Computational Systems Biology
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Lecture – 08
Representation of Biological Networks

So, let's now switch gears and start looking at biological networks and start with a very simple introduction to how do we represent biological networks and what kind of standards people have been developing for representing biological networks, in particular we will look briefly at something known as SBGN or systems biology graphical notation. How do you represent biological networks?

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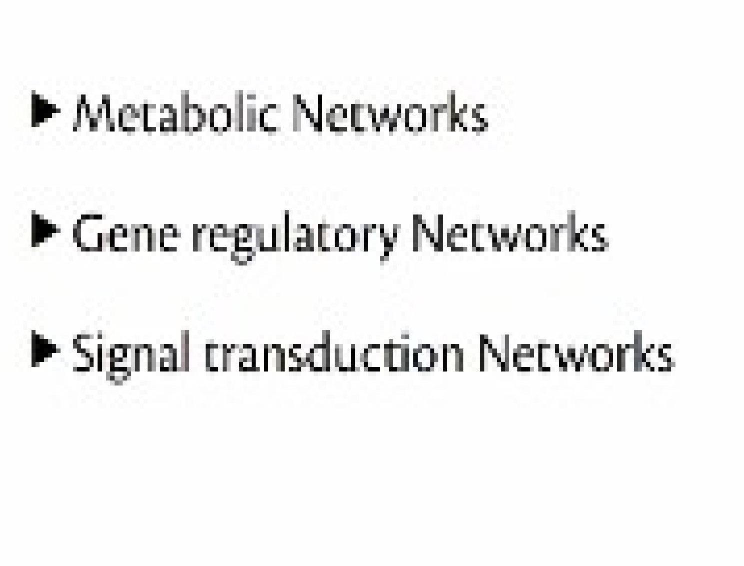

So, there are different types of networks that you observe in biology. You have metabolic networks which essentially catalogue the interactions between genes, proteins in fact, mostly proteins, metabolites and so on, so which reaction produces what. Then gene regulatory networks which essentially talk about which gene regulates what other gene, we will look at these in much more detail a little later on.

Signal transduction networks where the molecules are again proteins, small molecules but which can end up influencing any of the previous two processes. It can influence metabolism, it can influence gene transcription and so on. Protein interaction networks and so forth.

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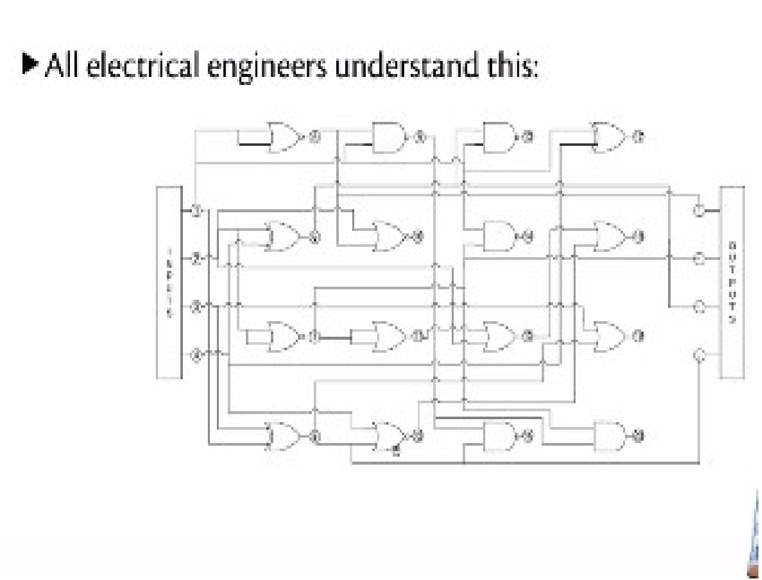

How do you represent these networks? So we will talk about graph theory shortly before we get into graph theory, how do you even represent these, how do you draw these networks, right? Because if you look at the rest of engineering, outside of biological engineering you will see there are fantastic standards. For example, all engineers understand this or even non electrical engineers would understand what this is.

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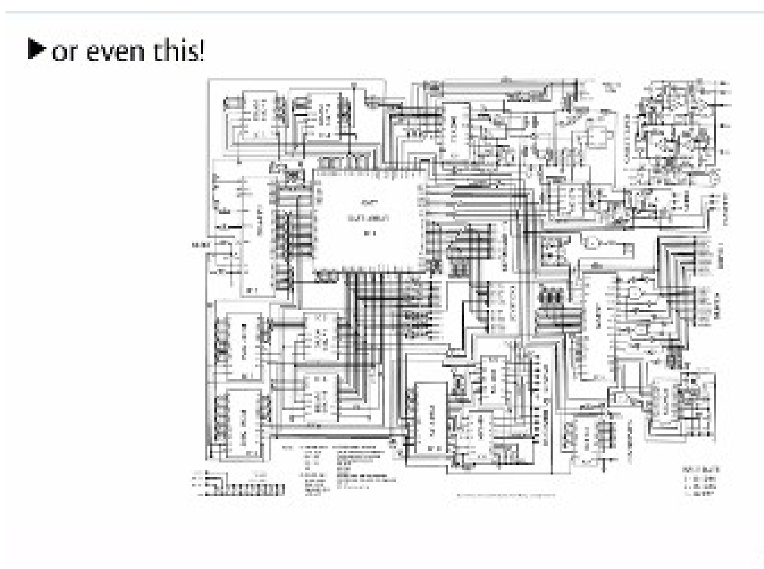

You know what is a AND gate, what is a NAND gate, what is an OR gate, what is a NOR gate and so on or even something as complex as this. This is not too difficult to understand for an electrical engineer I presume.

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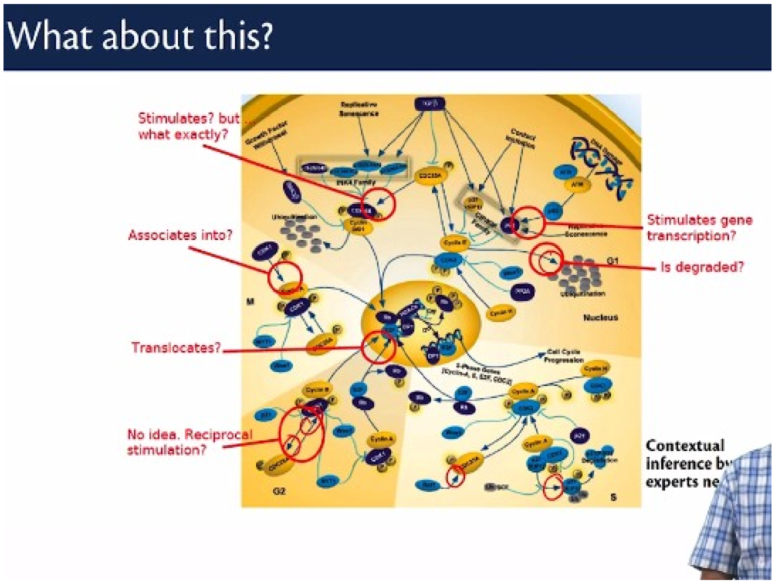

Whereas, what does this mean? This is a very iffy picture where the same arrow could be in multiple things. It could mean stimulates, it could mean associates, it could mean goes into this compartment and so this could be like reciprocal stimulation that you see here, this could be a translocation and so on and so forth. In fact, the same arrow and it's all represented by the same arrow, right? And the same arrow has taken on so many different meanings in this very slide, very picture.

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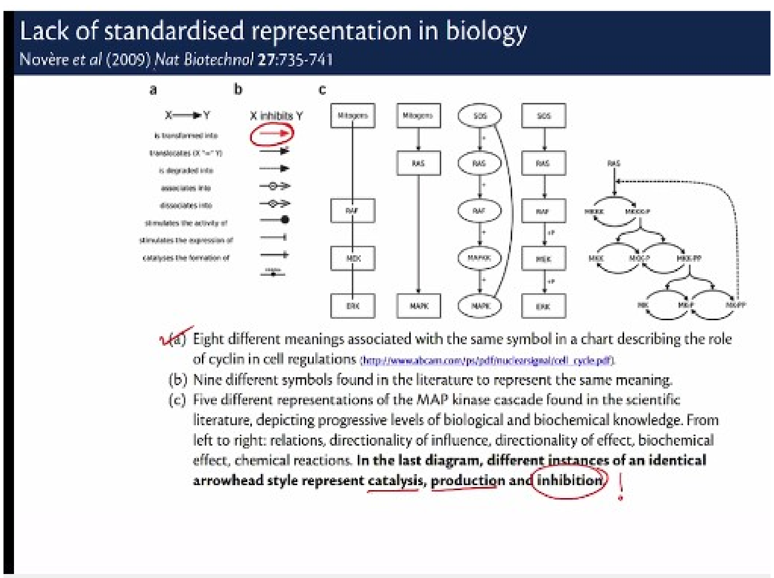

So, you need contextual inference by experts. So, there was a lot of argument and discussion about this and if you see more examples of the same thing just, so this is what we have already seen, eight different meanings associated with the same symbol and there are nine different symbols that have been found in some other picture. Look at this, for inhibition, there are so many different ways that one can represent inhibition.

The worst of them being a red arrow because when you print it in a paper, it gets mangled, when you make a black and white print and so on. So, all these become problems and here there are five different representations of the very same pathway, the MAP kinase pathway, a very popular path way, very popular signalling path way. And in the last diagram, you see the different instances of an identical arrowhead represent depending upon the case, catalysis, production or even inhibition.

So, it gets really challenging to read these figures, right? How do we make these figures? However I like to do it. So, a grad student make this nice figure and it just goes into the paper. There is no real gold standard which is normally followed which is what is addressed in this paper. I think you can take a look at this paper.

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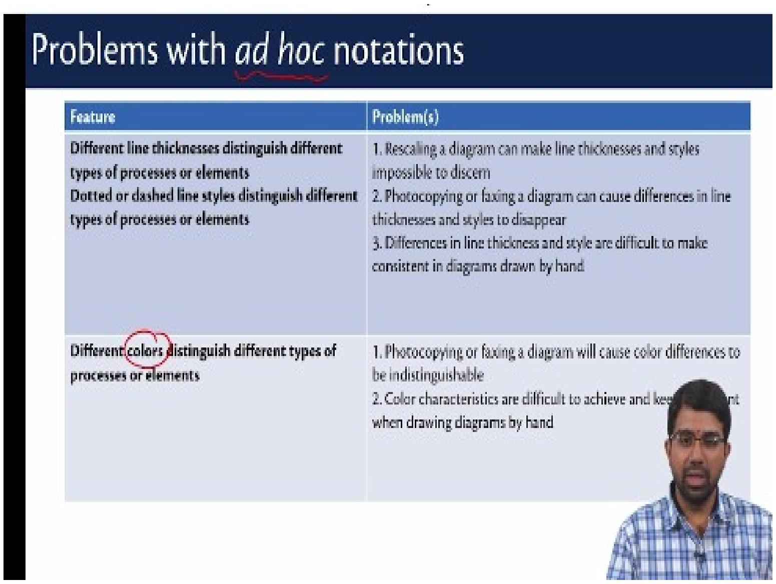

So, what are the problems? You have different line thicknesses to distinguish different kinds of process. Dotted or dashed lines distinguish different types of process and worst is different colours. And you can obviously imagine that all these will get mangled over a period of time, when you start photocopying and transmitting and so. And all these notations are adhoc, there is no standard.

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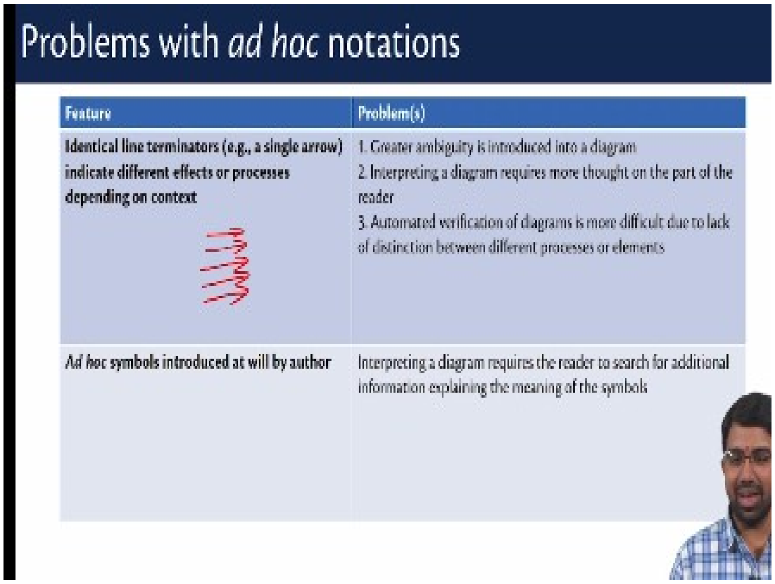

So, then and there are some more issues. In fact, adhoc symbols introduced at will by an author and identical line terminators which could mean different things. We just saw, right? This all these arrows mean different things depending upon where they are used. They all look the same but they all have a different meaning depending upon where they are used.

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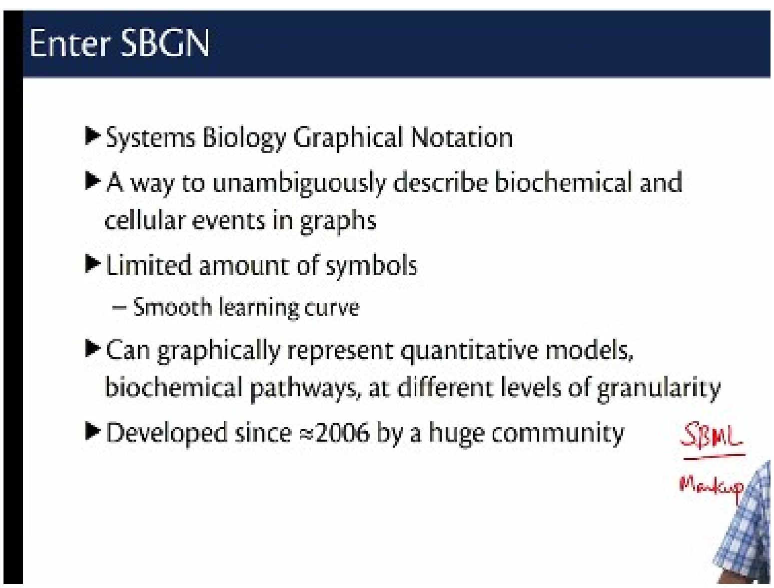

So, to basically surmount this issue where came SBGN, it stands for Systems Biology Graphical Notation. It’s a way to unambiguously describe biochemical and cellular events in graphs.

Limited amount of symbols therefore, you have a smooth learning curve and you can graphically represent several quantitative models of biochemical pathways at different levels of granularity. And this has been developed for the last ten plus years by a huge community which overlaps significantly with the SBML community.

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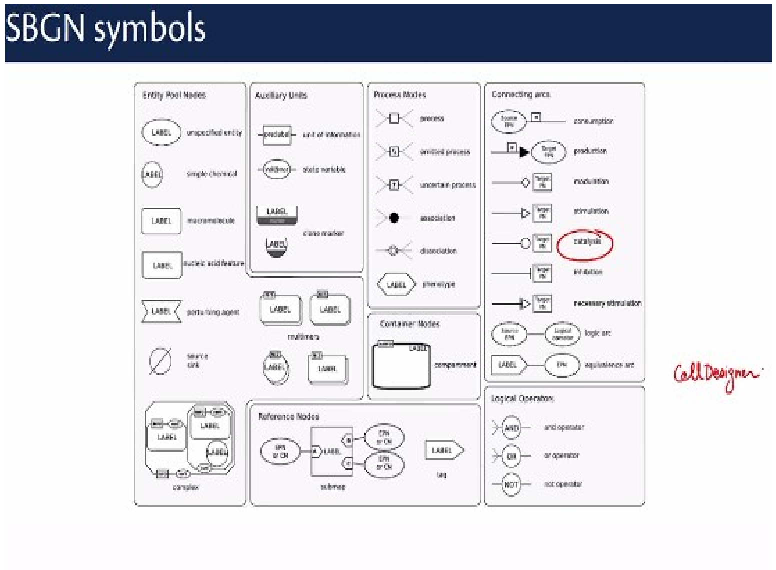

SBML stands for Systems Biology Markup language. So, we will try to look at an SBML file soon as well but for now, let's look at how SBGN works. This is all the symbols that you have in SBGN. So, this tries to surmount all the difficulties you had in previous methodologies for drawing, which was basically adhoc. Here you have a set of standards, you know that reactions have to happen in a particular way.

Catalysis has to happen in this fashion. AND, OR or NOT are expressly mentioned. And you have different types of node shapes for different kinds of molecules. This is some sort of a standard. The idea is to bring in some sort of engineering type language into biological graphics, biological diagrams, which is usually non-existent. So, if you see there are some nice papers you still the penetrance of this is occasionally not great.

So, you still do see papers where you have the same old arrows but you incrementally see a lot of papers starting to use these kinds of nice arrows and Cell Designer is one software which gives you very good access to this entire spectrum of symbols and arrows and so on but in practice, you have many different representations.

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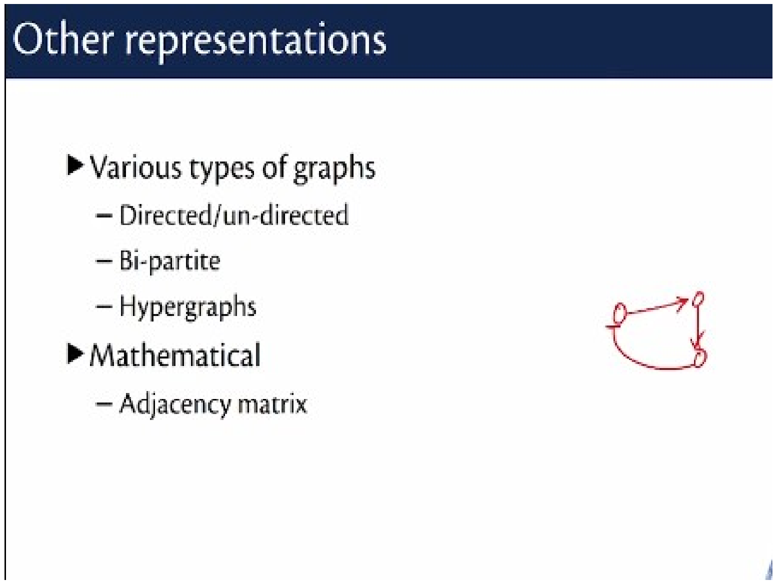

And we need to talk about the different types of graphs that exist, we will look at these shortly. And also the mathematical representations of various types of graphs. This brings us to what is a graph really? I think some of you are already familiar with graph theory but I will go over a formal introduction to graph theory. So, this is how graph looks like, so you typically have nodes and edges.

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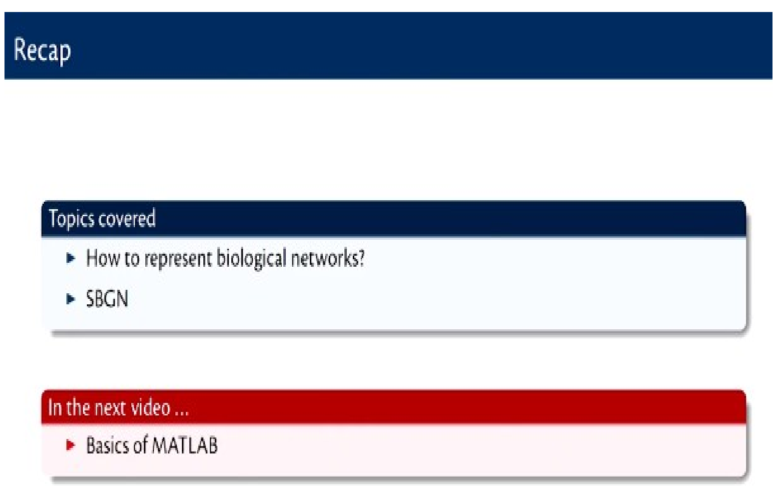

So, in today's video, we had a brief overview of how one tries to represent biological networks and how there are not really very good standards that have been used in the past by many authors but there is an evolving standard quality SBGN which is what we must use in the future to represent any biological network that you might work with in this course. So, in the next video, we will look at, we will do a lab where in we will cover the several basics of MATLAB.

We will do a series of videos wherein we look at a brief introduction to how we go about using MATLAB for systems biology.