# Detailed balance and complex balance: modern history of 130 year old laws

Alexander N. Gorban

Department of Mathematics
University of Leicester, UK

CRNT Workshop, Portsmouth, 2014

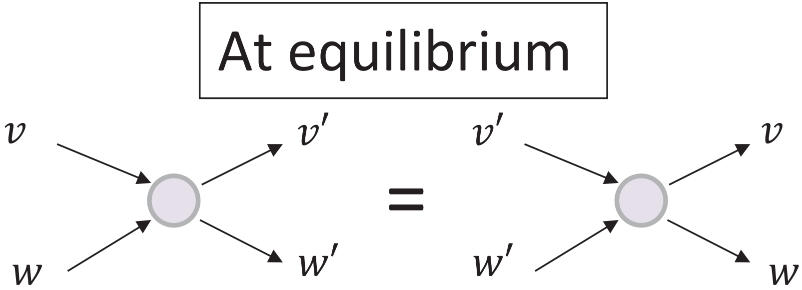
# Outline

1. The history of detailed and semidetailed balance
    - Boltzmann’s discovery
    - Timeline of the main events
2. The Michaelis–Menten–Stueckelberg theorem
    - Asymptotic assumptions
    - Michaelis–Menten versus Briggs–Haldane
    - Thermodynamics of fast equilibria
    - Generalized mass action law
3. Let some equilibria go to zero

# Outline

1. The history of detailed and semidetailed balance
   - Boltzmann’s discovery
   - Timeline of the main events
2. The Michaelis–Menten–Stueckelberg theorem
   - Asymptotic assumptions
   - Michaelis–Menten versus Briggs–Haldane
   - Thermodynamics of fast equilibria
   - Generalized mass action law
3. Let some equilibria go to zero

# Boltzmann's detailed balance (1872)



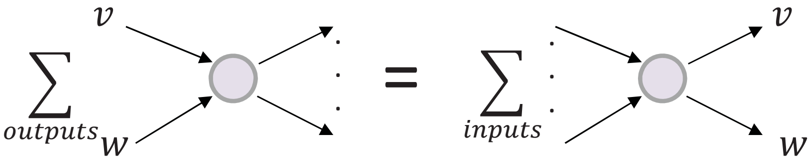
# Why detailed balance?

$1 \Rightarrow 2;\ 2\&3 \Rightarrow 4$

1. Dynamics is $T$-invariant.
2. Equilibrium is $T$-invariant.
3. $T$ transforms $v+w \to v'+w'$ into reverse collision $v'+w' \to v+w$.
4. At equilibrium, the rate of $v+w \to v'+w'$ is equal to the rate of $v'+w' \to v+w$.

# Boltzmann’s cyclic balance (1887) (or semi-detailed balance or complex balance)

At equilibrium



# Why cyclic balance?

- $v + w$ is a complex $\Theta$.
- At equilibrium, kinetics can be decomposed into a systems of cycles $\Theta_1 \to \Theta_n$ $(n = 2, \ldots)$ in such a way that each cycle is equilibrated (in each cycle and for any complex complex the input rate is equal to the output rate).
- This *cyclic decomposition* proves *cyclic balance*.

# Outline

1. The history of detailed and semidetailed balance
    - Boltzmann's discovery
    - Timeline of the main events
2. The Michaelis–Menten–Stueckelberg theorem
    - Asymptotic assumptions
    - Michaelis–Menten versus Briggs–Haldane
    - Thermodynamics of fast equilibria
    - Generalized mass action law
3. Let some equilibria go to zero

# From Boltzmann to Wegscheider

- In 1872 Boltzmann proved $H$-theorem on the basis of detailed balance;
- In 1887 Lorentz stated the nonexistence of inverse collisions for polyatomic molecules and impossibility of detailed balance for them;
- In the issue of the “Sitzungsberichte der Kaiserlichen Akademie” (1887) Boltzmann proposed the “cyclic balance” condition and proved $H$-theorem for systems with cyclic balance;
- In 1901 Wegscheider formulated detailed balance for chemical kinetics;

# From Einstein to Tolman

- In 1916 Einstein used detailed balance as the background for his quantum theory of radiation (Nobel prize);
- In 1925 Lewis published in PNAS “A new principle of equilibrium" with foundation of detailed balance;
- In 1932 Onsager used detailed balance in his work about reciprocal relations (Nobel prize);
- In 1938 Tolman published “The Principles of Statistical Mechanics” with analysis of Boltzmann's detailed balance;

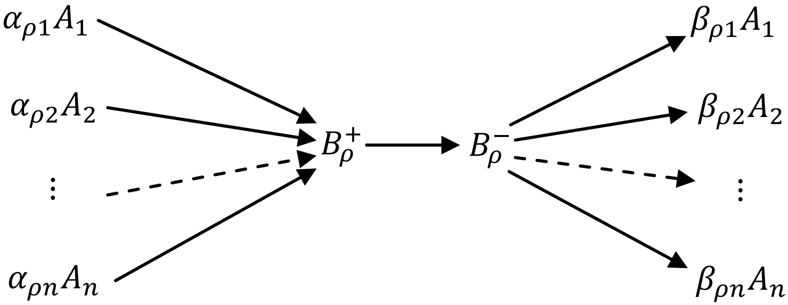
# From Heitler to Cercignani

- In 1944 Heitler analyzed Boltzmann's cyclic balance and in 1951 Coester proved Heitlers hypothesis about cyclic balance (the "Heitler-Coestler theorem of semi-detailed balance");
- In 1952 Stueckelberg demonstrated that cyclic balance holds for Markov microkinetics under condition that intermediates are in fast equilibrium and in small amount;
- In 1972 Horn and Jackson rediscovered cyclic (complex) balance for chemical kinetics.
- In 1981 Cercignani and Lampis demonstrated that the Lorenz arguments are wrong and the new Boltzmann relations are not needed, detailed balance should hold!

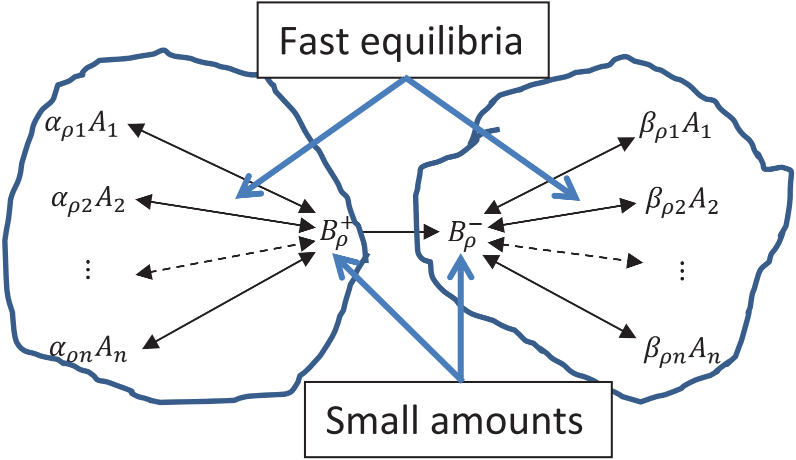
# Outline

1. The history of detailed and semidetailed balance
    - Boltzmann's discovery
    - Timeline of the main events
2. The Michaelis–Menten–Stueckelberg theorem
    - Asymptotic assumptions
    - Michaelis–Menten versus Briggs–Haldane
    - Thermodynamics of fast equilibria
    - Generalized mass action law
3. Let some equilibria go to zero

# 2*n*-tail scheme with intermediates — a starting point in the Stueckelberg asymptotic



# Reversible, fast and small



# Vocabulary

- $A_1, \dots, A_n$ – components;
- $B_1, \dots, B_m$ – intermediate compounds;
- $\nu_{ji} \geq 0$ $(i = 1, \dots, n,\ j = 1, \dots, m)$ – stoichiometric coefficients;
- $\Theta_j = \sum_i \nu_{ji} A_i$ – complexes;
- $\Theta_j \rightleftharpoons B_j$ – fast equilibria;
- $B_i \to B_j$ – intermediates' transitions;
- $c_i \geq 0$ – concentration of $A_i$;
- $\varsigma_j \geq 0$ – concentration of $B_j$.

# Michaelis–Menten trick (1913)

1. Equilibria are defined by thermodynamics;
2. We do not know kinetics of nonlinear reactions $\Theta_j \rightleftharpoons B_j$ but we know their equilibria;
3. If the reactions $\Theta_j \rightleftharpoons B_j$ are fast then we do not need kinetics for these reactions and thermodynamics gives the equilibria;
4. If all $\varsigma_j$ are small then only linear reactions with $B_j$ should be taken into account and their rates are linear in $\varsigma_j$.

Behind this trick we can imagine a general system of kinetic equations which has a Lyapunov function (free energy) and includes some small parameters.

# Outline

1. The history of detailed and semidetailed balance
   - Boltzmann's discovery
   - Timeline of the main events
2. The Michaelis–Menten–Stueckelberg theorem
   - Asymptotic assumptions
   - Michaelis–Menten versus Briggs–Haldane
   - Thermodynamics of fast equilibria
   - Generalized mass action law
3. Let some equilibria go to zero

# Briggs–Haldane (1925)

- The famous Michelis–Menten formula was produced by Briggs & Haldane (1925).
- Briggs and Haldane considered the simplest enzyme reaction $S+E \leftrightharpoons SE \to P+E$.
- They assumed mass action law kinetics for all elementary reactions.
- They mentioned that the total concentration of enzyme ($[E]+[SE]$) is “negligibly small” compared with the concentration of substrate $[S]$.
- After that they produced the now famous ‘Michaelis–Menten’ formula for the rate of the brutto–reaction $S+E \rightleftharpoons P+E$.

# Michaelis–Menten (1913)

- Michaelis & Menten considered the fully reversible mechanisms like $S+E \leftrightharpoons B_1 \leftrightharpoons B_2 \leftrightharpoons P+E$.
- They did not assume any kinetic formula for non-linear reactions.
- They assumed that equilibria $S+E \leftrightharpoons B_1$ and $B_2 \leftrightharpoons P+E$ are fast, and concentrations of compounds $B_{1,2}$ are small.
- They produced **mass action law kinetics for the brutto–reaction** $S+E \rightleftharpoons P+E$.

# Outline

# Free energy

- The basic hypothesis is that the compounds are the small admixtures to the system,
- That is, the amount of compounds $B_j$ is much smaller than amount of initial components $A_i$.
- Take the *energy* of their interaction with $A_i$ in the linear approximation in concentrations of $B_j$,
- Use the *perfect entropy* for $B_i$.
- Under these standard assumptions for a small admixtures get the free energy:

$$F = Vf(c,T) + VRT \sum_{j=1}^{q} \varsigma_j \left( \frac{u_j(c,T)}{RT} + \ln \varsigma_j - 1 \right)$$

# Standard equilibrium

The *standard equilibrium* concentration for $B_j$ is by definition:

$$\varsigma_j^*(c,T)=\exp\left(-\frac{u_j(c,T)}{RT}\right)$$

It is defined because of Boltzmann distribution ($\frac{1}{Z}\exp(-u/RT)$) with unite normalization factor (statistical sum) $Z=1$. With this notation

$$F=Vf(c,T)+VRT\sum_{j=1}^{q}\varsigma_j\left(\ln\left(\frac{\varsigma_j}{\varsigma_j^*(c,T)}\right)-1\right)$$

# Fast equilibria

- Use the formula for free energy to define the fast equilibria $\Theta_j \rightleftharpoons B_j$.
- Find the concentration of $B_i$, $\varsigma_i$ as a function of the concentrations $c_i$ of $A_i$.
- Such an equilibrium is the minimizer of the free energy on the straight line parameterized by $a$: $c_i = c_i^0 - a\nu_{ji}$, $\varsigma_j = a$.

$$\boxed{\varsigma_j = \varsigma_j^*(c,T)\exp\left(\frac{\sum_i \nu_{ji}\mu_i(c,T)}{RT}\right) + o(\varsigma)}$$

where $\mu_i = \frac{\partial f(c,T)}{\partial c_i}$ is the chemical potential of $A_i$.

# Outline

# Transformation of compounds

Linear kinetics of compounds is just a Markov chain (master equation)

$$\frac{\mathrm{d}\varsigma_j}{\mathrm{d}t} = \sum_{l,\,l\neq j} \left(\kappa_{jl}\varsigma_l - \kappa_{lj}\varsigma_j\right)$$

It should be in agreement with thermodynamics: the standard equilibrium should be a kinetic equilibrium:

$$\boxed{\sum_{l,\,l\neq j} \kappa_{jl}\varsigma_l^* = \sum_{l,\,l\neq j} \kappa_{lj}\varsigma_j^*}$$

# Quasiequilibrium elimination of compounds

In the quasiequilibrium approximation the rate of the brutto–process $\Theta_j \to \Theta_l$ is

$$w_{lj} = \kappa_{lj}\varsigma_j$$

In the same approximation

$$\boxed{w_{lj} = \kappa_{lj}\varsigma_j^*(c,T)\exp\left(\frac{\sum_i \nu_{ji}\mu_i(c,T)}{RT}\right) = \varphi_{lj}(c,T)\Omega_{lj}(c,t)}$$

where $\varphi_{lj}$ is the *kinetic factor* and $\Omega_{lj}$ is the *Boltzmann factor*

$$\Omega_{lj} = \exp\left(\frac{\sum_i \nu_{ji}\mu_i(c,T)}{RT}\right), \quad \varphi_{lj} = \kappa_{lj}\varsigma_j^*(c,T)$$

# Complex balance

The complex balance condition appears as a trivial re-writing of the condition that the Boltzmann equilibrium of compounds $\varsigma^*$ should be an equilibrium of Markov kinetics:

$$\boxed{\sum_{l} \varphi_{lj} = \sum_{l} \varphi_{jl}}$$

This condition is sufficient for the thermodynamic behavior of the system because the perfect entropy is the Lyapunov function for Markov kinetics.

# Restart of the formalism: GMAL+complex balance

Now, we can:

- “Forget” about the compounds (temporarily, at least);
- Start from the formulas for $w_{lj}$, the Boltzmann factor $\Omega_{lj}$ and the system of non-negative kinetic factors $\varphi_{jl}$;
- Kinetic factors should satisfy the complex balance condition.

This asymptotic representation of the kinetics that goes through intermediates, which (1) are in small amounts and (2) persist in fast equilibria with the components is the

*Michaelis–Menten–Stuekelberg theorem*

.

# A simple cycle with detailed balance

Consider a simple cycle

$$A_1 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} A_2 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} A_3 \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} A_1$$

with equilibrium $c^{\rm eq} = (c_1^{\rm eq}, c_2^{\rm eq}, c_3^{\rm eq})$ and detailed balance:

$$k_i c_i^{\rm eq} = k_{-i} c_{i+1}^{\rm eq}$$

(here, $c_{3+1} = c_1$). The perfect free energy

$$F = \sum_i RTVc_i \left( \ln \left( \frac{c_i}{c_i^{\rm eq}} \right) - 1 \right).$$

# The classical thermodynamics has no limit but the kinetic equations have

- Let $c_1^{\mathrm{eq}} \to 0$ for given $c_{2,3}^{\mathrm{eq}} > 0$ and fixed $k_1, k_{\pm 2}, k_{-3} > 0$.
- The limit kinetic system exists

$$A_1 \xrightarrow{k_1} A_2 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} A_3 \underset{k_{-3}}{\leftarrow} A_1 \, .$$

- The limit free energy does not exist.

Two questions arise:

1. Which system appear as the limits of systems with detailed balance when some reaction rate constants tend to zero?
2. Do these systems have Lyapunov functions?

# The extended principle of detailed balance

A system which obey the generalized mass action law is the limits of the systems with detailed balance when some of the reaction rate constants tend to zero if and only if:

- **The principle of detailed balance is valid for the reversible part.** (This means that for the set of all reversible reactions there exists a positive equilibrium where all the elementary reactions are equilibrated by their reverse reactions.)
- **The convex hull of the stoichiometric vectors of the irreversible reactions has empty intersection with the linear span of the stoichiometric vectors of the reversible reactions.** (Physically, this means that the irreversible reactions cannot be included in oriented cyclic pathways.)

The Lyapunov functions have been constructed too.

# Example: $H_2$+$O_2$ system

Consider a standard mechanism with 8 components $H_2$, $O_2$, $OH$, $H_2O$, $H$, $O$, $HO_2$, and $H_2O_2$ and 20 elementary reactions. Some of them are “almost irreversible”. Consider their irreversible limits.

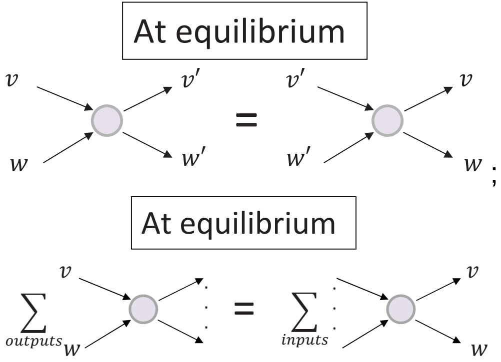
Let reactions $H_2 + O_2 \rightleftharpoons 2OH$, $H_2 + OH \rightleftharpoons H_2O + H$, $H_2 + O \rightleftharpoons OH + H$, $H_2O_2 \rightleftharpoons 2OH$, $H + H_2O_2 \rightleftharpoons H_2 + HO_2$, $OH + H_2O_2 \rightleftharpoons H_2O + HO_2$ be reversible. Find the maximal sets of reactions which may be irreversible.

There are two maximal sets, the following one and the set of reverse reactions:

$OH + HO_2 \to O_2 + H_2O$, $H + HO_2 \to 2OH$, $O + HO_2 \to O_2 + OH$, $2H \to H_2$, $OH + H \to H_2O$, $H + O \to OH$, $2O \to O_2$, $H + HO_2 \to H_2 + O_2$, $2HO_2 \to O_2 + H_2O_2$.

# Main message 1

Boltzman introduced detailed (1872) and complex (1887) balance:

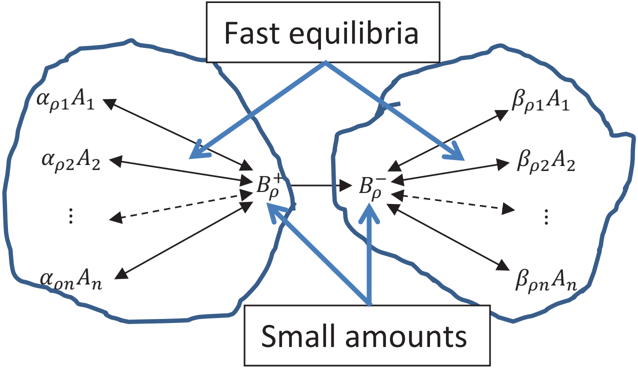


At equilibrium

At equilibrium

# Main message 2

The generalized mass action law with the complex balance condition appear in the limit


Fast equilibria

Small amounts

# Main message 3

There exists extended detailed balance when some reactions become irreversible. It consists of two parts:

- The principle of detailed balance is valid for the reversible part.
- The convex hull of the stoichiometric vectors of the irreversible reactions has empty intersection with the linear span of the stoichiometric vectors of the reversible reactions.

# References: some history

- Boltzmann, L. Weitere Studien über das Wärmegleichgewicht unter Gasmolekülen. *Sitzungsber. keis. Akad. Wiss.* **1872**, *66*, 275–370. Translation: In *Kinetic Theory of Gases*; Imperial Colledge Press: London, UK, 2003.
- Boltzmann, L. Neuer Beweis zweier Sätze über das Wärmegleichgewicht unter mehratomigen Gasmolekülen. Sitzungsberichte der Kaiserlichen Akademie der Wissenschaften in Wien. **1887**, *95*, 153–164.
- Wegscheider, R. Über simultane Gleichgewichte und die Beziehungen zwischen Thermodynamik und Reactionskinetik homogener Systeme, Monatshefte für Chemie / Chemical Monthly 32(8) (1901), 849–906.

# References: some history

- Lewis, G.N. A new principle of equilibrium, *PNAS* March 1, 1925 vol. 11 no. 3 179-183.
- Coester, F. Principle of detailed balance. *Phys. Rev.* **1951**, *84*, 1259.
- Stueckelberg, E.C.G. Theoreme *H* et unitarite de *S*. *Helv. Phys. Acta* **1952**, *25*, 577–580.
- Horn, F.; Jackson, R. General mass action kinetics. *Arch. Ration. Mech. Anal.* **1972**, *47*, 81–116.
- Feinberg, M. Complex balancing in general kinetic systems. *Arch. Ration. Mech. Anal.* **1972**, *49*, 187–194.
- Yablonskii, G.S.; Bykov, V.I.; Gorban, A.N.; Elokhin, V.I. *Kinetic Models of Catalytic Reactions*; Elsevier: Amsterdam, The Netherlands, 1991.

# References

- Gorban, A.N.; Shahzad, M. The Michaelis – Menten – Stueckelberg Theorem. *Entropy* **2011**, *13*, 966–1019. Corrected postprint: arXiv:1008.3296 [physics.chem-ph]
- A.N. Gorban, G.S. Yablonskii, Extended detailed balance for systems with irreversible reactions, *Chem. Eng. Sci.* 66 **2011** 5388–5399; arXiv:1101.5280 [cond-mat.stat-mech].
- D. Grigoriev, P.D. Milman, Nash resolution for binomial varieties as Euclidean division. A priori termination bound, polynomial complexity in essential dimension 2, *Advances in Mathematics*, 231 (6) **2012**, 3389–3428.

# References

- A.N. Gorban, E.M. Mirkes, G.S. Yablonskii, Thermodynamics in the Limit of Irreversible Reactions, *Physica A* 392 **2013** 1318–1335, arXiv:1207.2507 [cond-mat.stat-mech]
- A. N. Gorban, General H-theorem and entropies that violate the second law, *Entropy* **2014**, 16(5), 2408–2432, Extended postprint arXiv:1212.6767 [cond-mat.stat-mech].
- Gorban, A.N., Sargsyan, H.P., and Wahab, H.A. Quasichemical Models of Multicomponent Nonlinear Diffusion, *Mathematical Modelling of Natural Phenomena*, Volume 6 / Issue 05, **2011**, 184-262.