

LECTURE #3

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EXAMPLES OF COMPLEX NETWORKS

Biochemical Reaction Networks

2

- Well-stirred systems of molecular species in thermal equilibrium at fixed volume.
- The probability that a randomly selected combination of reactant molecules at time t , associated with the m -th reaction, to react accordingly during $[t, t + dt)$ is proportional to dt .
- The proportionality factor κ_m is known as the specific probability rate constant of the reaction.

Biochemical Reaction Networks

3

- Given that $\mathbf{X}(t) = \mathbf{x}$, if $\gamma_m(\mathbf{x})$ is the number of distinct subsets of molecules that can form a reaction complex for reaction m at time t , then

$$\gamma_m(\mathbf{x}) = \prod_{n=1}^N [x_n \geq v_{nm}] \binom{x_n}{v_{nm}} = \prod_{n=1}^N [x_n \geq v_{nm}] \frac{x_n!}{v_{nm}!(x_n - v_{nm})!}$$

Iverson bracket

https://en.wikipedia.org/wiki/Iverson_bracket

$X_1 \rightarrow X_2$ (monomolecular) $\Rightarrow \gamma(x_1) = x_1$, for $x_1 \geq 1$

$X_1 + X_1 \rightarrow X_2$ (bimolecular with **same** reactants) $\Rightarrow \gamma(x_1, x_2) = x_1(x_1 - 1)/2$, for $x_1 \geq 2$

$X_1 + X_2 \rightarrow X_3$ (bimolecular with **different** reactants) $\Rightarrow \gamma(x_1, x_2) = x_1 x_2$, for $x_1, x_2 \geq 1$

Biochemical Reaction Networks

4

- Each of the distinct combinations $\gamma_m(\mathbf{x})$ of the reactant molecules of the m -th reaction has probability $\kappa_m dt$ to react and probability $1 - \kappa_m dt$ of not reacting.
- Hence, the probability that a particular one of the $\gamma_m(\mathbf{x})$ reactant combinations does react during $[t, t + dt)$ is given by

$$\kappa_m dt (1 - \kappa_m dt)^{\gamma_m(\mathbf{x})-1} \simeq \kappa_m dt \quad \text{for } dt \simeq 0$$

Biochemical Reaction Networks

5

- Now, the probability that any of the $\gamma_m(\mathbf{x})$ distinct reactants will react during $[t, t + dt)$ is given by the sum of all probabilities:

$$\sum_{i=1}^{\gamma_m(\mathbf{x})} \kappa_m dt (1 - \kappa_m dt)^{\gamma_m(\mathbf{x})-1} \simeq \sum_{i=1}^{\gamma_m(\mathbf{x})} \kappa_m dt = \kappa_m \gamma_m(\mathbf{x}) dt \quad \text{for } dt \simeq 0$$

- In this case, the propensity functions are given by

$$\pi_m(\mathbf{x}) = \kappa_m \gamma_m(\mathbf{x}) = \kappa_m \prod_{n=1}^N [x_n \geq \nu_{nm}] \binom{x_n}{\nu_{nm}}$$

- These propensity functions are said to follow the mass-action law.

Pharmacokinetic Networks

6

- Used to study absorption, distribution, metabolism, and elimination of chemicals and drugs by the body of animals and humans.
- A model for studying the effect of tetrachloroethylene (widely used solvent) on carcinogenesis.
- This model divides the body into the lungs (central compartment) and fat tissue, poorly perfused tissue (muscles and skin), richly perfused tissue (central nervous system and viscera, except liver), and liver.

Pharmacokinetic Networks

7

- Let X_n be the solvent present in the n -th compartment
- We have 5 species and 10 reactions:

$\emptyset \rightarrow X_1$ (injection of one solvent molecule into lung blood)

$\left. \begin{array}{l} X_1 \rightarrow X_2 \\ X_2 \rightarrow X_1 \end{array} \right\}$ (exchange of one solvent molecule between lung blood and fat tissue)

$\left. \begin{array}{l} X_1 \rightarrow X_3 \\ X_3 \rightarrow X_1 \end{array} \right\}$ (exchange of one solvent molecule between lung blood and poorly perfused tissue)

$\left. \begin{array}{l} X_1 \rightarrow X_4 \\ X_4 \rightarrow X_1 \end{array} \right\}$ (exchange of one solvent molecule between lung blood and richly perfused tissue)

$\left. \begin{array}{l} X_1 \rightarrow X_5 \\ X_5 \rightarrow X_1 \end{array} \right\}$ (exchange of one solvent molecule between lung blood and the liver)

$X_5 \rightarrow \emptyset$ (metabolic clearance of one solvent molecule by the liver)

Pharmacokinetic Networks

8

- Let us assume that:
 - ▣ All compartments are homogeneous.
 - ▣ Injection of solvent into the lung blood takes place at constant rate κ_1 .
 - ▣ The probability of a randomly selected solvent molecule to move from compartment n to compartment n' within $[t, t + dt)$ is proportional to dt with proportionality constant $\kappa_{nn'}$.
- Then, the pharmacokinetic network can be modeled as a Markovian reaction network with linear propensity functions.

Pharmacokinetic Networks

9

- In this case, we have that:

$$\begin{aligned}\pi_1(\mathbf{x}) &= \kappa_1, & \pi_2(\mathbf{x}) &= \kappa_{12}x_1, & \pi_3(\mathbf{x}) &= \kappa_{21}x_2 \\ \pi_4(\mathbf{x}) &= \kappa_{13}x_1, & \pi_5(\mathbf{x}) &= \kappa_{31}x_3, & \pi_6(\mathbf{x}) &= \kappa_{14}x_1 \\ \pi_7(\mathbf{x}) &= \kappa_{41}x_4, & \pi_8(\mathbf{x}) &= \kappa_{15}x_1, & \pi_9(\mathbf{x}) &= \kappa_{51}x_5 \\ \pi_{10}(\mathbf{x}) &= \kappa_5x_5\end{aligned}$$

- The n -th element x_n of vector \mathbf{x} denotes the population of tetrachloroethylene in the n -th compartment.

Pharmacokinetic Networks

10

- If however we assume that tetrachloroethylene metabolism in the liver is saturable according to the [Michaelis-Menten mechanism](#), then

$$\pi_{10}(\mathbf{x}) = \frac{Vx_5}{K + x_5}$$

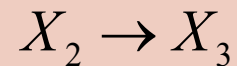
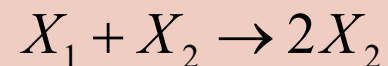
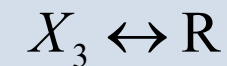
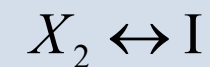
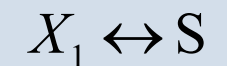
- This is a nonlinear hyperbolic propensity function.

https://en.wikipedia.org/wiki/Michaelis-Menten_kinetics

Epidemiological Networks

11

- These networks study the spread of infectious diseases or agents through a population of individuals.
- **SIR model:**
 - Susceptible (S) individuals.
 - Infected (I) individuals.
 - Resistant (R) individuals.
- We have 3 species and 2 reactions:



Epidemiological Networks

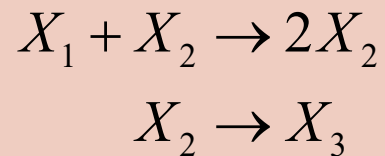
12

- We can assume that:
 - ▣ The probability of a randomly selected susceptible individual at time t to become infected by a randomly selected infectious individual during $[t, t + dt)$ is proportional to dt , with proportionality factor κ_1 that does not depend on the particular individuals involved.
 - ▣ The probability of a randomly selected infected individual at time t to become resistant to the disease during $[t, t + dt)$ is proportional to dt , with proportionality factor κ_2 that does not depend on the particular individual.

Epidemiological Networks

13

- In this case, the interactions lead to a Markovian reaction network with propensity functions:



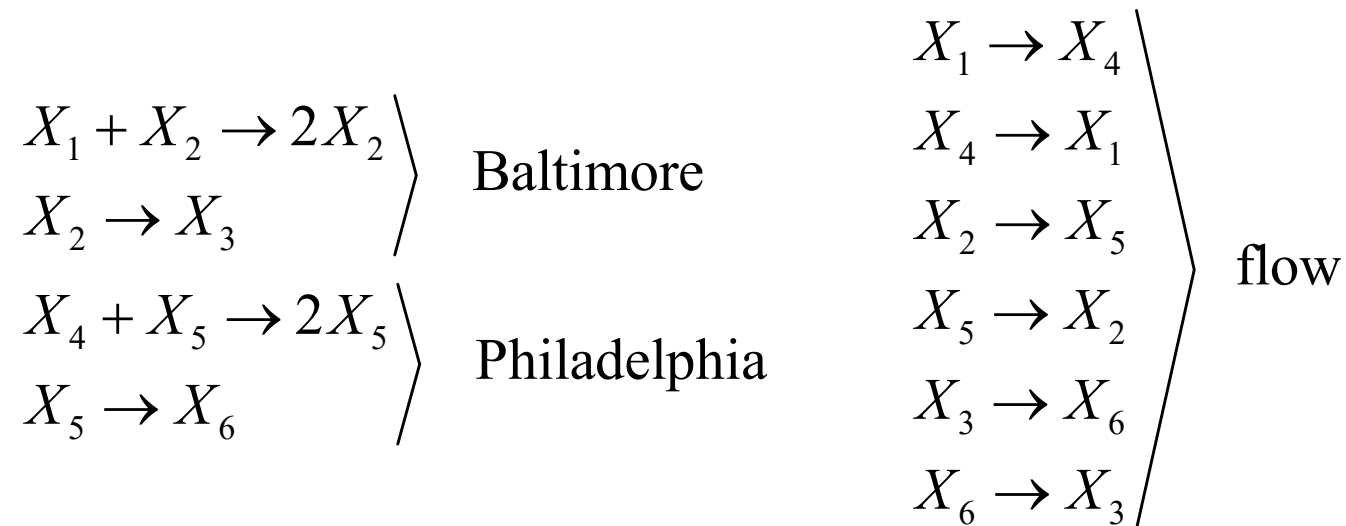
$$\begin{aligned} \pi_1(x_1, x_2, x_3) &= \kappa_1 x_1 x_2 \\ \pi_2(x_1, x_2, x_3) &= \kappa_2 x_2 \end{aligned}$$

- x_1, x_2, x_3 are the populations of the susceptible, infected and resistant individuals.

Epidemiological Networks

14

- A more complicated network involves two different cities and flow of individuals between these cities:



Ecological Networks

15

- Study interactions among organisms living in a particular ecosystem as well as between these organisms and nonliving physical components of the environment (air, soil, water, sunlight).
- Model how mass and energy are transferred from primary producers to predators.

Ecological Networks

16

- Food web comprised of:

X_1 : grass

X_2 : rabbits

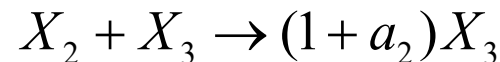
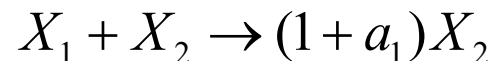
X_3 : wolves

- Let $X_1(t), X_2(t), X_3(t)$ be the net mass of grass, rabbits and wolves at time t .
- $X_1(t) = x$ means that, at time t , the mass of grass equals x -times some reference value (taken to be 1), and likewise for rabbits and wolves.

Ecological Networks

17

- We can assume that changes in mass distribution are caused by discrete steps in body size as predators eat prey, as well as by the mortality that comes with this process.
- We can model the predation of grass by rabbits and rabbits by wolves with the following reactions:

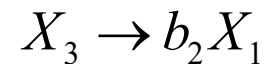
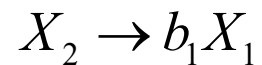


- $a_1, a_2 > 0$ are constants representing the conversion factors of mass.

Ecological Networks

18

- We can also model the fact that when rabbits or wolves die, for reasons other than predation, they fertilize the grass using the following reactions:



- $b_1, b_2 > 0$ are recycling constants.
- Consequently, we have a network with 3 species and 4 reactions.

Ecological Networks

19

- Under appropriate assumptions, the previous interactions lead to a Markovian reaction network with mass action propensity functions given by:

$$\pi_1(\mathbf{x}) = \kappa_1[x_1 \geq 1, x_2 \geq 1]x_1x_2$$

$$\pi_2(\mathbf{x}) = \kappa_2[x_2 \geq 1, x_3 \geq 1]x_2x_3$$

$$\pi_3(\mathbf{x}) = \kappa_3[x_2 \geq 1]x_2$$

$$\pi_4(\mathbf{x}) = \kappa_4[x_3 \geq 1]x_3$$

- The Iverson bracket $[P]$ is used to make sure that the reactions occur only when the net mass of a reactant species is at least as large as the corresponding reference value 1.

Social Networks

20

- Opinion formation in social networks.
- A group of interacting individuals in a social network that may support or dismiss an established theory.
- Individuals endowed with two separate opinions: a publicly pronounced and a privately held opinion for/against the established theory.

Social Networks

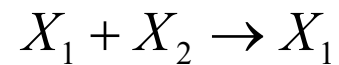
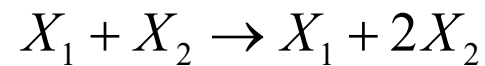
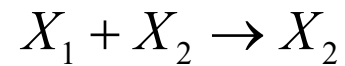
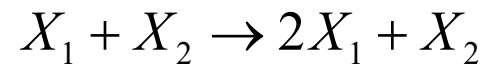
21

- Consider a fixed homogeneous group of $2L$ individuals who react in the same manner to a given situation.
- An individual holds simultaneously a public and a private opinion that each takes values $1/2$ (for the established theory) and $-1/2$ (against the established theory).
- X_1 is the net public opinion (sum of the publicly held opinions of all individuals).
- X_2 is the net private opinion (sum of the privately held opinions of all individuals).

Social Networks

22

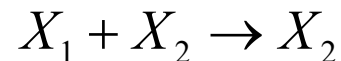
- We are dealing with 2 species interacting with 4 reactions:



Social Networks

23

□ Reactions



model the influence of net private opinion X_2 on the net public opinion X_1 that results in a single individual changing their public opinion in support of (first reaction) or against (second reaction) the established theory.

- In this case, the net private opinion remains unchanged, whereas, the net public opinion is increased by one in the first reaction [due to a value change from $-1/2$ (against) to $1/2$ (for)] and decreased by one in reaction 2 [due to a value change from $1/2$ (for) to $-1/2$ (against)].

Social Networks

24

□ Reactions

$$X_1 + X_2 \rightarrow X_1 + 2X_2$$

$$X_1 + X_2 \rightarrow X_1$$

model the influence of net public opinion X_1 on the net private opinion X_2 that results in a single individual changing their private opinion in support of (first reaction) or against (second reaction) the established theory.

Social Networks

25

- The following propensity functions have been suggested:

$$X_1 + X_2 \rightarrow 2X_1 + X_2$$

$$X_1 + X_2 \rightarrow X_2$$

$$X_1 + X_2 \rightarrow X_1 + 2X_2$$

$$X_1 + X_2 \rightarrow X_1$$

$$\pi_1(\mathbf{x}) = \kappa_1(L - x_1)\exp(a_1x_1 + a_2x_2)$$

$$\pi_2(\mathbf{x}) = \kappa_1(L + x_1)\exp(-a_1x_1 - a_2x_2)$$

$$\pi_3(\mathbf{x}) = \kappa_2(L - x_2)\exp(a_3x_1)$$

$$\pi_4(\mathbf{x}) = \kappa_2(L + x_2)\exp(-a_3x_1)$$

Social Networks

26

$$X_1 + X_2 \rightarrow 2X_1 + X_2$$

$$X_1 + X_2 \rightarrow X_2$$

$$X_1 + X_2 \rightarrow X_1 + 2X_2$$

$$X_1 + X_2 \rightarrow X_1$$

$$\pi_1(\mathbf{x}) = \kappa_1(L - x_1) \exp(a_1 x_1 + a_2 x_2)$$

$$\pi_2(\mathbf{x}) = \kappa_1(L + x_1) \exp(-a_1 x_1 - a_2 x_2)$$

$$\pi_3(\mathbf{x}) = \kappa_2(L - x_2) \exp(a_3 x_1)$$

$$\pi_4(\mathbf{x}) = \kappa_2(L + x_2) \exp(-a_3 x_1)$$

- x_1, x_2 represent the net values of all publicly and privately held opinions.
- $-L \leq x_1, x_2 \leq L$, where $-L$ and L represent total disapproval and total approval of the established theory.

Social Networks

27

$$X_1 + X_2 \rightarrow 2X_1 + X_2$$

$$X_1 + X_2 \rightarrow X_2$$

$$X_1 + X_2 \rightarrow X_1 + 2X_2$$

$$X_1 + X_2 \rightarrow X_1$$

$$\pi_1(\mathbf{x}) = \kappa_1(L - x_1)\exp(a_1x_1 + a_2x_2)$$

$$\pi_2(\mathbf{x}) = \kappa_1(L + x_1)\exp(-a_1x_1 - a_2x_2)$$

$$\pi_3(\mathbf{x}) = \kappa_2(L - x_2)\exp(a_3x_1)$$

$$\pi_4(\mathbf{x}) = \kappa_2(L + x_2)\exp(-a_3x_1)$$

- $a_1 \geq 0$ controls pressure inflicted on public opinion.
- $a_2 \geq 0$ controls the influence of privately held beliefs on publicly stated opinions.
- a_3 controls the reinforcement (for $a_3 > 0$) or the weakening (for $a_3 < 0$) effect that the net public opinion has on the net private opinion in support of the established theory.

Social Networks

28

- When the values of a_1 and a_3 vary, an abrupt change from supporting the established theory to no supporting this theory may occur.
- This is reminiscent to the well-known phenomenon of phase transition.
- Does this phenomenon occur in other networks?
- What is the cause of such abrupt transition?
- Is this associated with emerging complexity in Markovian reaction networks?

https://en.wikipedia.org/wiki/Phase_transition

Neural Networks

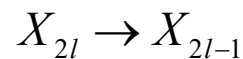
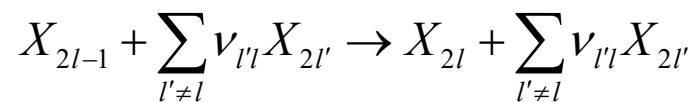
29

- We consider a model that consists of L neurons.
- Each neuron can be in either of two states: quiescent or active.
- X_{2l-1} denotes a quiescent neuron l .
- X_{2l} denotes an active neuron l .

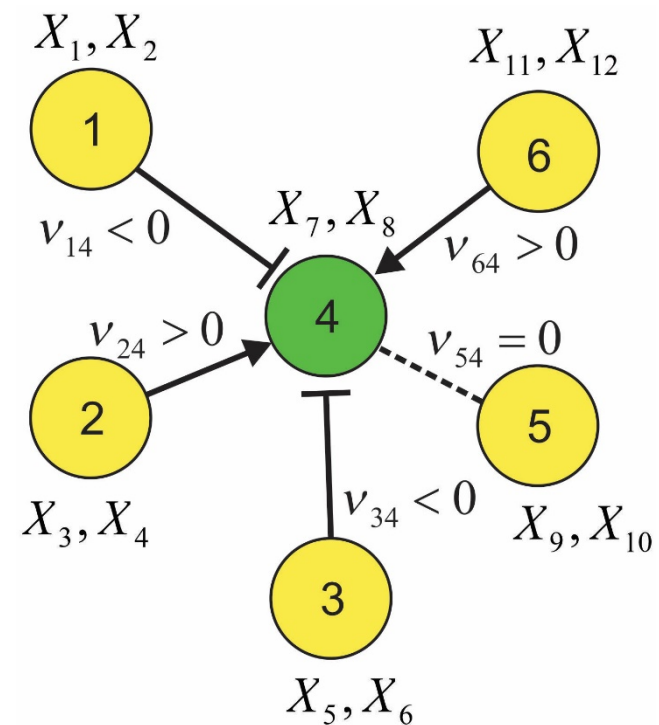
Neural Networks

30

- We assign the following two reactions to the l -th neuron:

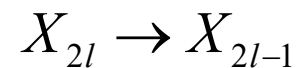
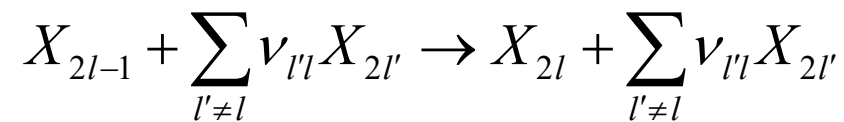


- ν_{ij} measures the synaptic weight between neurons i and j .
- A positive value of ν_{ij} indicates an excitatory synapsis and a negative value indicates an inhibitory synapsis.



Neural Networks

31



- The first reaction models transition of the l -th neuron from the quiescent to the active state.
- The second reaction models transition of the l -th neuron from the active to the quiescent state.
- We obtain a reaction network with $2L$ species and $2L$ reactions.

Neural Networks

32

- We can describe this system by a $2L \times 1$ state vector \mathbf{x} with binary-valued 0/1 elements x_{2l-1}, x_{2l} indicating the state of the l -th neuron (with 0 being quiescent and 1 being active).
- We must satisfy the “mass conservation” relationships:

$$x_{2l-1} + x_{2l} = 1, \quad \text{for } l = 1, 2, \dots, L$$

Neural Networks

33

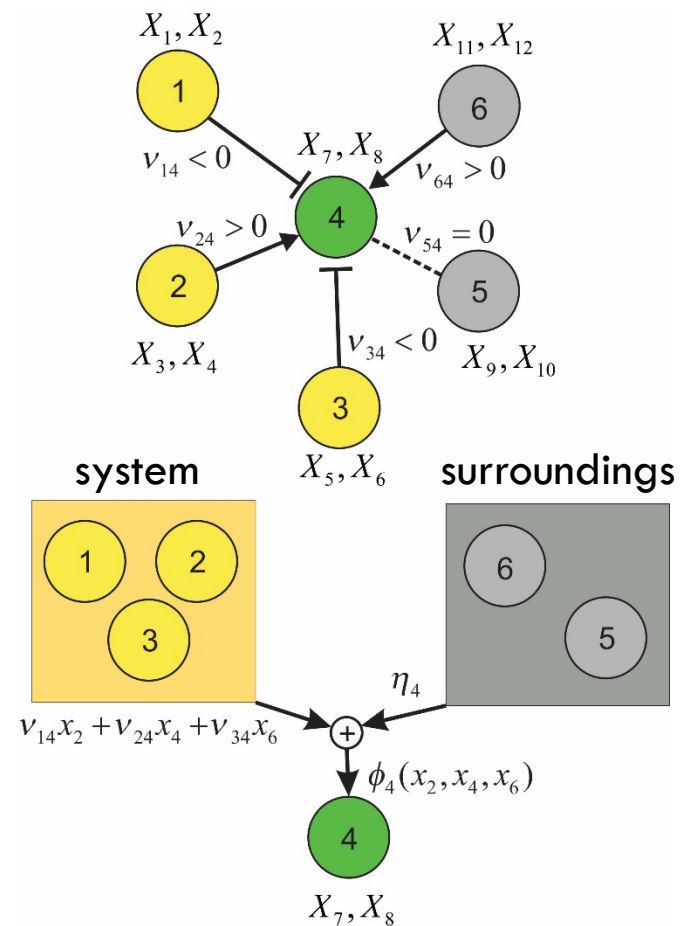
- It has been suggested that the probability of the l -th neuron becoming active during $[t, t + dt)$, given that the neuron is quiescent at time t , can be taken to be

$$x_{2l-1}[\phi_l(\mathbf{x}) > 0] \tanh[\phi_l(\mathbf{x})] dt$$

- $\phi_l(\mathbf{x})$ is the net synaptic input to the l -th neuron, given by

$$\phi_l(\mathbf{x}) = \sum_{l' \neq l} v_{ll'} x_{2l'} + \eta_l$$

external input



Neural Networks

34

$$X_{2l-1} + \sum_{l' \neq l} v_{ll'} X_{2l'} \rightarrow X_{2l} + \sum_{l' \neq l} v_{ll'} X_{2l'}$$
$$X_{2l} \rightarrow X_{2l-1}$$

- The propensity functions will now be given by

$$\pi_{2l-1}(\mathbf{x}) = x_{2l-1} [\phi_l(\mathbf{x}) > 0] \tanh[\phi_l(\mathbf{x})]$$
$$\pi_{2l}(\mathbf{x}) = \gamma_l x_{2l}$$

Multi-Agent Networks

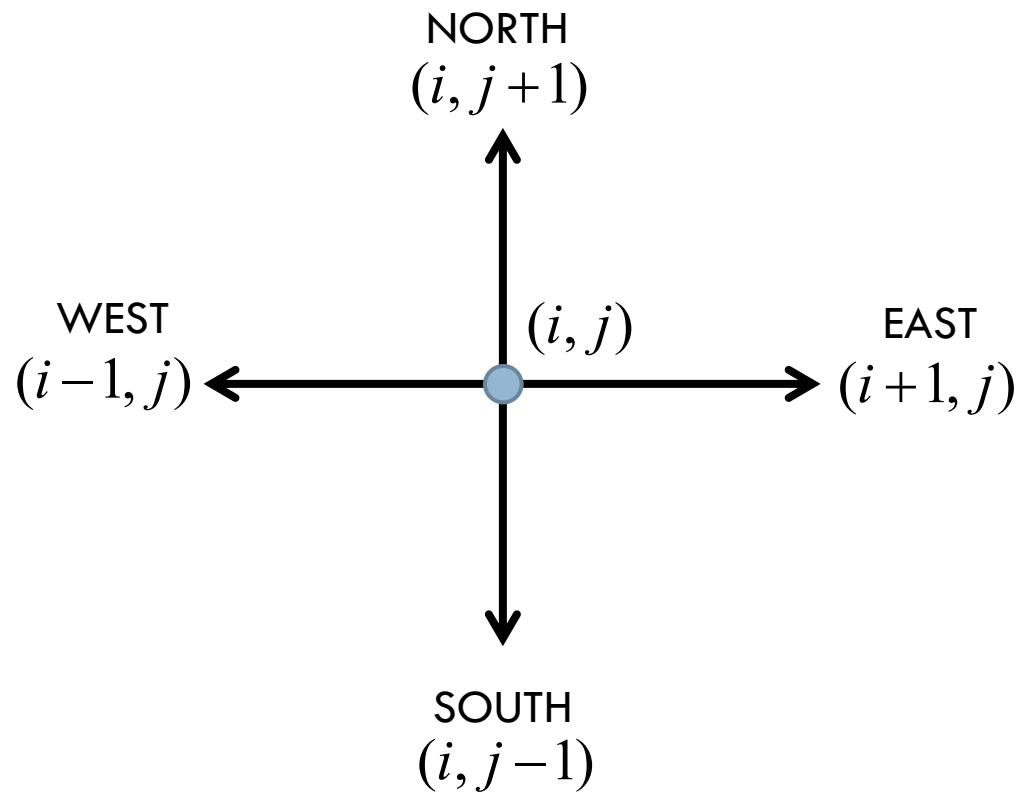
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- Systems of intelligent agents, such as autonomous vehicles, which observe and act upon their environment and interact with each other to achieve a certain goal.
- Consider a system of L autonomous unmanned vehicles (AUVs) that can move over a two-dimensional bounded rectangular space in a discrete fashion.

Multi-Agent Networks

36

- An AUV located at a discrete point (i, j) in space can move towards one of four possible directions:



Multi-Agent Networks

37

- Develop a model to describe vehicular motion so that the AUVs reach a spatial configuration \mathbf{x} at steady-state with desired probability $\rho(\mathbf{x})$.
- We want the probability mass function $\rho(\mathbf{x})$ to assign high probability over configurations that maximize a given design objective and low or zero probability over the remaining configurations.

Multi-Agent Networks

38

- Employ two species X_{2l-1} and X_{2l} whose populations x_{2l-1} and x_{2l} denote the position of the l -th AUV on the two-dimensional grid.
- We can characterize the motion of all AUVs by a multi-agent network comprised of $2L$ species and the following $4L$ reactions:

$$X_{2l-1} + X_{2l} + \sum_{l' \neq l} (X_{2l'-1} + X_{2l'}) \rightarrow 2X_{2l-1} + X_{2l} + \sum_{l' \neq l} (X_{2l'-1} + X_{2l'})$$

$$X_{2l-1} + X_{2l} + \sum_{l' \neq l} (X_{2l'-1} + X_{2l'}) \rightarrow X_{2l} + \sum_{l' \neq l} (X_{2l'-1} + X_{2l'})$$

$$X_{2l-1} + X_{2l} + \sum_{l' \neq l} (X_{2l'-1} + X_{2l'}) \rightarrow X_{2l-1} + 2X_{2l} + \sum_{l' \neq l} (X_{2l'-1} + X_{2l'})$$

$$X_{2l-1} + X_{2l} + \sum_{l' \neq l} (X_{2l'-1} + X_{2l'}) \rightarrow X_{2l-1} + \sum_{l' \neq l} (X_{2l'-1} + X_{2l'})$$

$$l = 1, 2, \dots, L$$

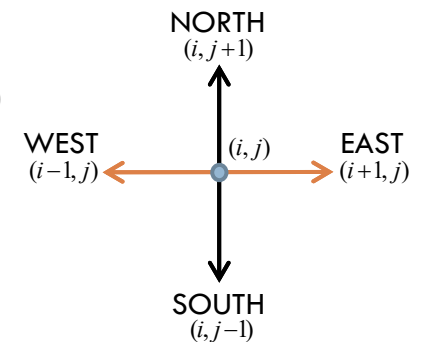
Multi-Agent Networks

39

- The reactions below model one-step motion of the l -th AUV towards east/west.

$$X_{2l-1} + X_{2l} + \sum_{l' \neq l} (X_{2l'-1} + X_{2l'}) \rightarrow 2X_{2l-1} + X_{2l} + \sum_{l' \neq l} (X_{2l'-1} + X_{2l'})$$

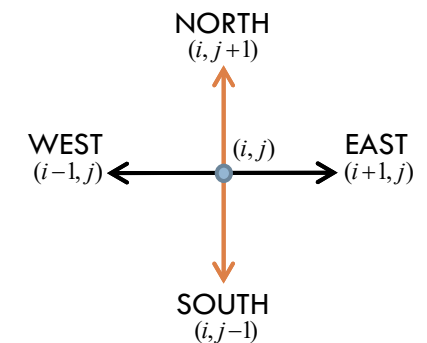
$$X_{2l-1} + X_{2l} + \sum_{l' \neq l} (X_{2l'-1} + X_{2l'}) \rightarrow X_{2l} + \sum_{l' \neq l} (X_{2l'-1} + X_{2l'})$$



- The reactions below model one-step motion of the l -th AUV towards north/south.

$$X_{2l-1} + X_{2l} + \sum_{l' \neq l} (X_{2l'-1} + X_{2l'}) \rightarrow X_{2l-1} + 2X_{2l} + \sum_{l' \neq l} (X_{2l'-1} + X_{2l'})$$

$$X_{2l-1} + X_{2l} + \sum_{l' \neq l} (X_{2l'-1} + X_{2l'}) \rightarrow X_{2l-1} + \sum_{l' \neq l} (X_{2l'-1} + X_{2l'})$$



Multi-Agent Networks

40

- Let us define the potential energy $\bar{V}(\mathbf{x})$ of the reaction system being in configuration \mathbf{x} at steady-state by

$$\bar{V}(\mathbf{x}) = \begin{cases} -\ln \frac{\rho(\mathbf{x})}{\rho(\mathbf{x}_*)}, & \text{for } \mathbf{x} \in \mathcal{D} \\ \infty, & \text{otherwise} \end{cases}$$

- \mathcal{D} is the set of all permissible vehicle configurations.
- $\mathbf{x}_* \in \mathcal{D}$ is a configuration of zero potential energy, taken to be the one with the highest probability $\rho(\mathbf{x})$.

Multi-Agent Networks

41

- Given that $\mathbf{X}(t) = \mathbf{x}$, we will assume:
 - ▣ The probability that the l -th AUV initiates motion within $[t, t + dt)$ is proportional to dt , with proportionality factor κ_l .
 - ▣ Given that the l -th AUV initiates motion during $[t, t + dt)$, it moves EAST with probability $\sim \exp\{-\bar{V}(\mathbf{x} + \mathbf{s}_{4l-3})\}$, where \mathbf{s}_m is the m -th column of the net stoichiometric matrix of the reaction network.

Multi-Agent Networks

42

- The parameter κ_l controls the rate by which the l -th vehicle initiates motion.
- The probability $\sim \exp\{-\bar{V}(\mathbf{x} + \mathbf{s}_{4l-3})\}$ implies that the AUV will be moving EAST with higher probability if the motion produces a larger reduction in potential energy.
- We can make similar assumptions for vehicle motion in the other three directions.

Multi-Agent Networks

43

- It turns-out that the resulting reaction network is Markovian with propensity functions:

$$\pi_m(\mathbf{x}) = \kappa_l e^{-\bar{V}(\mathbf{x} + \mathbf{s}_m)}$$

for $m = 4l - 3, 4l - 2, 4l - 1, 4l$, $l = 1, 2, \dots, L$.

- The resulting master equation governing the population process $\mathbf{X}(t)$ has a unique stationary distribution $\bar{p}_X(\mathbf{x}) = \lim_{t \rightarrow \infty} p_X(\mathbf{x}; t)$, which is given by the [Gibbs distribution](https://en.wikipedia.org/wiki/Gibbs_distribution) of statistical physics

$$\bar{p}_X(\mathbf{x}) = \frac{1}{\zeta} e^{-\bar{V}(\mathbf{x})}$$
$$\zeta = \sum_{\mathbf{x}} e^{-\bar{V}(\mathbf{x})} \quad (\text{partition function})$$

https://en.wikipedia.org/wiki/Gibbs_measure

Multi-Agent Networks

44

$$\bar{V}(\mathbf{x}) = \begin{cases} -\ln \frac{\rho(\mathbf{x})}{\rho(\mathbf{x}_*)}, & \text{for } \mathbf{x} \in \mathcal{D} \\ \infty, & \text{otherwise} \end{cases}$$
$$\bar{p}_X(\mathbf{x}) = \frac{1}{\zeta} e^{-\bar{V}(\mathbf{x})}$$
$$\zeta = \sum_{\mathbf{x}} e^{-\bar{V}(\mathbf{x})}$$

- From these equations, we have that $\bar{p}_X(\mathbf{x}) = \rho(\mathbf{x})$, as desired.