

Computational Systems Biology
Karthik Raman
Department of Biotechnology
Indian Institute of Technology – Madras

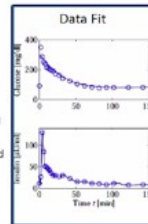
Lecture – 07
Some Example Models

In today's video, we will look at some example models which are interesting because you want to understand whether you know a model is mechanistic or dynamic or stochastic and so on and what are the assumptions that go into a model. So, to fixate all the ideas that we looked at in the last few videos, let us look at a few interesting example models.

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Insulin-Glucose Dynamics (*The Minimal Model*)

- **What does it model?**
 - The concentrations of interstitial insulin and glucose over time, and the interactions between the two.
- **What does it neglect?**
 - The reaction of the pancreas to glucose, among many other finer, sub-first-order interactions.
- **Characteristics of the Model**
 - **Mathematical**
 - **Deterministic** – The result and equation are deterministic for a given person
 - **Closed** – All necessary interactions are encompassed within the model
 - **Correlative** – The curve is fit and equations are derived based on experimental values
 - **Empirical** – The models are typically tested with data from experiments where glucose is injected intravenously and insulin and glucose concentrations are measured at regular time intervals.
 - **Continuous** – The result is a differential equation, which can provide concentrations of insulin and glucose at any given time, given the initial concentrations.
- **Salient Features of the Model**
 - **Two compartment model** – Lowest complexity known to model this system
 - Parameters change depending on the person
 - Use in diagnosis and in patient treatment
 - Should ideally lead to an artificial pancreas in the future
- **Mathematics of the model**



$$\frac{dx_1}{dt} = -(p_1 + x_2)x_1 + p_1 g_e \quad ; \quad \frac{dx_2}{dt} = -p_2 x_2 + p_3 (u - i e)$$

where g_e and i_e represent the equilibrium values of glucose and insulin, x_1 is the concentration of blood glucose and x_2 is proportional to the concentration of interstitial insulin. p_1 , p_2 and p_3 are parameters defined by the characteristics of the person of interest.

Welcome back, let's just take a closer look at some nice example models and try to understand various aspects of it, you know the modelling process that we discussed earlier about what is the scope, whether it's a continuous model, empirical model, correlatory model, dynamic model and so on. This is a classic very, very simple model of insulin-glucose dynamics.

It is a minimal model. What does it model? It just models interstitial insulin and glucose over time and the interactions between the two. It neglects so many other things, right? Now, there is pancreas, there is glucagon and there is a very complicated signalling network, there is some receptors involved. All that is ignored. It's a very, very simple simplified model of what happens to glucose and insulin.

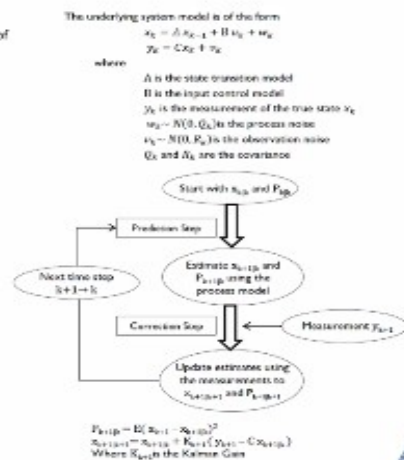
So, this is a deterministic model. No stochasticity is considered. It's a closed model, It's a correlative model. It's also somewhat empirical in the sense, it's not a mechanistic model, it's continuous of course because it varies with time and it's considered as a two compartment model. You have one box with glucose, one box with insulin. It is a two compartment model and very simple equations, right? Just two differential equations to explain.

So, this is a very simple example, this is a kind of what I want you to work on in your assignment, your first assignment where you want to make a single slide about a particular model.

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Kalman Filter

- Kalman filter is an empirical model used in finding a statistically optimal state estimates of the system from noisy input data.
 - It is a recursive estimator with two phases.
- Assumption**
- The underlying system dynamics is linear.
 - All noises have a Gaussian distribution.
- Applications**
- Navigation systems
 - Time series analysis
 - Radar tracker
- Advantages**
- It can run real time with present input measurements and previous state estimate.
 - There is no need for storage of past estimates.
- Disadvantages**
- Most noises are not gaussian.
 - Covariance of noise cannot be easily estimated.



Another example is the Kalman filter which is till date remains a very, very popular model for handling noise and so on, so I will not go through the details.

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Gambler's Ruin

- Stochastic model that employs random walks to predict the outcome of a game of gambling
- Parameters in the model are the probabilities of winning and losing a particular game, say p and q and the amount placed as bet by the gambler
- For a given initial amount of money the model predicts whether the gambler reaches his/her objective or goes broke
- This model can be reduced to a Markov chain:
for an initial state i , the probability of reaching a state a , before state b based on p and q



Figure showing the chain when the objective is 4 and stakes are of worth 1

- Model used to predict probability of win/ruin in a fair game, i.e $p=q=0.5$ when
 - Opponent is infinitely rich
 - Stakes are increased or reduced



But this is another example model which talks about Gambler's ruin. It's a stochastic model that employs some random walks to predict what happens in a game. Similarly, a very good example is you can actually model a tennis game. So, you can have just setup a Markovian process wherein you have every state will be a particular score in the game and you can transit to different states and similarly, you can have a set of states for the match and so on and so forth.

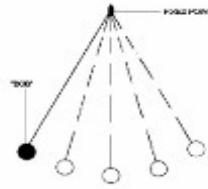
So and this is potentially a model. You say that a player 1 wins with a probability P and player 2 wins with probability $1 - p$ and you can actually set up equations and say what is the probability of player 1 winning the match, right? That can be derived based on, so that would be a, it would be a stochastic model because each time you run it, you will get a different set of results.

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Newton's model of Motion

A continuous and analytical model developed by Isaac Newton to describe the motion of bodies due to forces.

Governing Equations



Limitations

Applications

- This model is governed by the three laws of motion developed by him:
 - Every body persists in its state of being at rest or of moving uniformly straight forward, except insofar as it is compelled to change its state by force impressed
 - The alteration of motion is ever proportional to the motive force impress'd; and is made in the direction of the right line in which that force is impress'd.
 - To every action there is always an equal and opposite reaction: or the forces of two bodies on each other are always equal and are directed in opposite directions.

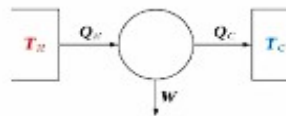
Isaac Newton, The Principia, A new translation by I. D. Cohen and A. Whitman, University of California press, Berkeley, 1999.

- Small particles and velocities close to the speed of light cannot be handled by this model.
- The conservation of momentum was derived using the third law from the first section. An analytical explanation could not be given for Kepler's laws.

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Model: The Carnot Engine

- It is a continuous and theoretical system. First proposed by Sadi Carnot (1796-1832).



- Follows laws of thermodynamics;
- Carnot efficiency = $1 - (T_h/T_c) = 1 - (Q_h/Q_c)$ (Where h-heat in; c-heat out);
- $dS = dQ/dT$ and Clausius inequality are notable contributions that came out of this model;

- Carnot engine, though hypothetical, gave a great deal of theoretical understanding and mathematical equivalents for each concept, in thermodynamics, and helped us to understand the concept of entropy in particular.
- It gave engineers an upper limit, a functional end point, a limit that can be achieved by any heat engine.
- But Carnot engine considers uniform resistance and absence of friction thus equations derived have to be modified to include friction.

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Zipf's law

- Empirical law in statistics. Originally found to describe word frequencies (1932) and city sizes (1949)
- Discrete power law distribution. $\log cf_i = \log c + k \log i$
 i = rank, cf_i = collection frequency

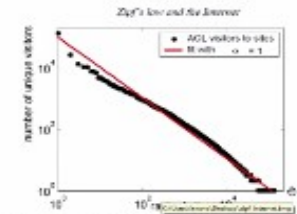


Figure 3. Sites ranked by the number of unique AOL visitors they received Dec. 2000. AOL, America Online, is the largest Internet service provider in the United States. The fit is a Zipf distribution, $\alpha = 1$.

Superseded Pareto distributions and provided a more general framework to Benford's law (financial fraud etc.)

Describes features of social networks such as the Internet; even used in web-caching strategies.

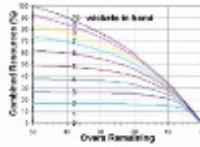
Unlike Gaussian distributions, the
are scale-free

Good old Newton's model of motion or the Carnot engine. Zipf's law, this is actually a very interesting law particularly in the context of what we will study couple of classes down the line. So, this study is the word frequencies in English text, so what it finds, what do you see? What do you see here? It is a power law kind of thing, right? So, you have the log-log plot. It's linear, so for, okay this is the internet but this doesn't actually describe Zipf's law.

The Zipf's law was originally for word frequencies. So, what would you expect if you looked at word frequencies in the English language? You will have few words that are repeated an astronomical number of times and the rest of the words all have much lower frequencies and so on. So, majority of the words will have very low frequencies and a few words like, "A", "the", prepositions and so on and some other you know conjunctions all of those will have a very high usage. So, you end up finding a power law kind of distribution and this is something we will see in biological networks as well as we go on.

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Duckworth-Lewis Model



- The basic principle is that each team in a limited-overs match has two available resources: wickets remaining and overs to play
- Attempts to set a statistically fair target for the second team's innings, based on the score achieved by the first team, taking their wickets lost and overs played into account
- In 2004, the D/L method was split into a Professional Edition and a Standard Edition
- The Standard Edition preserves the use of a single table and simple calculation
- The Professional Edition uses substantially more sophisticated statistical modelling, and requires the use of a computer (used in ODIs)

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Of course, Duckworth Lewis, right? Our favourite model. So, essentially there are various ways to characterise these models, so you want to understand deterministic, stochastic, dynamic and empirical, correlative, mechanistic all of these things is what you need to think of when you analyse any model, when you want to understand the characteristics of a model. So, this is just a basic recap of what we did earlier.

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Topics covered

- ▶ Some Example Models

In the next video ...

- ▶ How to represent biological networks?
- ▶ SBGN

So, with this, we have sort of done with some of the fundamentals of mathematical modelling. So, in the next video, let's start looking at how we represent biological networks and something known as SBGN or systems biology graphical notation.