

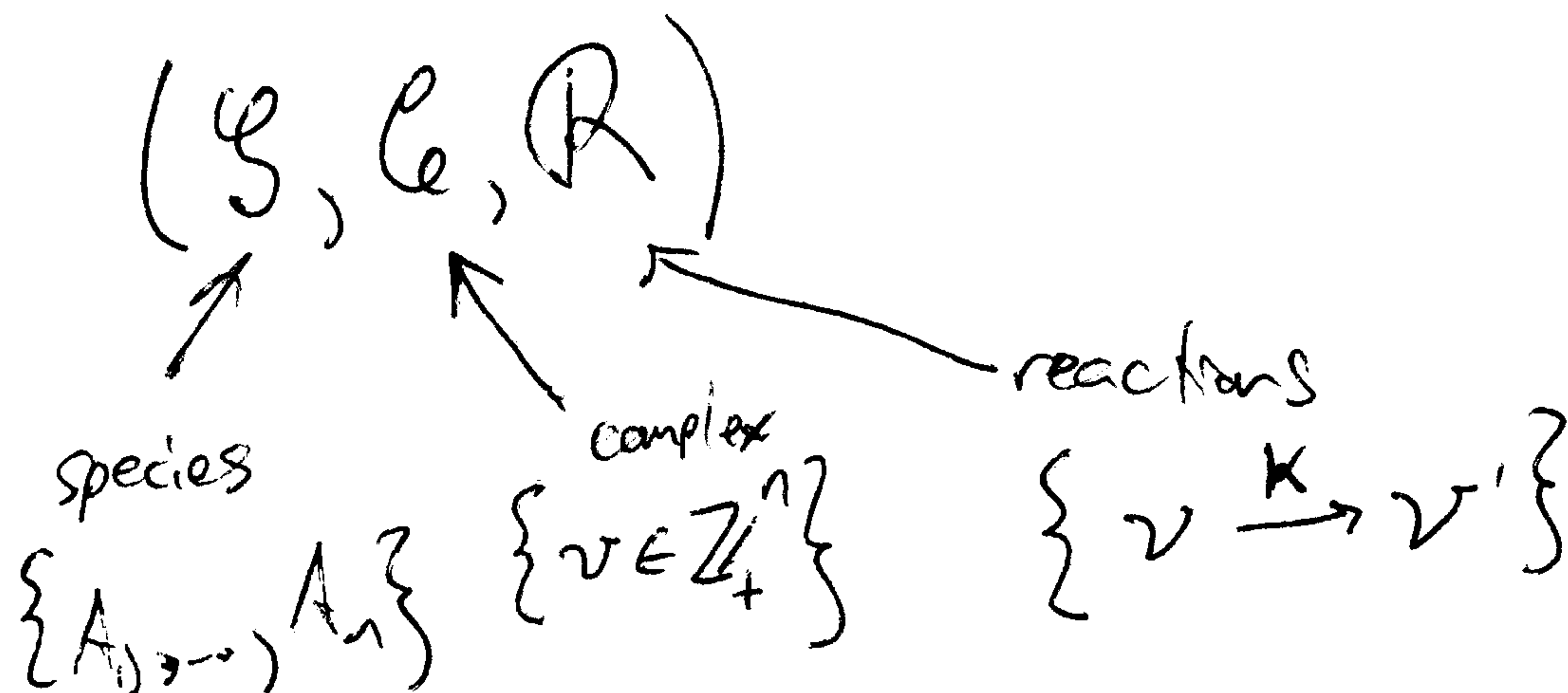
Notes by Alex Bilk

McZ 289

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Biochemical Reaction Networks



Markov Chain Model

$$\{X(t), t \geq 0\} \quad X(t) = \begin{pmatrix} X_1(t) \\ \vdots \\ X_n(t) \end{pmatrix}$$

$X_i(t)$ = # of molecules of species i at time t

$N_1, \dots, N_K$
independent rate 1
Poisson processes

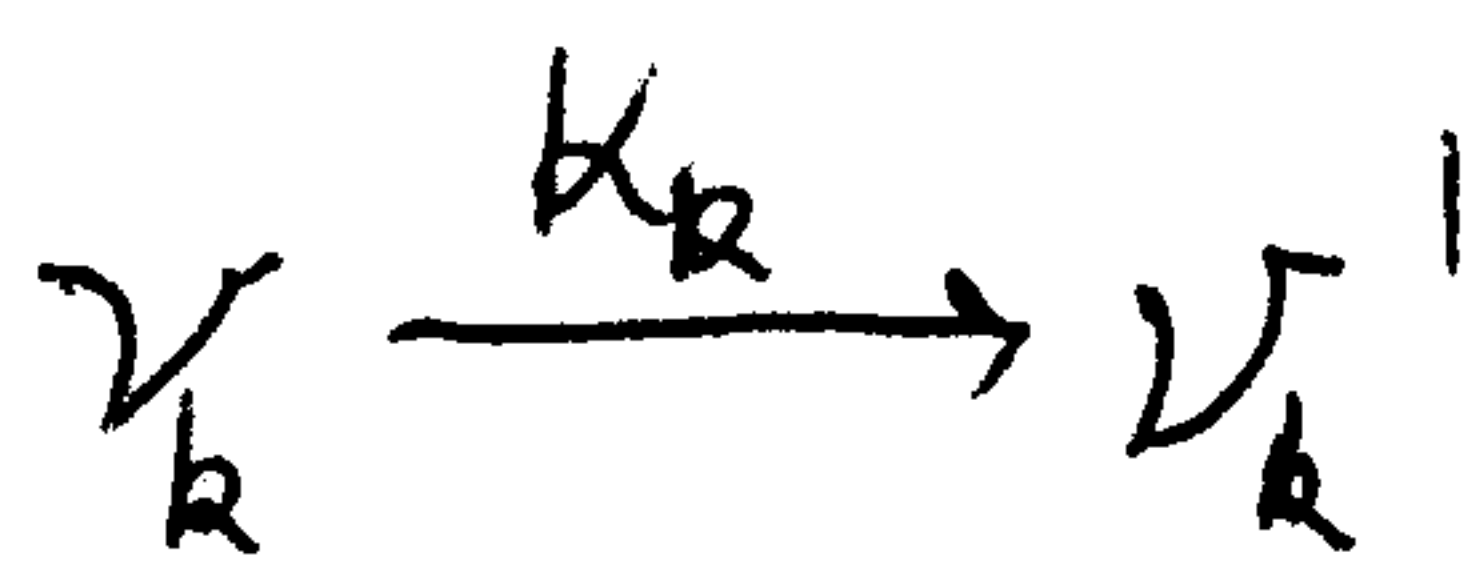
K = # of reactions

Then we have:
$$X(t) = X(0) + \sum_{k=1}^K N_k \left(\int_0^t \chi_k(X(s)) ds \right)$$

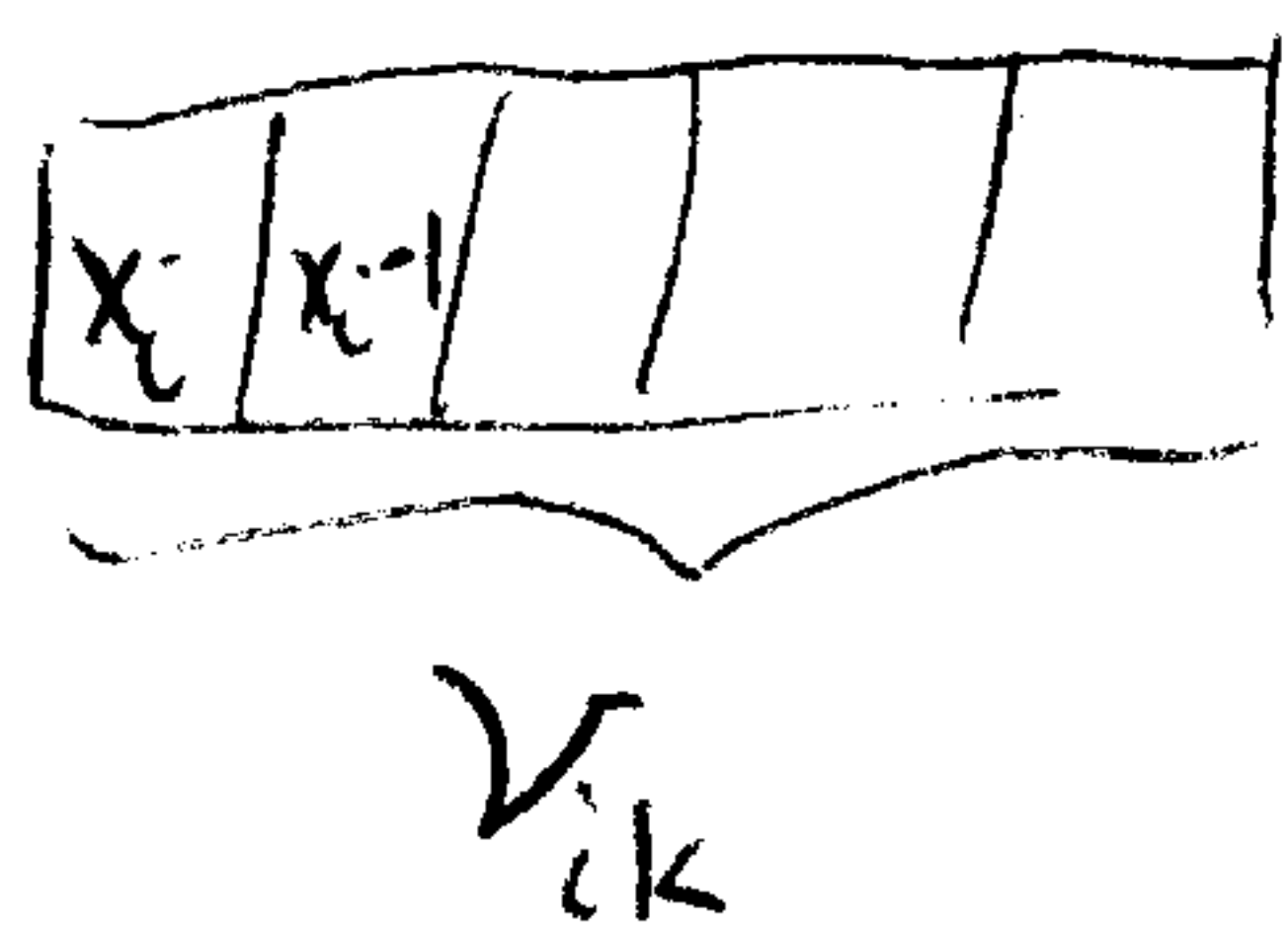
$\chi_k = (v_k' - v_k)$

The "microscopic" stochastic Model

Mass Action Kinetics



$$\lambda_k(x) = k_k \prod_{i=1}^n \nu_{ik}! \binom{x_i}{\nu_{ik}}$$



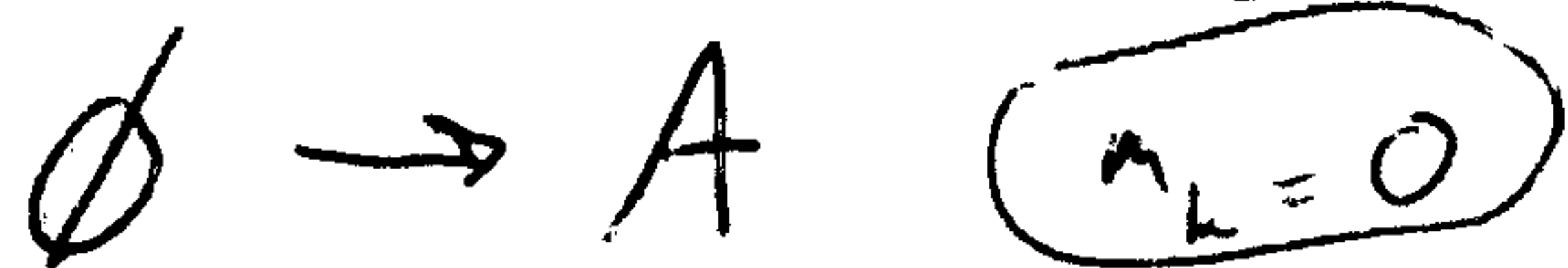
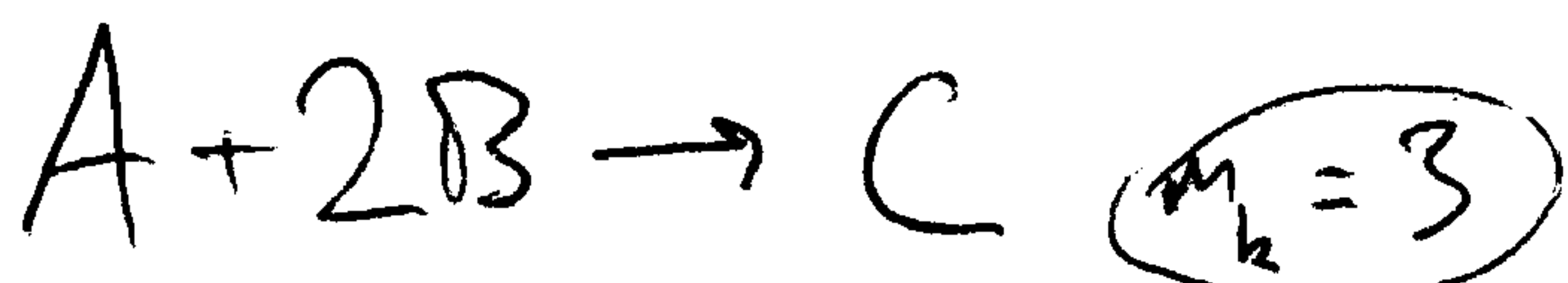
x_i = # of molecules of species i currently available

If V is volume for system, Gillespie's argument gives that:

$$k_k \propto \frac{1}{V^{m_k-1}}$$

m_k = # of molecules involved in reaction k

$$= \sum_{i=1}^n \nu_{ik}$$



Define $\tilde{k}_k = k_k V^{m_k-1}$

$$\text{i.e. } K_k^V = \tilde{k}_k / V^{m_k-1}$$

so that $\tilde{k}_k$ independent of V

Let $r = V$ (goes to ∞ through a sequence,

i.e. $r_m \rightarrow \infty$ as $m \rightarrow \infty$)

Sequence of networks

$$\begin{aligned}
 \chi_k^r(x) &= \frac{\tilde{K}_k}{r^{m_k}} \prod_{i=1}^n x_i (x_i - 1) \cdots (x_i - v_{ik} + 1) \\
 &\quad \text{exactly one } r \text{ for every term, so let} \\
 &= r^{\tilde{K}_k} \prod_{i=1}^n \left\{ c_i \left(c_i - \frac{1}{r} \right) \cdots \left(c_i - \frac{(v_{ik} - 1)}{r} \right) \right\} \quad \left. \begin{array}{l} c_i = \frac{x_i}{r} \end{array} \right\} \\
 &\quad \boxed{f_k^r(c)}
 \end{aligned}$$

In r th system:

$$\bar{X}^r(t) = \frac{X^r(t)}{r} = \frac{X^r(0)}{r} + \sum_{k=1}^K \frac{1}{r} N_k \left(\int_0^t f_k^r(\bar{X}^r(s)) ds \right) (v_k' - v_k)$$

Initial conditions:

$$\bar{X}^r(0) \Rightarrow \bar{X}_0 \quad \text{as } r \rightarrow \infty$$

$\uparrow$
 finite r.v.

Now $\{\bar{X}^r\}$ is a sequence of processes in $\mathbb{D}(L_0^\infty, \mathbb{R}_{\geq 0}^K)$

Criterion for C-tightness

$\{\bar{X}^r\}$ is C-tight if $\forall T > 0, \forall \varepsilon > 0, \exists \delta^* = \delta(\varepsilon, T)$

$\exists K^* = K(\varepsilon, T)$ and $r^* = r(\varepsilon, T)$ st. $\forall r \geq r^*$

(i) $P(\|\bar{X}^r\|_T \geq K^*) < \varepsilon$

(ii) $P(\omega(\bar{X}^r, \delta^*, T) \geq \varepsilon) < \varepsilon$

Strong Approximation

Can choose prob. space on which $N_1, \dots, N_K$ are defined such that it also supports independent standard one-dimensional

Brownian motions $W_1, \dots, W_K$ and

$$\eta_k(t) \equiv \frac{N_k(t) - t - W_k(t)}{(\log t) \sqrt{2}}, \quad t \geq 0, \quad k=1, \dots, K$$

$$\xi_k \equiv \sup_{t \in (0, \infty)} |\eta_k(t)| < \infty \text{ a.s. for each } k$$

$$E[e^{x \xi_k}] < \infty \quad \forall k \text{ for some } x > 0$$

define:

$$l(t) \equiv \log t \sqrt{2}$$

then

$$N_k(t) = t + W_k(t) + l(t) \eta_k(t)$$

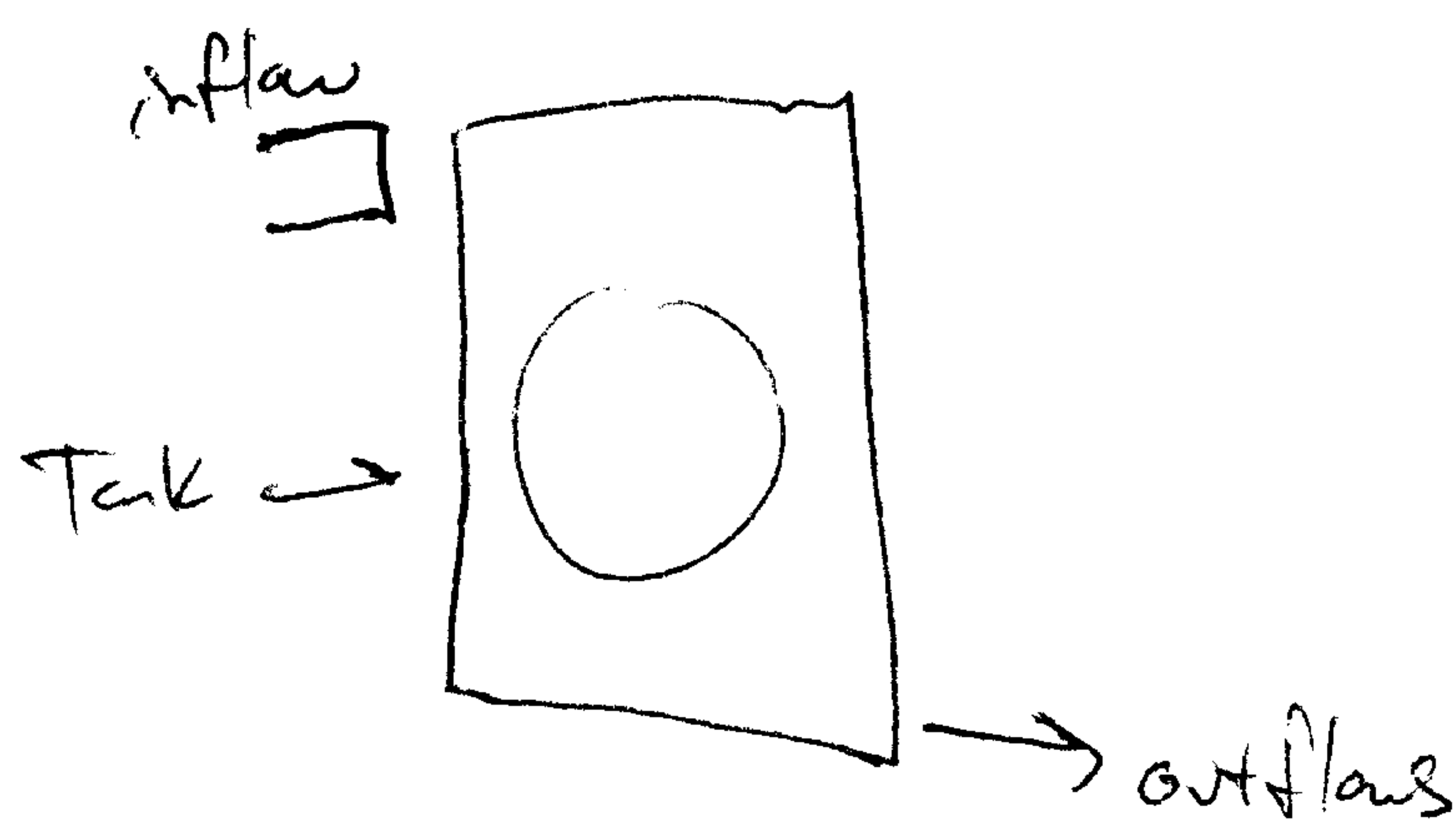
back to our $\bar{X}^r(t)$ equation:

$$\bar{X}^r(t) = \bar{X}^r(0) + \sum_{k=1}^K \frac{1}{r} \left(\int_0^t r f_k^r(\bar{X}^r(s)) ds \right) (V_k' - V_k)$$

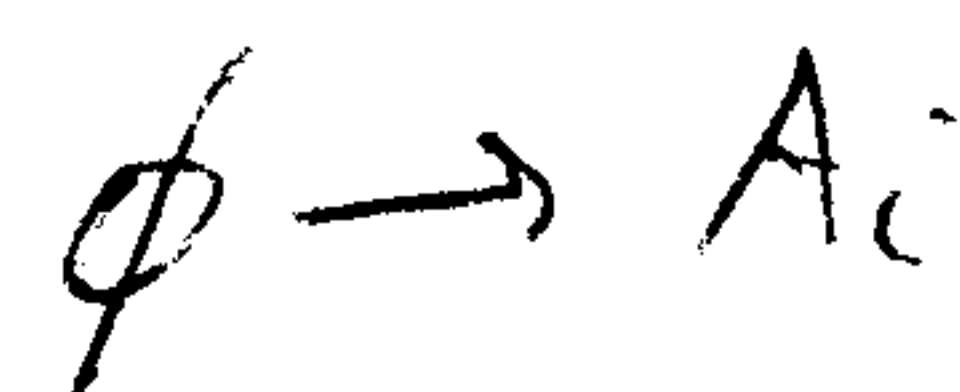
$$+ \sum_{k=1}^K \frac{1}{r} W_k \left(r \int_0^t f_k^r(\bar{X}^r(s)) ds \right) (V_k' - V_k) + \rightarrow$$

$$+ \sum_{k=1}^K \frac{1}{V} \ell \left(r \int_0^t f_k^r(\bar{X}^r(s)) ds \right) \eta_k \left(r \int_0^t f_k^r(\bar{X}^r(s)) ds \right) (v_k' - v_k)$$

"Mass" of network



Inflow reactions



Outflows



↑
[Continuous flow stirred tank reactor]

Conserved quantities

A vector $m \in \mathbb{R}_{>0}^n$ is a conserved quantity if

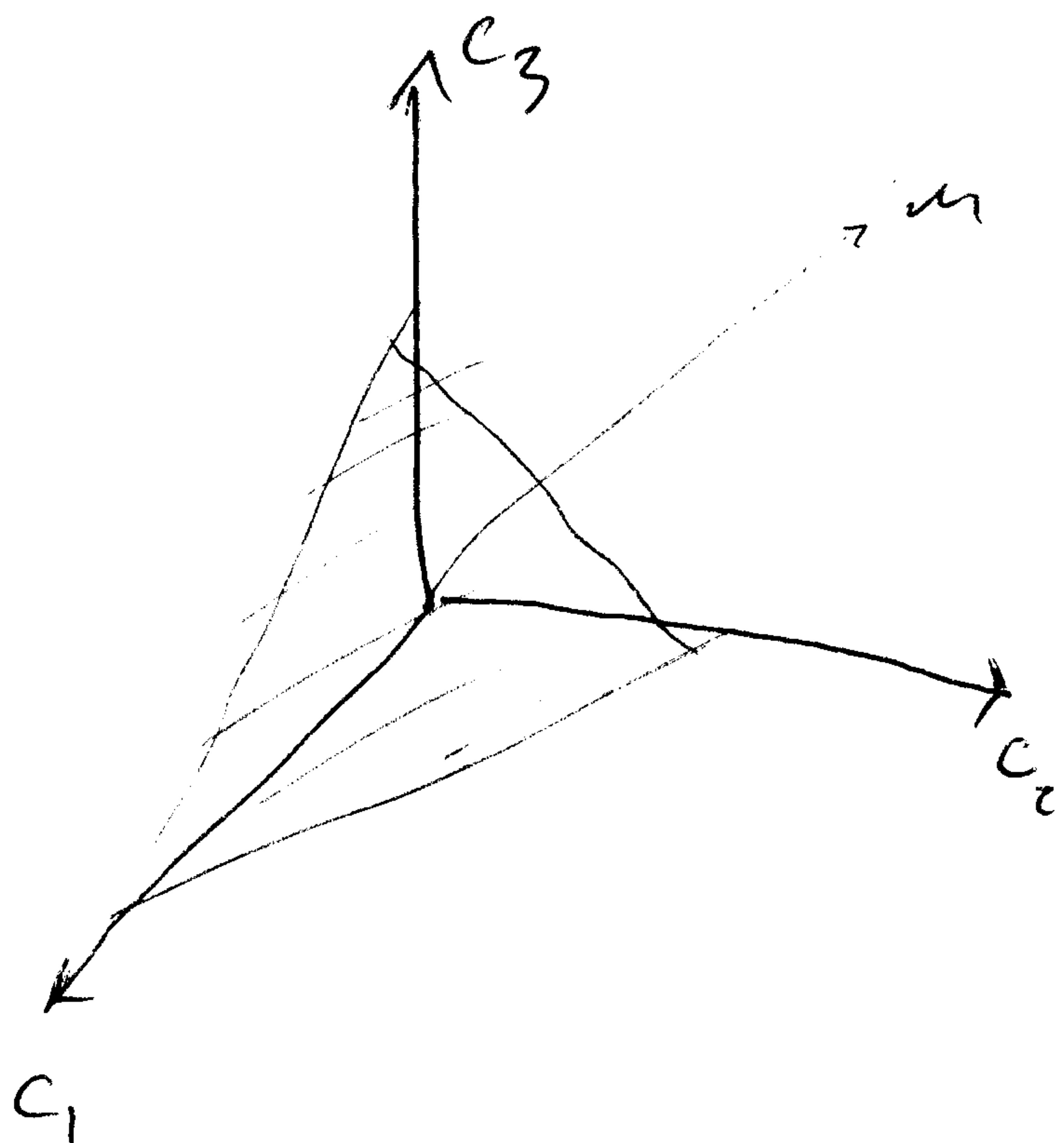
$$m \cdot (v_k' - v_k) = 0 \quad \text{for } k = 1, \dots, K$$

in which case $m \cdot \bar{X}^r(t) = m \cdot \bar{X}^r(0) \quad \forall t \geq 0$

Example: $A + B \rightarrow C$

$$S = \begin{pmatrix} -1 \\ -1 \\ 1 \end{pmatrix} = (v' - v)$$

$m = (1, 1, 2)$ is a conserved quantity



Suppose that a subset $k = 1, \dots, K_1$ of reactions are conservative, i.e.

$$\exists m \in \mathbb{R}_{>0}^n \text{ s.t. } m \cdot (v_k' - v_k) = 0 \quad k = 1, \dots, K_1$$

and $k = K_1 + 1, \dots, K_2$ correspond to outflows (so that $v_k' - v_k = -v_k$),

and $k = K_2 + 1, \dots, K$ correspond to inflows

$$m \cdot \bar{X}'(t) \leq m \cdot \bar{X}'(0) + \sum_{\substack{k=K_2+1 \\ (\text{inflows})}}^K \frac{1}{r} N_k \left(r \int_0^t f_k^n(\bar{X}'(s)) ds \right) \underbrace{m \cdot v_k'}_{m_k'}$$

For inflow reaction: $\phi \rightarrow A_i$,

$$f_k^n(c) = \tilde{k}_k \quad (\text{no concentrations involved})$$

so we get a major simplification:

$$M \cdot \bar{X}'(t) \leq M \cdot \bar{X}'(0) + \sum_{k \geq K_2+1} \frac{m_k'}{r} \left[rt \tilde{K}_k + W_k(rt \tilde{K}_k) + \eta_k(rt \tilde{K}_k) \ell(rt \tilde{K}_k) \right]$$

$$= M \cdot \bar{X}'(0) + \sum_{k \geq K_2+1} m_k' t \tilde{K}_k + \sum_{k \geq K_2+1} m_k' |\xi_k| \frac{\log(rt \tilde{K}_k)}{r} \vee 2$$

$$+ \sum_{k \geq K_2+1} m_k' \frac{W_k(rt \tilde{K}_k)}{r}$$

Note: $\frac{W_k(rt \tilde{K}_k)}{r} \stackrel{d}{=} \sqrt{r} \frac{W_k(t \tilde{K}_k)}{r} \xrightarrow{as \ r \rightarrow \infty} 0$

Fix $T > 0$ & $\varepsilon > 0$, there is $K^* = K(\varepsilon, T)$,
 $r^* = r(\varepsilon, T)$

s.t. $\mathbb{P}(\|M \cdot \bar{X}'(\cdot)\|_T \geq K^*) < \varepsilon \quad \forall r \geq r^*$

Since $m > 0$, follows that

$$\mathbb{P}(\|\bar{X}'(\cdot)\|_T \geq \tilde{K}^*) < \varepsilon \quad \forall r \geq r^*$$

This gives us containment, as will flag next time.