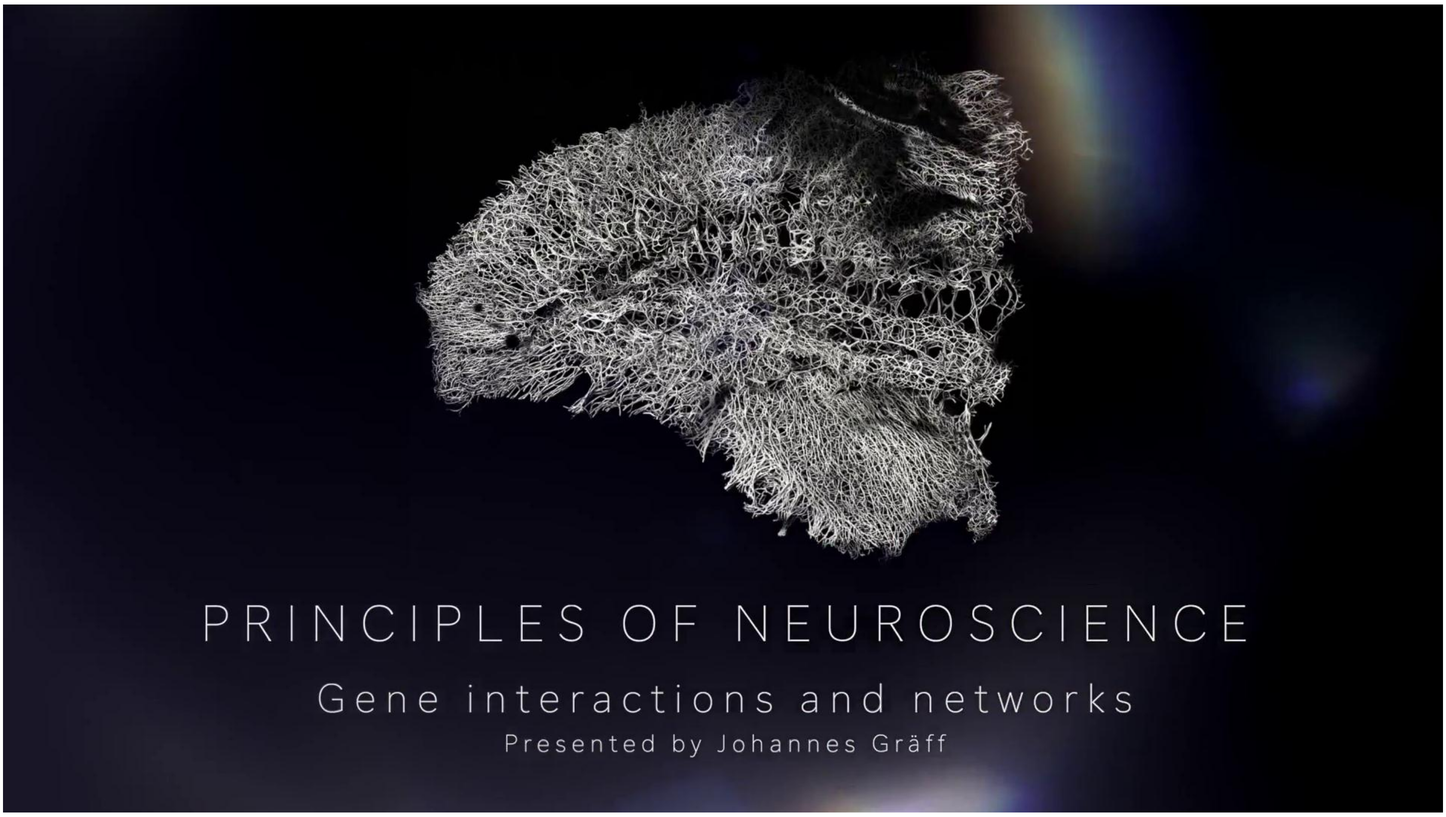

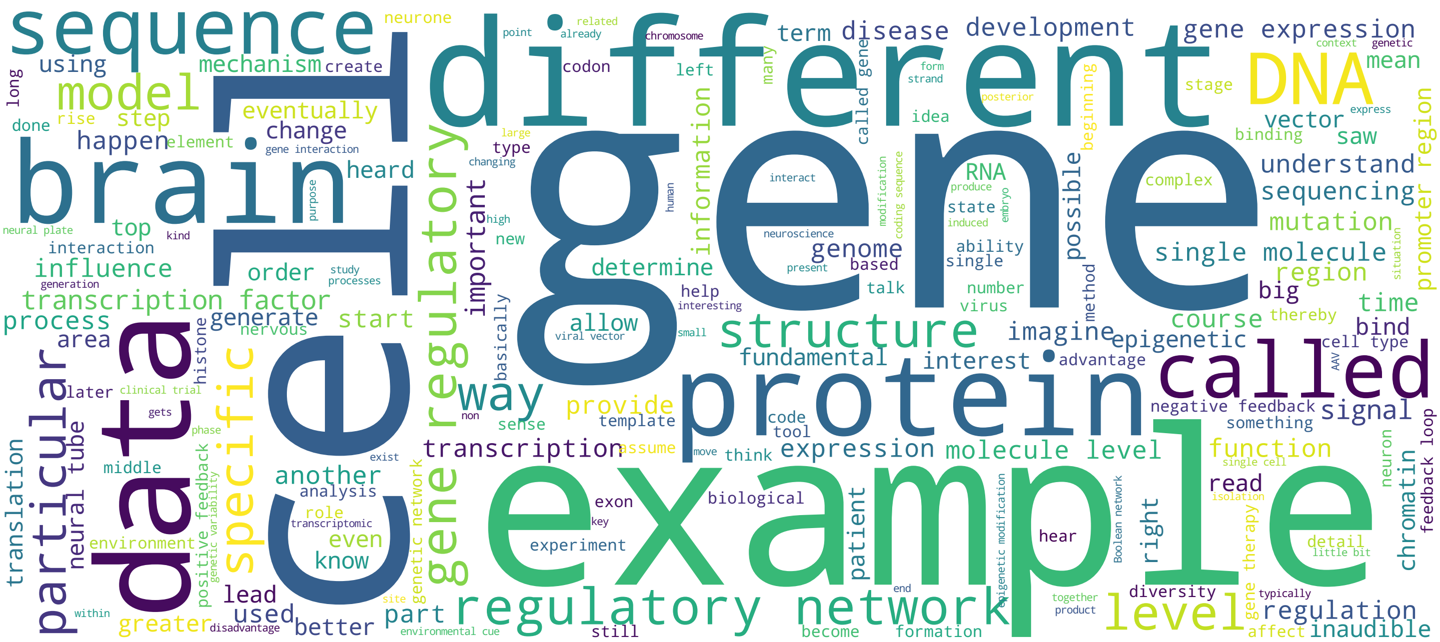

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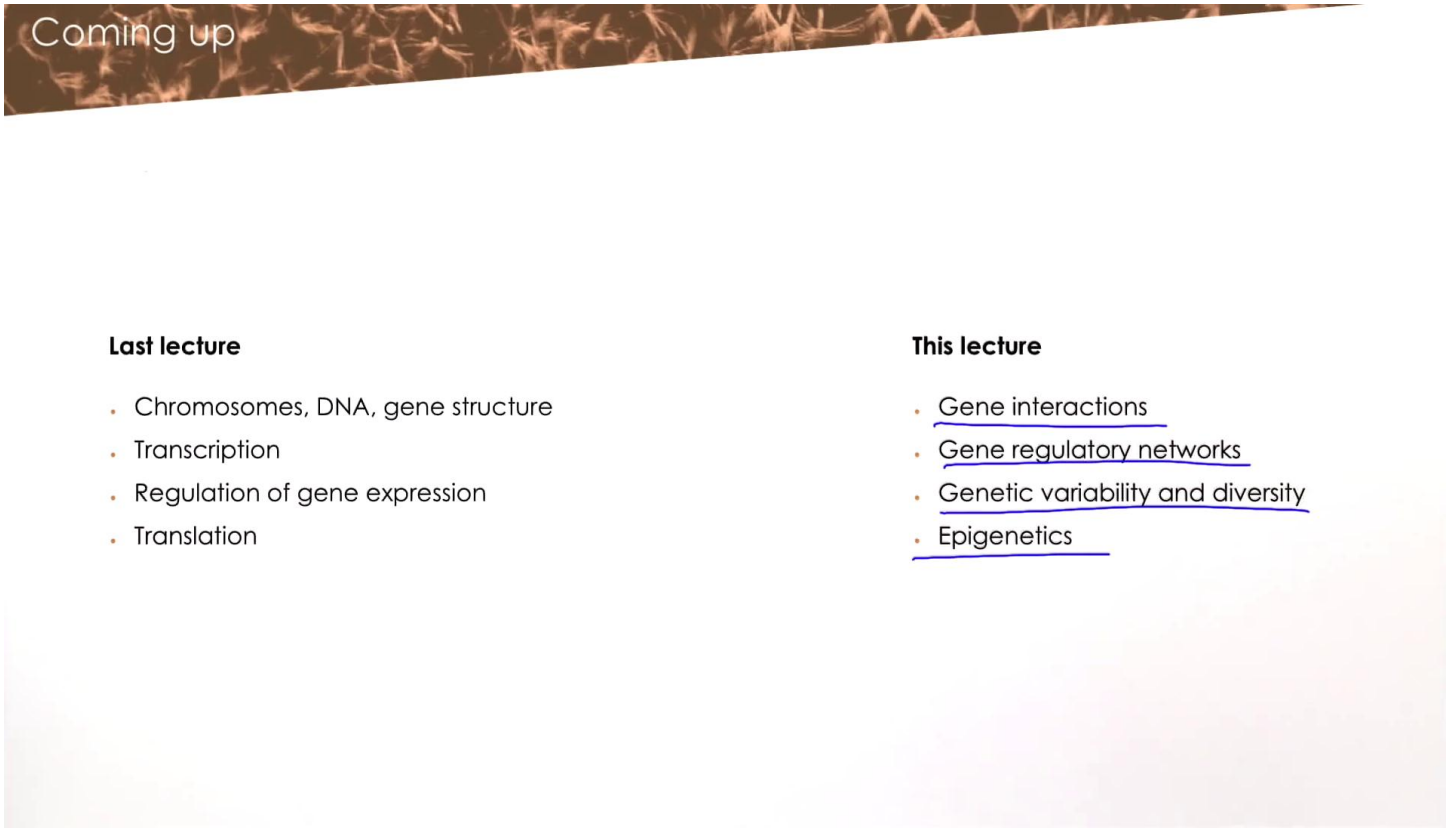
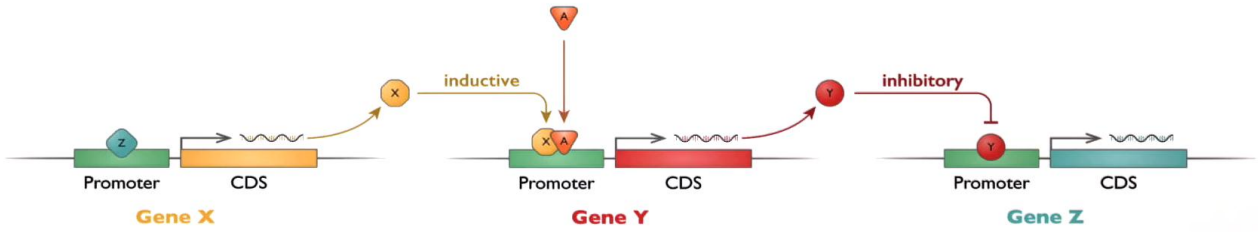


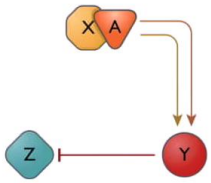
All right. In the last lecture, we heard about chromosomes, we heard about the DNA, we heard about chromatin and we heard about the gene structure, and we saw the essential steps of transcription which then leads to the regular of gene expression, and we briefly touched upon the final step on the way from a gene to a protein, which is the process of translation. In today's lecture, we're going to delve deeper into gene interactions and see how one gene can influence the expression of another, which leads then to the notion of so-called gene regulatory networks which are intricate interplays between different gene nodes, positive negative feedback loops and how the environment plays into this. We are then going to hear about genetic variability and diversity, its purpose on an evolutionary timescale and its importance for medicine. Finally we're also going to hear how genes can be tightly regulated in terms of their expression level by the mechanisms of epigenetics.

Notes

Summary

0m 10s





Gene interactions start with just one gene. We can imagine a gene X with its coding sequence in yellow and with its promoter region. We can further assume that upon the binding of a transcription factor C, the transcription of X is stimulated and ultimately gene X will be translated into a protein X. Now, gene X doesn't exist in isolation but will then also interact with a second gene which is called gene Y. Now, gene Y is thereby under the influence of gene X. If we now assume that gene X codes for a transcription factor, then this will lead to an inductive regulation of gene Y by gene X such that gene X, its protein, will bind to the promoter region of gene Y upon binding of which then the transcription and translation of Y is stimulated. Life is not always easy, so we can further imagine that gene Y is also under the influence of a core transcription of the regulator called A, which stipulates that both X and A in interaction are not to underpromote a region of Y will influence the transcription of Y. Now let's continue along this thought process and imagine that gene Y, which is induced by gene X and protein A will have an inhibitory effect of gene Z. Gene C is under a negative control of gene Y.

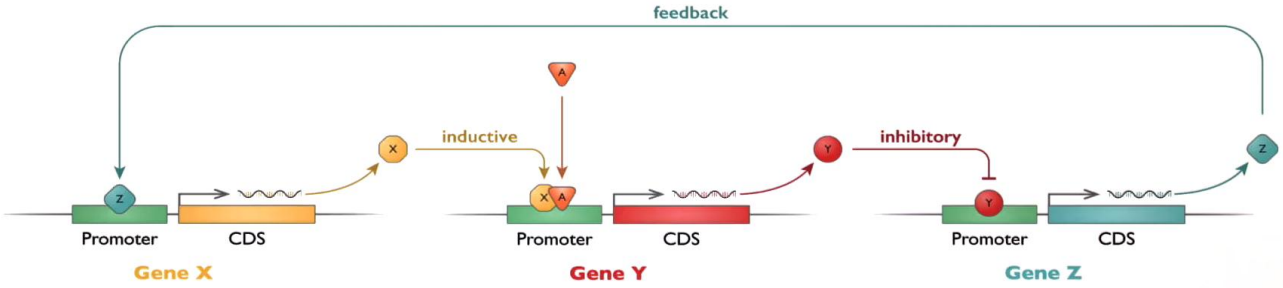
Notes

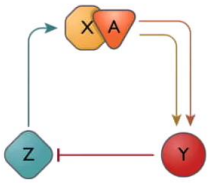
Summary

1m 16s

Gene interactions & networks

Genes, proteins, other molecules inside the cell, intra- and inter-cellular interactions, and the external environment all affect a given trait.
These interactions can be used to help understand the structure of complex genetic networks.



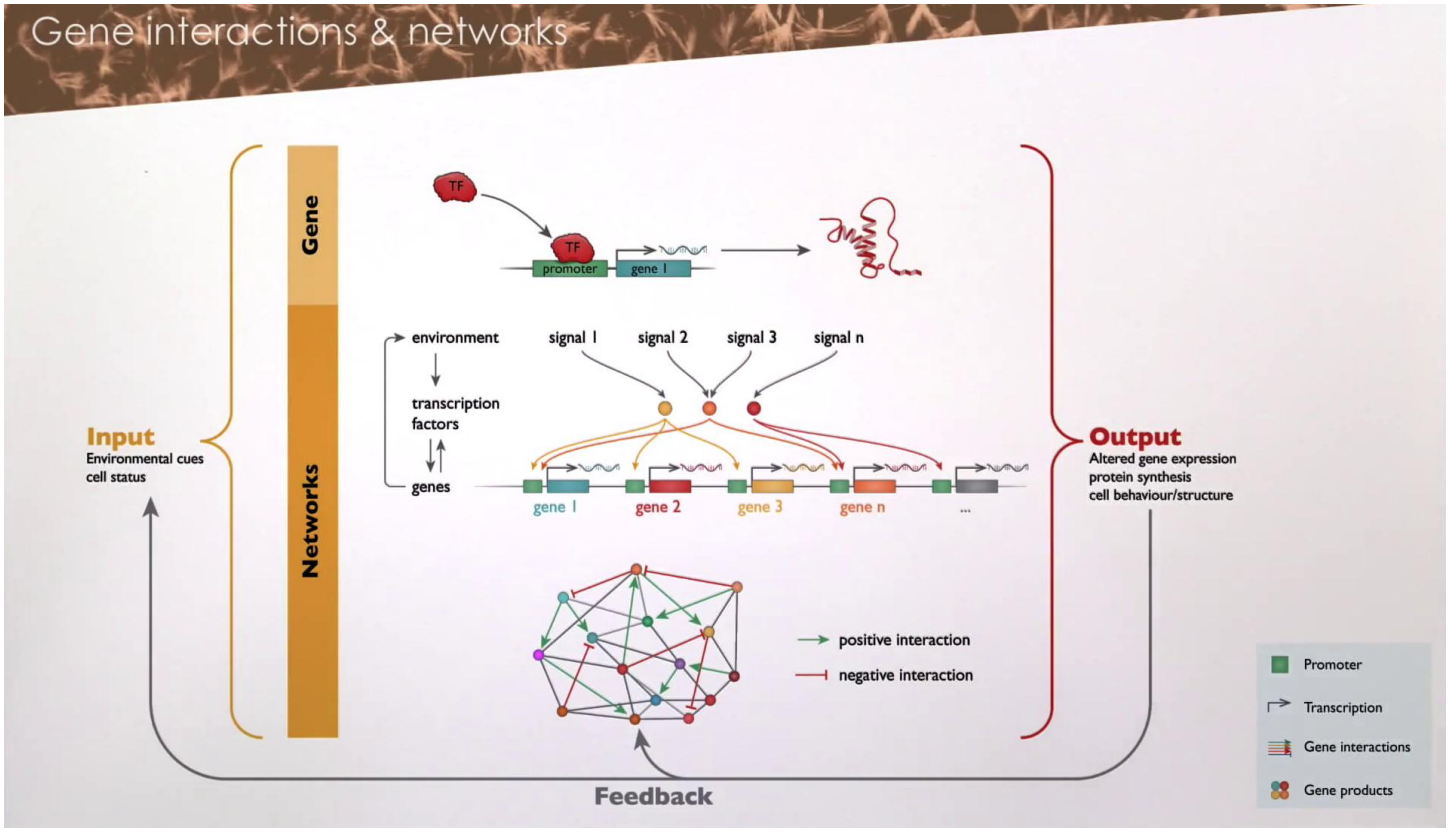


Let's imagine that we have gene C that will then code for this transcription factor that we saw at the beginning, which is regulating gene X to provide a positive feedback. This now provides an ideal situation for changing a positive feedback onto a negative feedback. This provides a perfect example of a positive feedback that is normally there from gene C to gene X that can be interrupted with a negative feedback regulation of this inhibitory intermediate that is gene Y. It is important to understand that genes, proteins, other molecules inside the cell, both intra and intracellular interactions as well as the external environment, all can affect a given trait. These interactions can then be used to help to understand the structure of complex genetic networks.

Notes

Summary

2m 51s

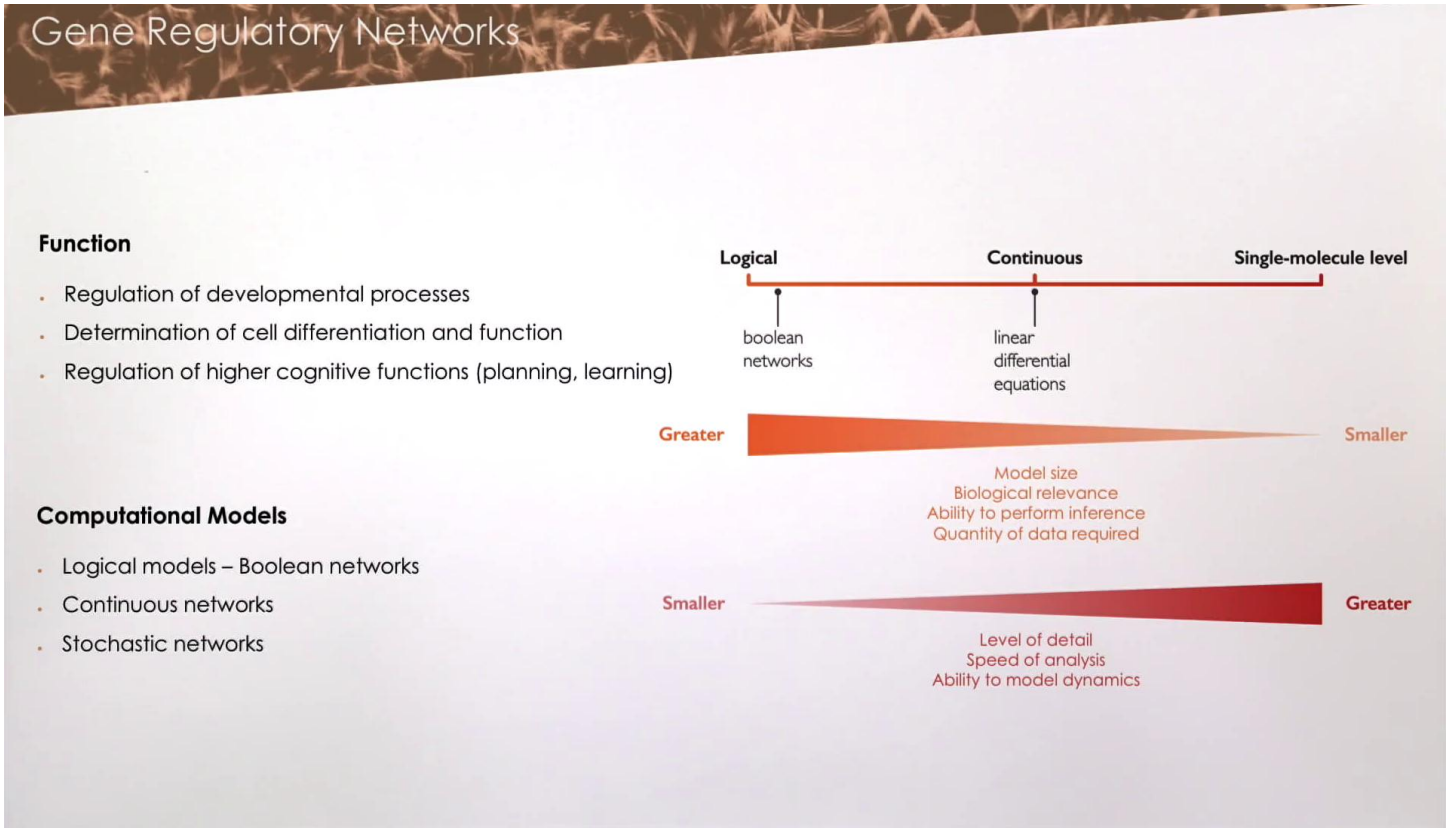


Such a genetic network is exemplified here. On the top we have a situation as we had it before, a transcription factor binding to a promoter region of interest which stimulates gene one. Then gene one would be in a cascade of genes that are placed on the genome one upon another, which will then react to different signals from the environment. We have signal one, two, three until N which influence the binding or in turn the expression of different transcription factors which will then bind or not to this regulatory cascade of different genes that we have here. The net sum of this will create an output of altered gene expression of altered protein synthesis and ultimately of an altered cellular behaviour. What we then have is this feedback loop that feeds back onto the input side such that environmental cues and the status of a cell will have a different effect now on the regulation of these genes and this regulation is controlled by both positive and negative interactions. We go from an environmental cue on the left through a gene regulatory network in the middle to an output product which can be a protein of interest. This eventually will then signal back to modify the input further.

Notes

Summary

3m 50s

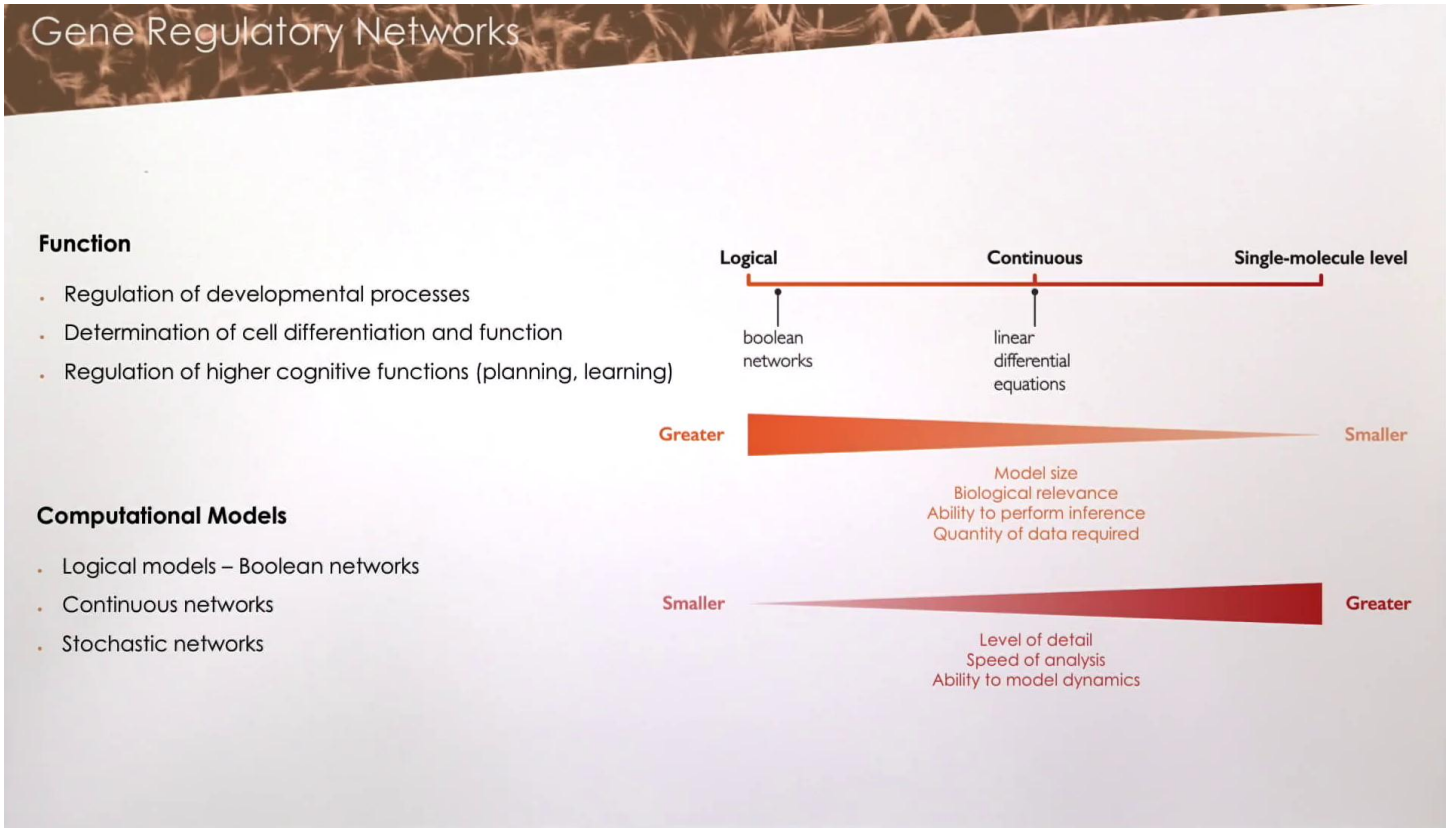


The function of gene regulatory networks are to regulate developmental processes, to determine cell differentiation and function and also to regulate higher cognitive functions such as executive planning and learning. Gene regulatory networks can be modelled computationally from a single molecule level here on the right to a Boolean network, which is a logical model here on the left, and in the middle we have something that is called a continuous model that is characterised by linear differential equations. All of these models have advantages and disadvantages. If we look on the single molecule level, the model size doesn't have to be very big in order to model a single molecule level and its behaviour. However, studying a single molecule in isolation is probably, biologically speaking, not so relevant. It is better to move to a Boolean network in order to have a bigger insight into the biological relevance of a gene regulatory network. The ability to perform interference, which means how gene regulatory networks influence one another, is better in a logical Boolean model. At the same time, the flip side of it is that the quantity of data required is enormous.

Notes

Summary

5m 16s



The level of detail is always going to be greater at the single molecule level, the speed of analysis is also going to be greater and the ability to model dynamics at the single-molecule level are going to be greater. However, the biological insights that we can gain with a single molecule level model of a gene regulatory network is by definition going to be limited.

Notes

Summary

6m 43s