Recall:

**Mass Action Kinetics:**

Deterministic fluid model: \( \dot{c} = f(c) = YA_k\Psi(c) \)

Complex balance solution: \( c \in \mathbb{R}_{\geq 0}^n \) such that \( A_k \Psi(c) = 0 \)

i.e., for each complex \( i \),

\[
\sum_{j \neq i} \bar{K}_{j \rightarrow i} c_j = \sum_{l \neq i} \bar{K}_{i \rightarrow l} c_l
\]

i.e., rate of flow into \( i \) = rate of flow out of \( i \)

**Theorem:** (see Gunawardena for proof)

Define the deficiency \( \delta = dim(\ker(Y) \cap \text{Image}(A_k)) \). Suppose that \( \delta = 0 \). Then the network has a complex balance solution if and only if the network is weakly reversible.

**Remark**

In fact, \( 0 \leq \delta \leq p - l - s \), where,

\[
\begin{align*}
p & = \text{No. of complexes} \\
l & = \text{No. of linkage classes: linkage classes are connected components of the complexes graph} \\
s & = \text{dimension of space spanned by } \nu_k' - \nu_k, k = 1, ..., K
\end{align*}
\]
Examples:

1. 
A + E \leftrightarrow AE \rightarrow B + E 

\[ p = 3 \]
\[ l = 1 \]
\[ s = 2 \]
\[ \Rightarrow p - l - s = 0 \]
\[ \Rightarrow \delta = 0 \]

This reaction network is not weakly reversible.

2. 
A \leftrightarrow 2B 
A + C \leftrightarrow D 
D \rightarrow B + E 
B+E \rightarrow A + C 

\[ p = 5 \]
\[ l = 2 \]
\[ s = 3 \]
\[ \Rightarrow p - l - s = 0 \]
\[ \Rightarrow \delta = 0 \]

This reaction network is weakly reversible, hence there is a complex balance equilibrium.

Note: When you have weak reversibility, \( \delta = p - l - s \).

Theorem: (Horn and Jackson, '72, Feinberg '72, Gunawardena '03)

Suppose \( \exists \) a complex balance solution. Then,

- The network is weakly reversible.
• Every $c \in \mathbb{R}^n_{>0}$ such that $f(c) = 0$ is a complex balance solution.

• Let $Z = \{c \in \mathbb{R}^n_{>0} : f(c) = 0\}$, then for any $c^* \in Z$,
  $Z = \{c \in \mathbb{R}^n_{>0} : ln(c) - ln(c^*) \in S^\perp\}$, where
  $S = \text{span}\{\nu_k - \nu_k : k = 1, \ldots, K\}$

• There is one and only one complex balance solution in each set of the form,
  $(c + S) \cap \mathbb{R}^n_{>0} \neq \emptyset$, $c \in \mathbb{R}^n_{>0}$, in other words, a positive stoichiometric compatibility class that is non empty.

• Each complex balance solution in a given positive stoichiometric compatibility class is locally asymptotically stable within that class.

Connection between complex balance solutions for fluid models and product form stationary distributions for stochastic models: (Anderson, Craciun, Kurtz)

Stochastic Model:

\[
X(t) = \# \text{ of molecules of each species at time } t \\
= X(0) + \sum_{k=1}^{K} N_k \left( \int_0^t \lambda_k(X(s)) \, ds \right) (\nu_k' - \nu_k)
\]

where \( \lambda_k(x) = \kappa_k \prod_{i=1}^{n} x_i(x_i - 1) \ldots (x_i - \nu_{ik} + 1) \)

Consider the fluid model with \( \dot{c} = f(c) = YA_k \Psi(c) \) (rate constants are \( \kappa_k \) and not \( \tilde{\kappa}_k \)). Assume that there is a complex balance solution $c$ for this fluid model.

Recall:

$X$ is a continuous time Markov chain. $X$ takes values in $Z^n_+ = \mathbb{N}^n$.

$x \leftrightarrow y$ (state $x$ communicates with state $y$) iff

$P(X(t) = y \text{ for some } t \geq 0 \mid X(0) = x) > 0$ and

$P(X(t) = x \text{ for some } t \geq 0 \mid X(0) = y) > 0$.
So, we can partition $\mathbb{Z}_+^n$ into equivalence classes of communicating states.

- All states in a given communicating class are of the same type, i.e., either all transient or all recurrent.

- A recurrent class is closed in the sense that there are no “arrows” leading out of it.

**Claim:** (Anderson, Craciun and Kurtz)

Assume $c$ is a complex balance solution. Consider a closed communicating class $\Gamma$. Let

$$
\pi(x) = \frac{M c^x}{x!}, \quad x \in \Gamma \subset \mathbb{Z}_+^n
$$

where

$$
c^x = \prod_{i=1}^{n} c_i^{x_i}
$$

and

$$
x! = \prod_{i=1}^{n} x_i!
$$

$M$ is a normalizing constant such that $\sum_{x \in \Gamma} \pi(x) = 1$. Then $\pi$ is the unique stationary distribution for $X$ on $\Gamma$.

**Note:**

$$
\sum_{x \in \mathbb{Z}_+^n} \frac{c^x}{x!} < \infty
$$

because

$$
\sum_{j=1}^{\infty} \frac{c_j^j}{j!} = e^{c_i} < \infty
$$

**Proof:**

We give the proof for the case when

$$
\Gamma = \mathbb{Z}_+^n.
$$
Since $X$ is a continuous time Markov chain:

$$P(X(t + h) = x' | X(t) = x) = q_{xx'}h + o(h) \quad \forall x \neq x'$$

$Q$-matrix:

$$Q = (q_{xx'})$$

$$q_{xx} = -\sum_{x' \neq x} q_{xx'} \quad \text{(Row sums are zero)}$$

Since $\Gamma$ is the whole space and the MC $X$ does not explode in finite time, it suffices to show,

$$\pi'Q = 0$$

i.e.,

$$\sum_{x \in \mathbb{Z}_+^n} \pi(x)q_{xx'} = 0 \quad \forall x' \in \mathbb{Z}_+^n$$

$$\Leftrightarrow \sum_{x \neq x'} \pi(x)q_{xx'} = \pi(x')(q_{xx'}x) = \pi(x') \sum_{x \neq x'} (q_{xx'}) \quad \forall x' \in \mathbb{Z}_+^n$$

$x \rightarrow x'$ can occur via the $k$th reaction provided $x - \nu_k + \nu_k' = x'$ and $x - \nu_k$ is in the positive orthant (i.e., there are enough reactants in $x$ to make the reaction feasible). Similarly, $x' \rightarrow x$ can occur by the $k$th reaction provided $x'$ has enough of each of the species to make the reaction go and $x = x' + \nu_k' - \nu_k$.

So the above equation is equivalent to having the following for each $x'$ in $\mathbb{Z}_+^n$:

$$\sum_{k=1}^{K} \pi(x)\lambda_k(x)1_{\{x=x'-\nu_k'+\nu_k;x-\nu_k \in \mathbb{Z}_+^n\}} = \pi(x') \sum_{k=1}^{K} \lambda_k(x')1_{\{x'-\nu_k \in \mathbb{Z}_+^n\}}$$

where

$$\lambda_k(x) = \kappa_k \prod_{i=1}^{n} (x_i - 1)(x_i - \nu_{ik} + 1).$$

Proof to be continued.