turnover, species ○ remain conserved.

The stoichiometric matrix S



	r_1	r_2	r_3
x	-1	0	0
x'	1	0	0
y	0	-1	0
y'	0	1	0
z	0	0	0
z'	0	0	0
A	-1	0	1
B	1	-1	0
C	0	2	-1

$$\mathrm{x} + \mathrm{A} \xrightarrow{r_1} \mathrm{B} + \mathrm{x}'$$
$$\mathrm{y} + \mathrm{B} \xrightarrow{r_2} \mathrm{C} + \mathrm{y}'$$
$$\mathrm{z} + \mathrm{C} \xrightarrow{r_3} \mathrm{A} + \mathrm{z}'$$

Note that a catalyst, which enters and exits a reaction with the same stoichiometry, has also well a zero entry in S. The yellow highlighted region is a restriction of the S to the autocatalytic cycle. The species in the cyan region are considered externl to the autocatalytic cycle, and are thought to be chemo-stated.

Autocatalytic cycle: Linear Algebra View

Definition: autocatalytic cycle

A set of species M and a set of reactions R form an autocatalytic cycle if:

1. R contains no reversible pair of reactions.
2. Every $m \in M$ is educt in one, and product in another reaction.
3. Every $r \in R$ has at least 1 educt and 1 product in M.
4. $\exists$ a strict positive integer vector w such that $S \cdot w > 0$.
5. w is minimal.

❷ +❸ restrics M to consists only of species that are catalytic or autocatalytic arranged in a cycle.

❹ states that all entries of the resul vector are non-negative, and at least 1 entry (the produced produced species) is strictly positive.

❺ expresses that no smaller autocatalytic cycle can be constructed by removing a species from M.

Minimal Autocatalytic Cycles

The previous definition translates into the following constrains for S to represent an autocatalytic cycle:

1. S must be a square matrix.
2. S must be invertible.
3. All diagonal entries of S must be negative.
4. All off-diagonal entries of S must be either zero or positive.

Enumeration results in 5 matrices (autocatalytic cores)

-1	2
1	-1

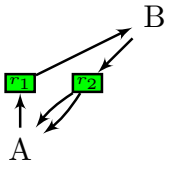
-1	1	0
1	-1	1
1	0	-1

-1	1	1
1	-1	0
1	0	-1

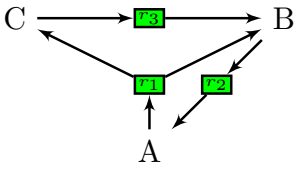
-1	1	0
1	-1	1
1	1	-1

-1	1	1
1	-1	1
1	1	-1

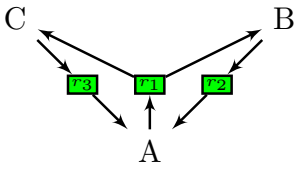
Incidence Graphs of Autocatalytic Cores



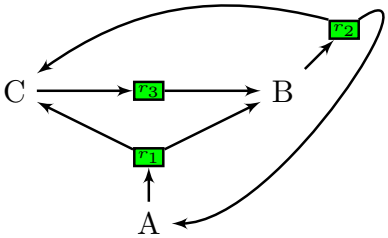
type 1



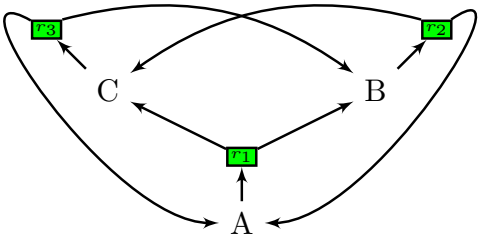
type 2



type 3



type 4



type 5

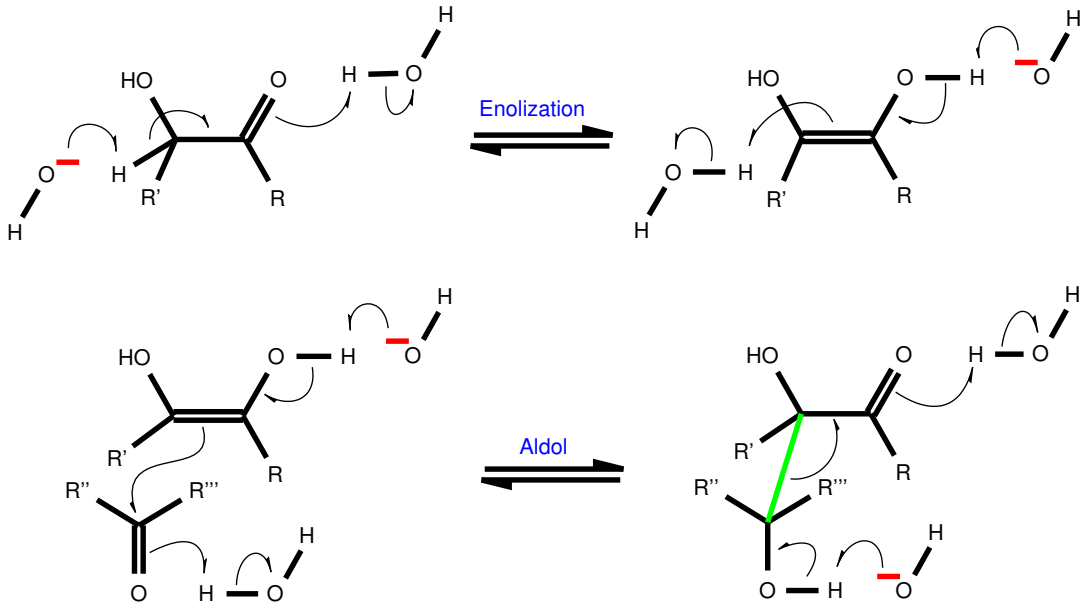
The autocatalytic cores [Blokhuis et al 2020], differ in the number of forks, reactions that split a single educt into two products. Type 1 to type 3 has 1 fork (r_1), type 4 has 2 forks (r_1, r_2) and type 5 has 3 forks (r_1, r_2, r_3).

Primer: Carbohydrate Chemistry $(CH_2O)_n$

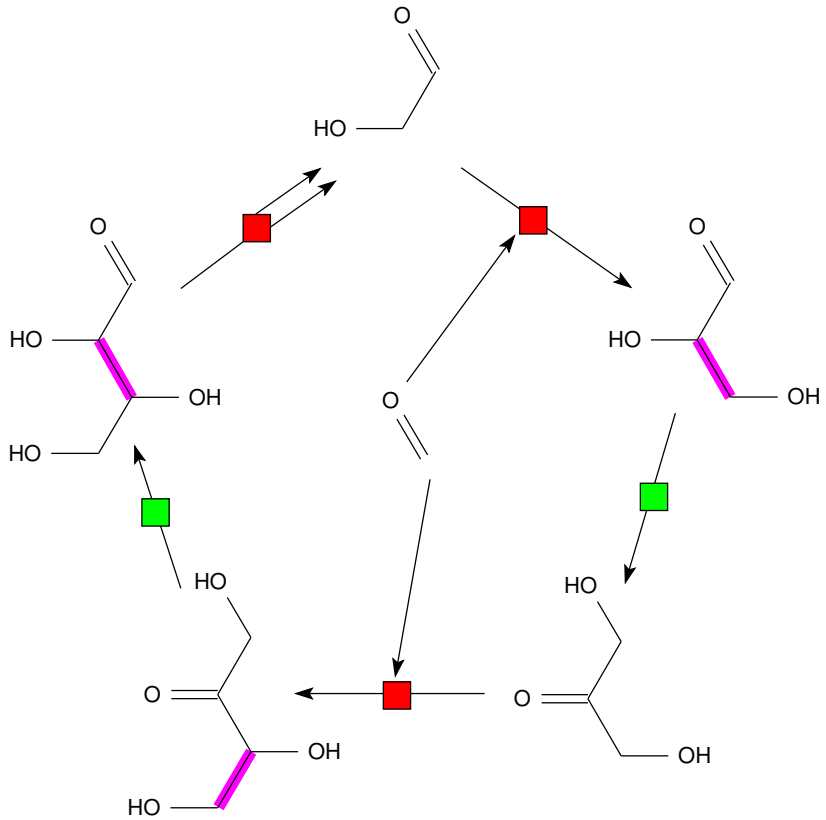
Sugars are organic compounds with an C:H:O ratio of 1:2:1.

The reactivity of sugars is largely dominated by the carbonyl group ($C=O$) and the vicinal alcohol groups ($HO-C-C-OH$).

The keto-enol isomerization reaction and the aldol condensation a $C-C$ bond formation reaction are of importance.

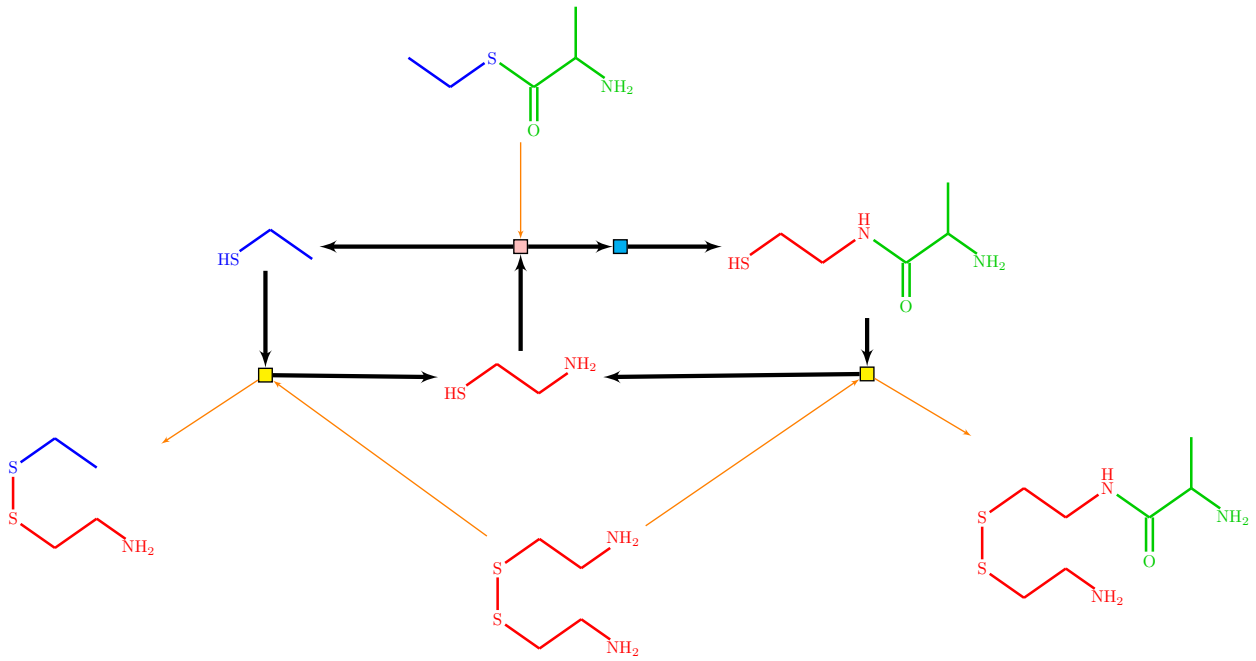


Formose Process



Type 1 autocatalytic core; ■ keto-enole isomerization, ■ Aldol / retro-Aldol reaction. Note that the reaction sequence from glycolealdehyde to erytrose is compressed into a single reaction (r_1) in the type 1 autocatalytic core figure. Butlerov AM (1861), Einiges über die chemische Structur der Körper, *Zeitschrift für Chemie* **4**:549-560;

Amino acid thioesters, cystamine autocatalytic system



Type 3 autocatalytic core; The reaction chemistry is thiol-disulfide exchange ■, thiol-thioester exchange ■ and native chemical ligation ■; orange arrows connect food or wast molecules to the autocatalytic cycle, which has a type 3 topology; cystamine (in the center) is the "autocatalyst"; [Semenov et al Nature 2016]

Further reading

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