

Bond Graph Clinic: Part 3

Biomolecular Systems

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Introduction

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Chemical Reactions

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Stoichiometry

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Conclusion

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References

Introduction

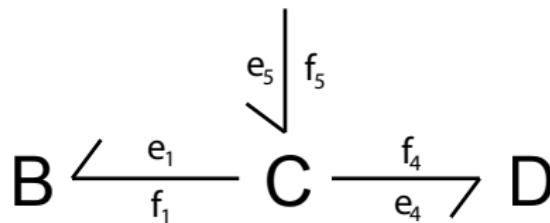
Chemical Reactions

Stoichiometry

Conclusion

Previously...

Network models of energetic systems



Bond Graphs capture:

- ▶ Energy transferred between B, C, D without loss via bonds.
- ▶ Power transfer represented by conjugate variables $P_i = e_i f_i$.
- ▶ Subsystem dynamics via constitutive relations $\Phi_B(e, f) = 0$

We've also looked at some examples.

Previously...

A Mathematicians Model of a Chemical System

A naive description of molecular systems is as follows:

1. A set of distinct quanta (molecules, complexes, atoms and free electrons) A, B, \dots move stochastically through a volume.
2. When A, B are sufficiently close they may bind to form complex C .
3. After some time τ , C may disassociate into a number of quanta E, \dots

All basic reaction types (synthesis, decomposition and replacement) can be represented in this way.

Clearly this is an example of a *reaction-diffusion* process.

This Clinic

Today we shall consider *reactions*.

Next clinic will consider *diffusion*.

Spatial Assumptions

Consider chemical reactions inside some vessel of fixed volume.

We assume that the chemical solution is well mixed, ie:

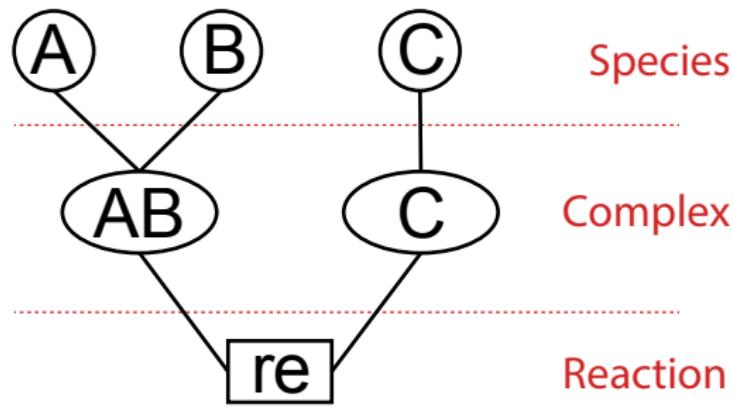
- ▶ The solution is actively stirred or,
- ▶ the diffusion rate across the volume is orders of magnitude faster than the fastest reaction rate.

This basically means we can work with average concentration, and ignore spatial effects inside the vessel.

Later, we will couple many vessels together to represent diffusion.

Chemical Reaction Networks

Chemical Reaction Network: Petri Net

Figure: Petri net of $A + B \rightleftharpoons C$

Chemical Reaction Network: Bond Graph

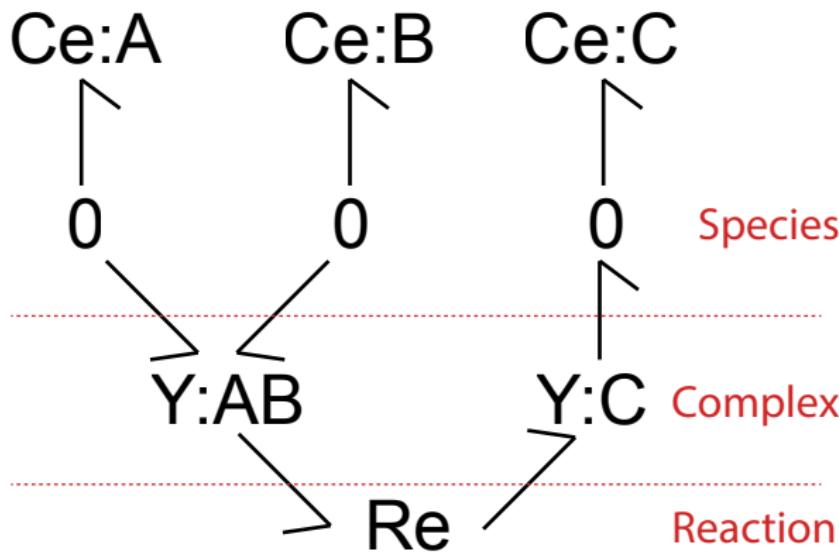


Figure: Bond Graph of $A + B \rightleftharpoons C$

Thermodynamic Assumptions

Consider chemical reactions inside some vessel of fixed volume. We assume that the solution is *isobaric* and *isothermal*. These assumptions allow us to define the chemical potential

$$\mu_A = \mu_A^\ominus + RT \ln \frac{x_A}{V_m}$$

- ▶ $R = N_A k_b \approx 8.314$ is the gas constant in $\text{JK}^{-1} \text{mol}^{-1}$
- ▶ $T \approx 300$ is temperature (in K)
- ▶ μ_A^\ominus is the chemical potential of a pure solution of A in J
- ▶ x_A the amount of species A in mol.
- ▶ V_m is volume of the solution in mol

This follows from the *Ideal Gas Law* and the *Fundamental Equation of Thermodynamics*.

Thermodynamic Assumptions

Consider chemical reactions inside some vessel of fixed volume.
We assume that the solution is *isobaric* and *isothermal*. These assumptions allow us to define the chemical potential

$$\mu_A = \mu_A^\emptyset + RT \ln \frac{x_A}{V_m}$$

$$\text{Energy} = x_A \cdot \mu_A \text{J}$$

$$\text{Power} = \dot{x}_A \cdot \mu_A \text{ Js}^{-1}$$

μ_A is *effort* or force-like

\dot{x}_A is the *flow* or flux-like.

Thermodynamic Assumptions

Consider chemical reactions inside some vessel of fixed volume. We assume that the solution is *isobaric* and *isothermal*. These assumptions allow us to define the chemical potential

$$\mu_A = \mu_A^\ominus + RT \ln \frac{x_A}{V_m}$$

Recall x_A is the molar amount of species A .

Question:

What happens to μ_A when $x_A \rightarrow 0$ but V_m is constant?
When might this occur and is this physical?

Components

Ce Constitutive Relation

$$\frac{e}{f} \nearrow \text{Ce}$$

Constitutive Relation for a Chemical Species:

$$\Phi_{\text{Ce}}(e, f) = e - \beta \ln kq = 0$$

Ce Constitutive Relation

$$\frac{e}{f} \nearrow \text{Ce}$$

Constitutive Relation for a Chemical Species:

$$\Phi_{\text{Ce}}(e, f) = e - \beta \ln kq = 0$$

This follows from substituting the parameters

$$k = \exp(\mu_A^\emptyset / RT) / V_m, \quad \beta = RT$$

and the state variables $\mu_A = e$, $\dot{x}_A = f$ and $x_A = q = q_0 + \int_0^t f dt$ into

$$\mu_A = \mu_A^\emptyset + RT \ln \frac{x_A}{V_m}.$$

Ce Constitutive Relation

$$\frac{e}{f} \nearrow \text{Ce}$$

Constitutive Relation for a Chemical Species:

$$\Phi_{\text{Ce}}(e, f) = e - \beta \ln kq = 0$$

$$\beta = RT, \quad k = \exp(\mu_A^\circ / \beta) / V_m$$

It will often be convenient for us to take $\beta = 1$

Chemical Kinetics

Reactions proceed according to the *Marcelin-de Donder* formula

$$v = \kappa \left(e^{A^f/RT} - e^{A^r/RT} \right)$$

Here:

- ▶ v is the reaction velocity or molar flow
- ▶ A^f, A^r are the forward and reverse chemical affinities
- ▶ κ is the reaction rate constant.
- ▶ R, T is the gas constant and temperature respectively.

Chemical Kinetics

Reactions proceed according to the *Marcelin-de Donder* formula

$$v = \kappa \left(e^{A^f/RT} - e^{A^r/RT} \right)$$

The mass flow in is v , hence the mass flow out is $-v$.

So

$$f_1 = v, \quad f_2 = -v$$

are natural *flow* variables.

Chemical Kinetics

Reactions proceed according to the *Marcelin-de Donder* formula

$$v = \kappa \left(e^{A^f/RT} - e^{A^r/RT} \right)$$

For a chemical reaction $\nu_A^f A + \nu_B^f B + \dots \rightleftharpoons \nu_A^r A + \nu_B^r B + \dots$ with forward and reverse stoichiometric coefficients ν^f and ν^r .

The forward (and similarly reverse) affinity is defined as

$$A^f = \nu_A^f \mu_A + \nu_B^f \mu_B + \dots$$

So the natural effort variables are

$$e_1 = A^f, \quad e_2 = A^r.$$

Re Constitutive Relation

$$\frac{e_1}{f_1} \nearrow \text{Re}_\kappa \swarrow \frac{f_2}{e_2}$$

Constitutive Relation for a reaction component:

$$\Phi_{Re}(\mathbf{e}, \mathbf{f}) = \left(\frac{\kappa[\exp(e_1/\beta) - \exp(e_2/\beta)] - f_1}{f_1 + f_2} \right) = 0$$

Where again $\beta = RT$ is often taken as $\beta = 1$.

Re Constitutive Relation

$$\frac{e_1}{f_1} \nearrow \text{Re}_\kappa \swarrow \frac{f_2}{e_2}$$

Constitutive Relation for a reaction component:

$$\Phi_{Re}(\mathbf{e}, \mathbf{f}) = \left(\frac{\kappa[\exp(e_1/\beta) - \exp(e_2/\beta)] - f_1}{f_1 + f_2} \right) = 0$$

This follows directly from the Marcelin-de Donder formula.

Putting it together



The above bond graph describes the reaction $A \rightleftharpoons B$.

$$\Phi_{\text{Ce}:A} = e_1 - \ln k_A \left[q_A(0) + \int (-f_1) dt \right] \quad (1)$$

$$\Phi_{\text{Re}}(\mathbf{e}, \mathbf{f}) = \left(\frac{\kappa [e^{e_1} - e^{e_2}] - f_1}{f_1 + (-f_2)} \right) \quad (3)$$

$$\Phi_{\text{Ce}:B} = e_2 - \ln k_B \left[q_B(0) + \int f_2 dt \right] \quad (2)$$

Recall that $q(t) = q_0 + \int_0^t f(t) dt$. So define

$$\dot{x}_A = \dot{q}_1 = -f_1 \quad \Rightarrow \quad q_1 = q_A(0) - \int_0^t f_1 dt \quad \Rightarrow \quad e^{e_1} = k_A q_1,$$

$$\dot{x}_B = \dot{q}_2 = f_2 \quad \Rightarrow \quad q_2 = q_B(0) + \int_0^t f_2 dt \quad \Rightarrow \quad e^{e_2} = k_B q_2.$$

The second line of (3) gives $f_1 = f_2$ which implies $-\dot{q}_1 = \dot{q}_2$, and the first gives the result

$$\dot{q}_1 = -\kappa (k_A q_1 - k_B q_2) = k_- q_2 - k_+ q_1 \quad \text{where} \quad k_+ = \kappa k_A, \quad k_- = \kappa k_B.$$

Complexes

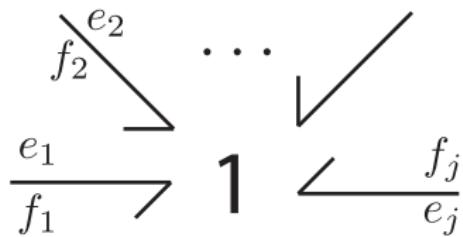
The reaction $A + B \rightleftharpoons C$ can be thought of

1. A and B collide forming a complex AB .
2. AB reacts to form C .

Clearly, the flow of A and the flow of B into this reaction are equal.

Hence, we *should* be able to represent the AB complex as a equal flow junction, and allow the reaction to drive what that flow is.

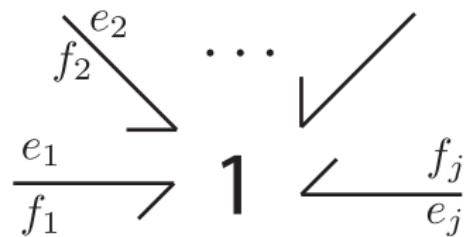
Revisiting the '1' junction



In clinic 2 we introduced the '1' junction and argued that its constitutive relation is given by

$$\Phi_1 = \begin{pmatrix} f_1 - f_2 \\ \cdots \\ f_{j-1} - f_j \\ e_1 + e_2 + \dots + e_j \end{pmatrix} = 0$$

Revisiting the '1' junction



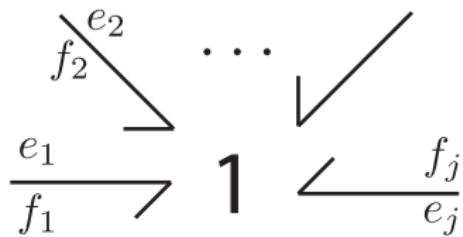
Alternatively

$$f_i = f_j \quad \forall i, j$$

and

$$\sum_i e_i = 0$$

Revisiting the '1' junction



Alternatively

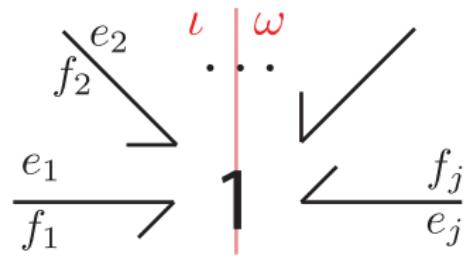
$$f_i = f_j \quad \forall i, j$$

and

$$\sum_i e_i = 0$$

This deviates from the literature and may cause problems (thanks to Peter Gauthrop for pointing this out.).

Revisiting the '1' junction

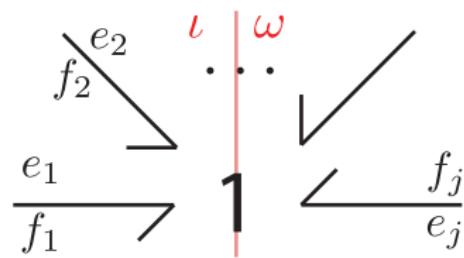


To fix this, we must instead think of the 1 junction as having two ends (call the sets ι and ω) so that all flows at ι are equal, all flows at ω are equal, and any flow at ω is in the opposite direction to any other at ι .

We can then define:

$$\sigma_k = \begin{cases} 1 & \text{if } k \in \iota, \\ -1 & \text{if } k \in \omega. \end{cases}$$

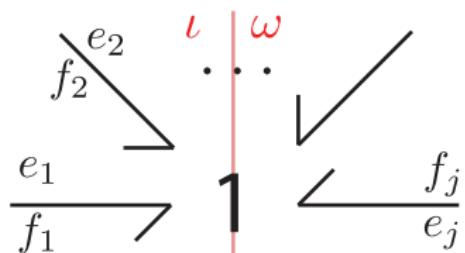
Revisiting the '1' junction



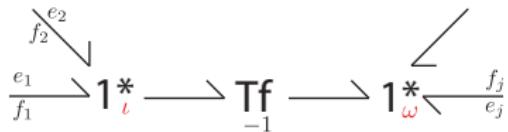
The redefined constitutive relation then becomes

$$\Phi_1 = \begin{pmatrix} \sigma_1 f_1 - \sigma_2 f_2 \\ \dots \\ \sigma_{j-1} f_{j-1} - \sigma_j f_j \\ \sum_{k=1}^j \sigma_k e_k \end{pmatrix} = 0, \quad \sigma_k = \begin{cases} 1 & \text{if } k \in \iota, \\ -1 & \text{if } k \in \omega. \end{cases}$$

Revisiting the '1' junction

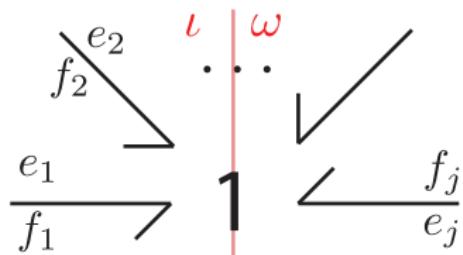


This is equivalent to the following bond graph



Where $\Phi_{1^*} = \begin{pmatrix} f_1 - f_2 \\ \dots \\ f_{j-1} - f_j \\ e_1 + e_2 + \dots + e_j \end{pmatrix}$ as before.

Revisiting the '1' junction



The relations can be simplified by associating the direction of a connecting bond with σ , ie; bond pointing out implies $\sigma = -1$.

$$\Phi_1 = \begin{pmatrix} \sigma_1 f_1 - \sigma_2 f_2 \\ \dots \\ \sigma_{j-1} f_{j-1} - \sigma_j f_j \\ \sum_{k=1}^j \sigma_k e_k \end{pmatrix} = 0, \quad \sigma_k = \begin{cases} 1 & \text{if connecting bond points in,} \\ -1 & \text{if connecting bond points out.} \end{cases}$$

This is standard practice, but this means that the 1 component needs to know what it's connected to.

Reaction Bond Graphs

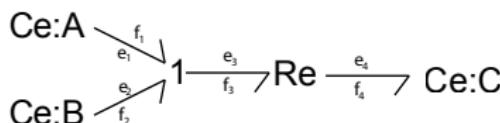


Figure: Bond Graph of $A + B \rightleftharpoons C$

$$\Phi_{Ce:A} = e_1 - \ln k_A(q_1), \quad (4)$$

$$\Phi_{Re} = \left(\frac{\kappa [e^{e_3} - e^{e_4}] - f_3}{f_3 + (-f_4)} \right), \quad (7)$$

$$\Phi_{Ce:B} = e_2 - \ln k_B(q_2), \quad (5)$$

$$\Phi_1 = \begin{pmatrix} e_1 + e_2 - e_3 \\ f_1 - f_3 \\ f_2 - f_3 \end{pmatrix} \quad (8)$$

$$\Phi_{Ce:B} = e_2 - \ln k_C(q_3) \quad (6)$$

Clearly

$$e_3 = e_1 + e_2 \implies \exp(e_3) = \exp(\ln k_A q_1 + \ln k_B q_2) = k_A k_B q_1 q_2.$$

Since $f_4 = q_4$, it follows from (12) that

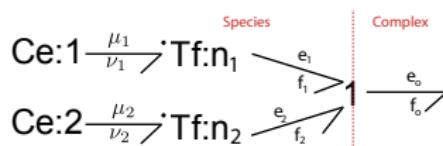
$$\dot{q}_4 = \kappa k_A k_B q_1 q_2 - \kappa k_C q_4 = k_+ q_1 q_2 - k_- q_4.$$

From (12) and (13) we have $\dot{q}_4 = f_4 = f_3 = f_2 = f_1$.

Combining this with $f_1 = -\dot{q}_1$ and $f_2 = -\dot{q}_2$ completes the picture.

Stoichiometric Coefficients

Transformers can be used to introduce stoichiometry (see [1] and [2])



Here n_1 and n_2 represent the stoichiometric coefficient, and the \circ on identifies the transformer primary winding.

Hence, the reaction forward affinity is given by

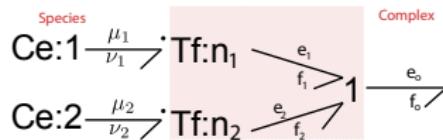
$$e_o = n_1 \mu_1 + n_2 \mu_2$$

and the flow rates

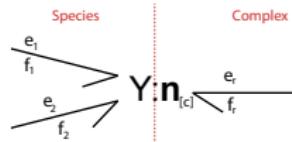
$$\nu_1 = n_1 f_0, \quad \nu_2 = n_2 f_0$$

are in terms of the reaction flow f_0 as expected.

Complexes

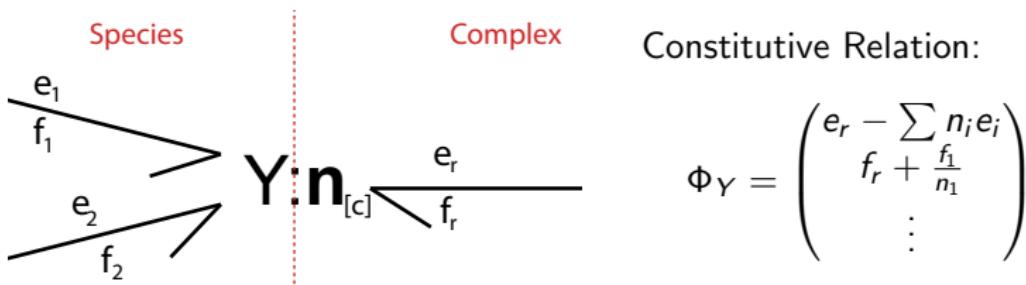


can be replaced by



Where \mathbf{n} is the forward or reverse (truncated) stoichiometric vector which in this case $\mathbf{n} = (n_1, n_2)$. Here $[c]$ identifies which port is associated with the complex.

Complexes II



Y is power conserving. Multiplying the top line by f_r gives

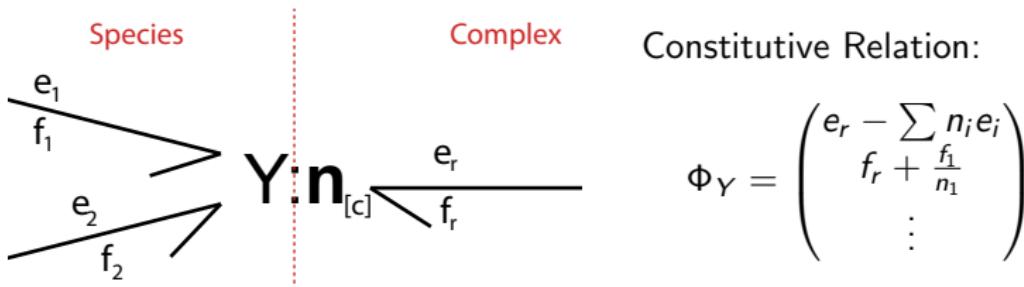
$$0 = e_r f_r - f_r \sum e_i n_i = e_r f_r - \sum e_i (n_i f_r)$$

Since $n_i f_r = -f_i$, the result follows from

$$0 = e_r f_r - \sum e_i (n_i f_r) = e_r f_r + \sum e_i f_i.$$

This is no surprise as Y is built from conserving components.

Complexes II



The through junction Y

- ▶ is power conserving,
- ▶ is unambiguous,
- ▶ is symbolically consistent,
- ▶ maps cleanly on existing C.R.N. theory.

Reaction Bond Graphs

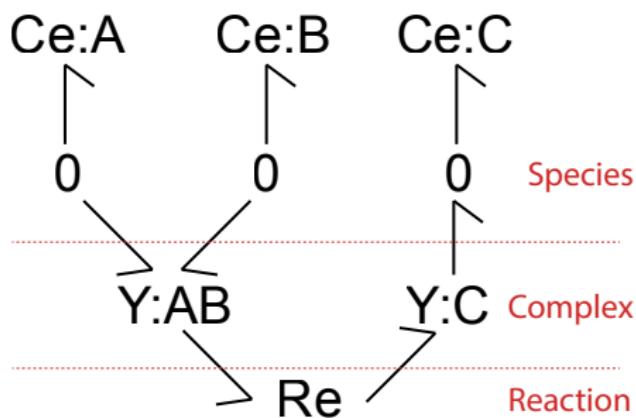
$$A + B \rightleftharpoons C: \text{ final form!}$$


Figure: Bond Graph of $A + B \rightleftharpoons C$

In the above figure we have added standard 0 junctions. While this is redundant in this above reaction, it allows us to use the same species for many reactions. Also, note that Y:C is the identity (*prove it!*) and may be omitted.

In Review

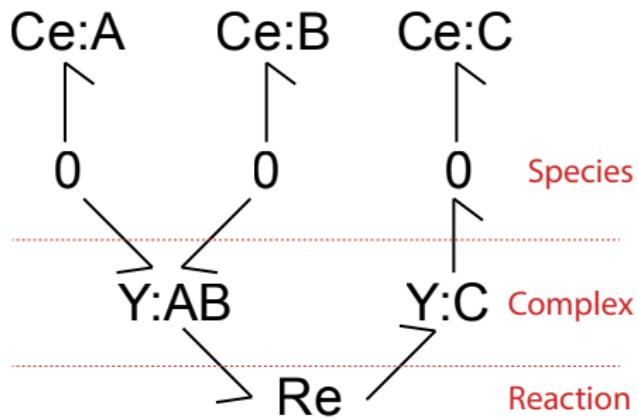


Figure: Bond Graph of $A + B \rightleftharpoons C$

The Ce is a one port component representing a store of a particular chemical species and has a constitutive relation that captures the usual definition of *chemical potential energy*.

In Review

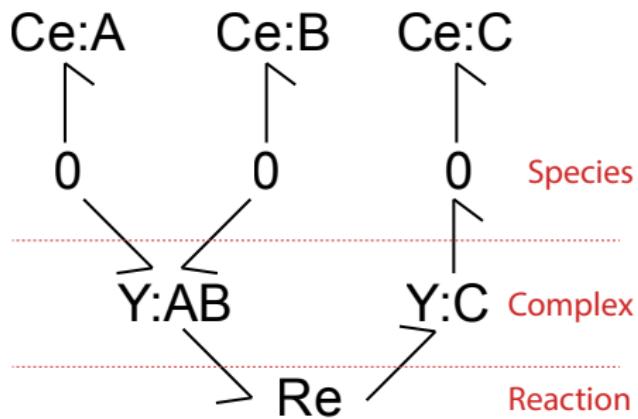


Figure: Bond Graph of $A + B \rightleftharpoons C$

The zero junctions allow species A B and C to be shared across reactions other than the one modelled in this graph.

In Review

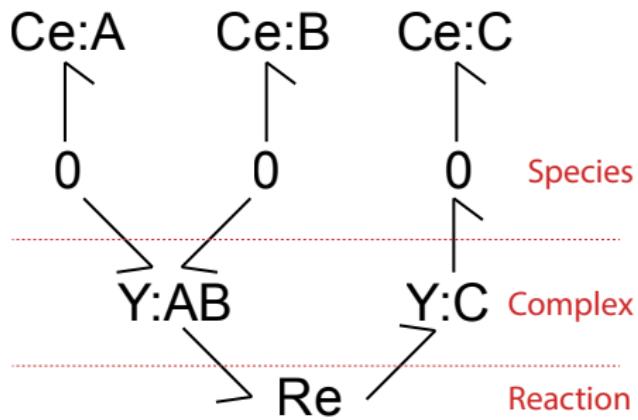


Figure: Bond Graph of $A + B \rightleftharpoons C$

The Y component is a power conserving through junction, which captures the forward (in the case of Y:AB) and reverse stoichiometry of this reaction.

In Review

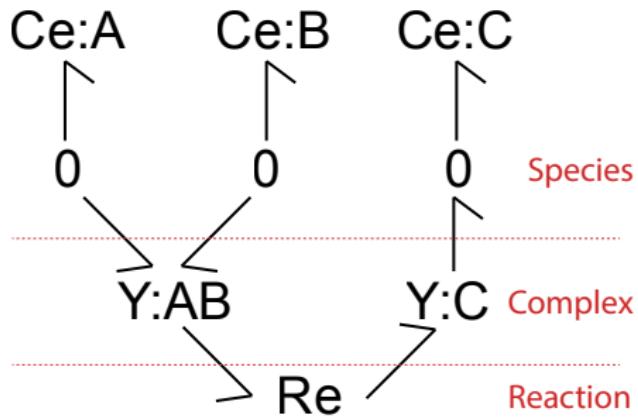


Figure: Bond Graph of $A + B \rightleftharpoons C$

The Re component models how the complex $A + B$ transmutes into C .
 The reaction proceeds according to the *Marcelin-de Donder* formula.

Try for yourself

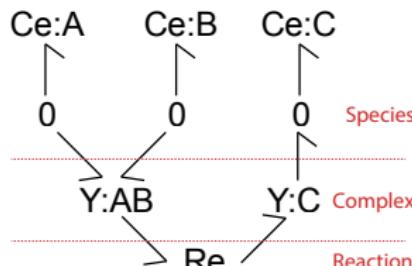
Try drawing bond graphs of these common reactions:

- ▶ $A + B \rightleftharpoons D + C$
- ▶ $A + B \rightleftharpoons B + C$
- ▶ $E + S \rightleftharpoons ES \rightleftharpoons E + P$

$$\Phi_{Ce}(e, f) = e - \ln k(q),$$

$$\Phi_{Re}(e_f, f_f, e_r, f_r) = \left(\frac{\kappa [e^{e_f} - e^{e_r}] - f_f}{f_f + f_r} \right)$$

$$\Phi_Y(e_0, f_0, e_1, f_1, \dots) = \left(\begin{array}{c} e_0 - \sum n_i e_i \\ f_0 + f_i/n_i \\ \vdots \end{array} \right)$$



References

-  Oster, G. F.; Perelson, A. S.; Katchalsky, A. *Quarterly Reviews of Biophysics* **1973**, 6, 1–134.
-  Gawthrop, P. J.; Crampin, E. J. *Proceedings. Mathematical, Physical, and Engineering Sciences / The Royal Society* **2014**, 470, 20140459.