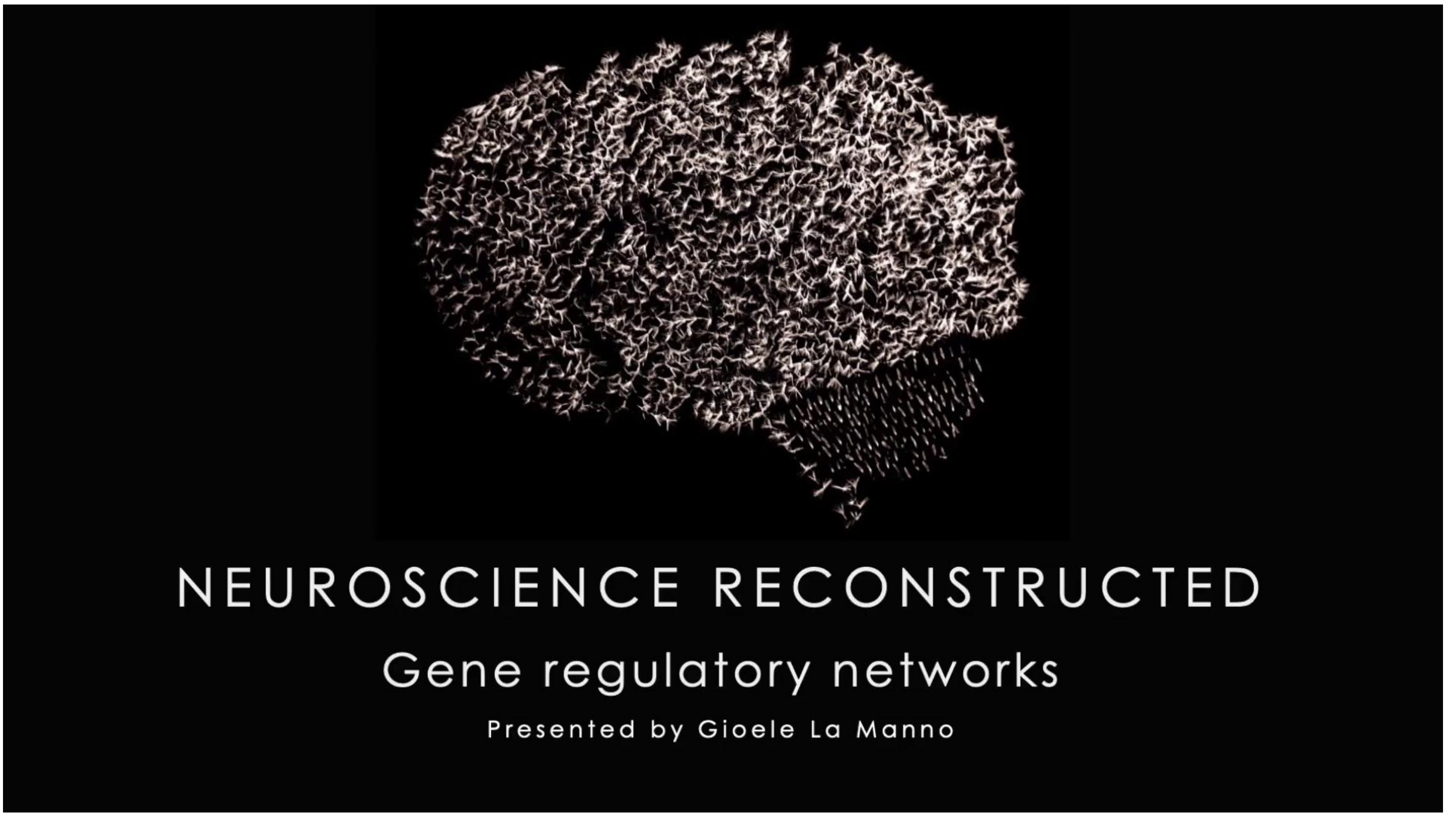

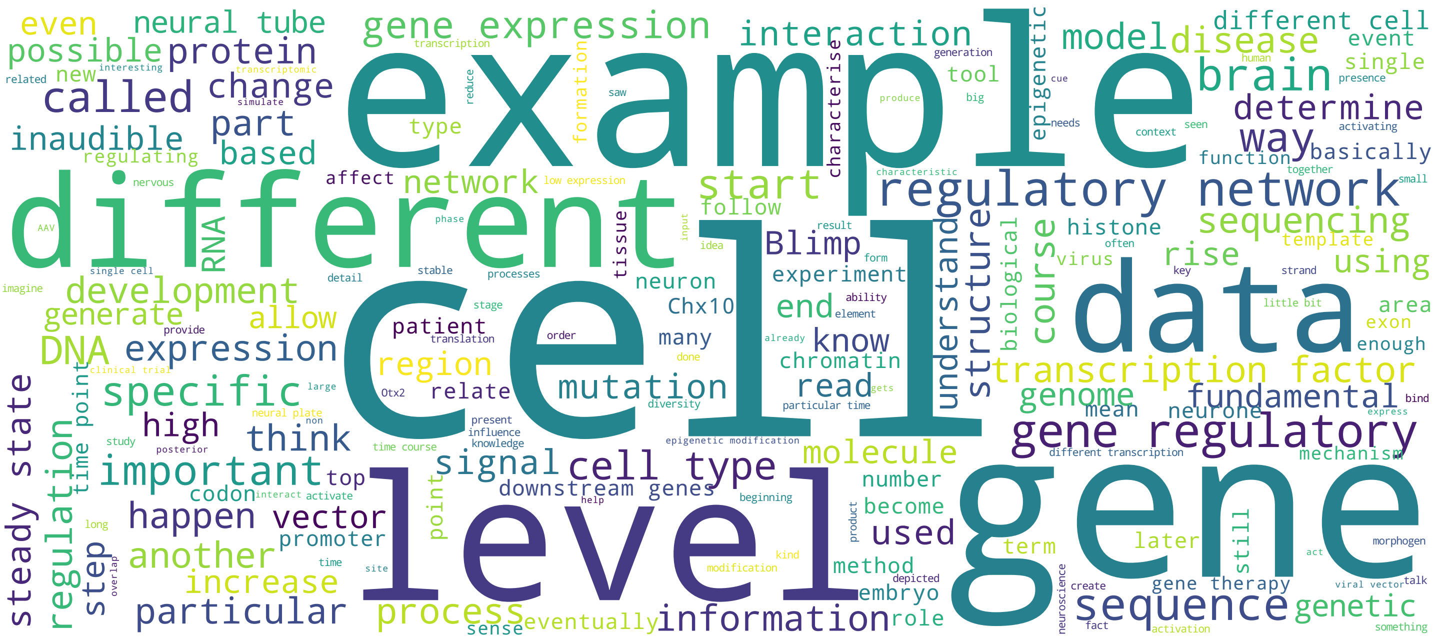

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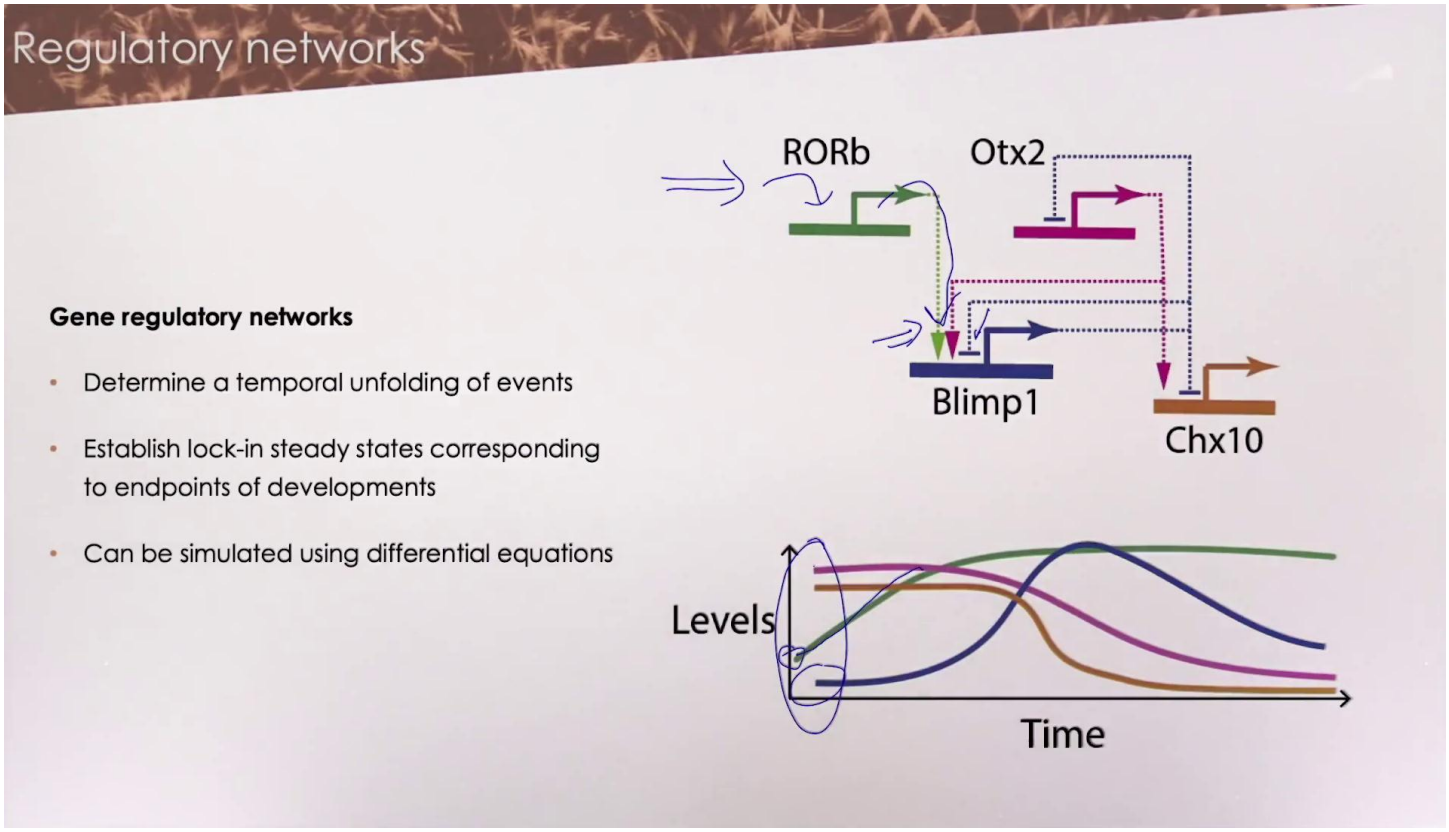
Video

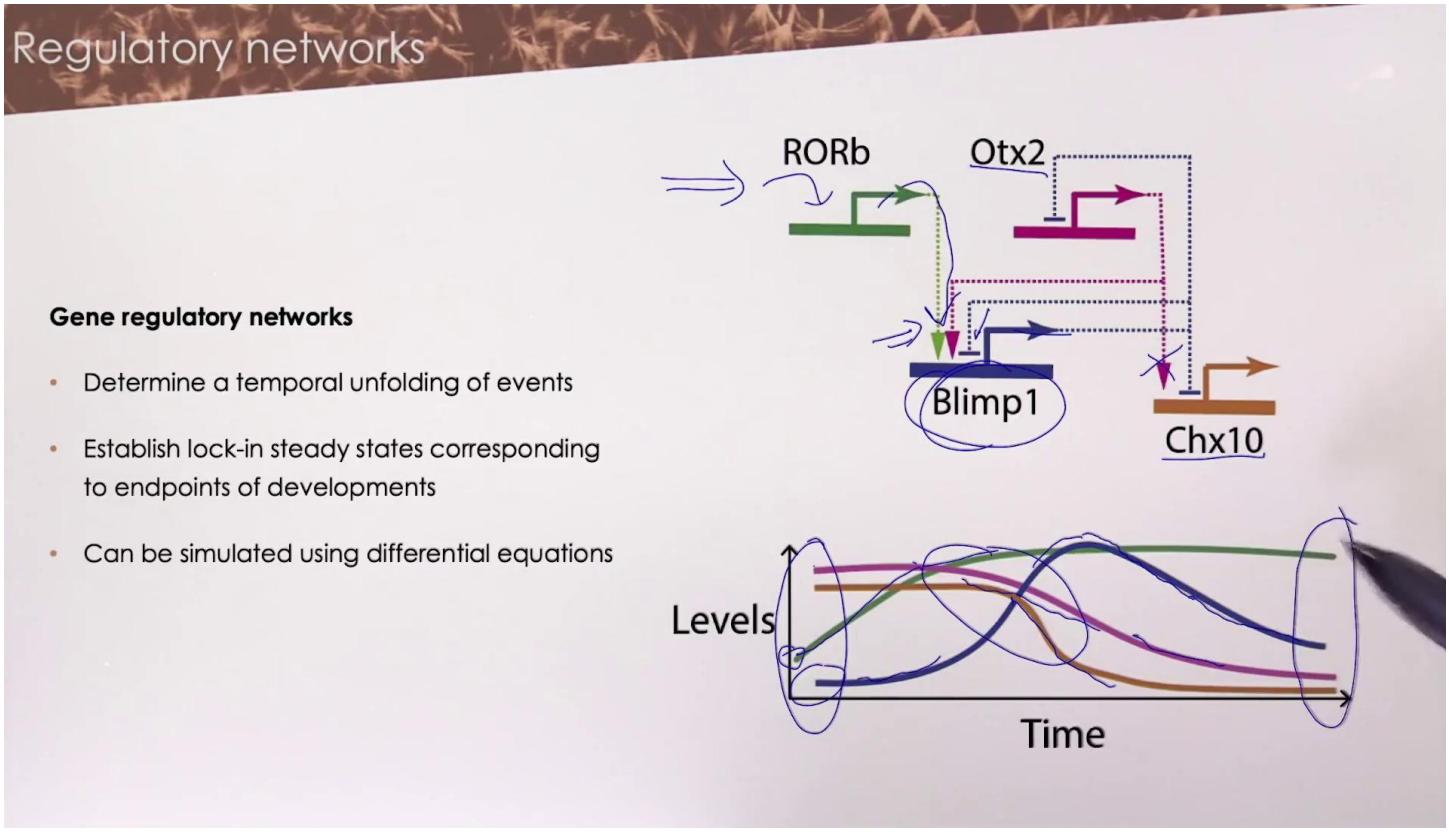


You already heard about some gene regulatory networks, but it's important for understanding development to see how a gene regulatory network with interactions between different transcription factors and the regulation of the set of downstream genes can be fundamentally important and can encode really a time course of changes for the cell. How does this happen? We're going to see this with this example. We have here four partners, transcription factors that have relation of activation indicated work from this pointed arrow is or this flat tip of the arrow is going to indicate an inhibition. We're going to see an example of how this particular gene regulatory network can determine a particular unfolding of event in a cell. A cell that starts at a particular time point with gene expression level that is as follows. If you follow the colour, this cell has a gene, very high gene expression for Otx2, and the same for Chx10, but a very low expression of Blimp1 and an average low expression of RORb. What happens if now a signal coming from the outside the cell, now in a strain signal, increases and transactivate RORb. RORb is going to start to increase its level of expression and therefore, inducing an activation on Blimp 1.

Notes

Summary

0m 05s

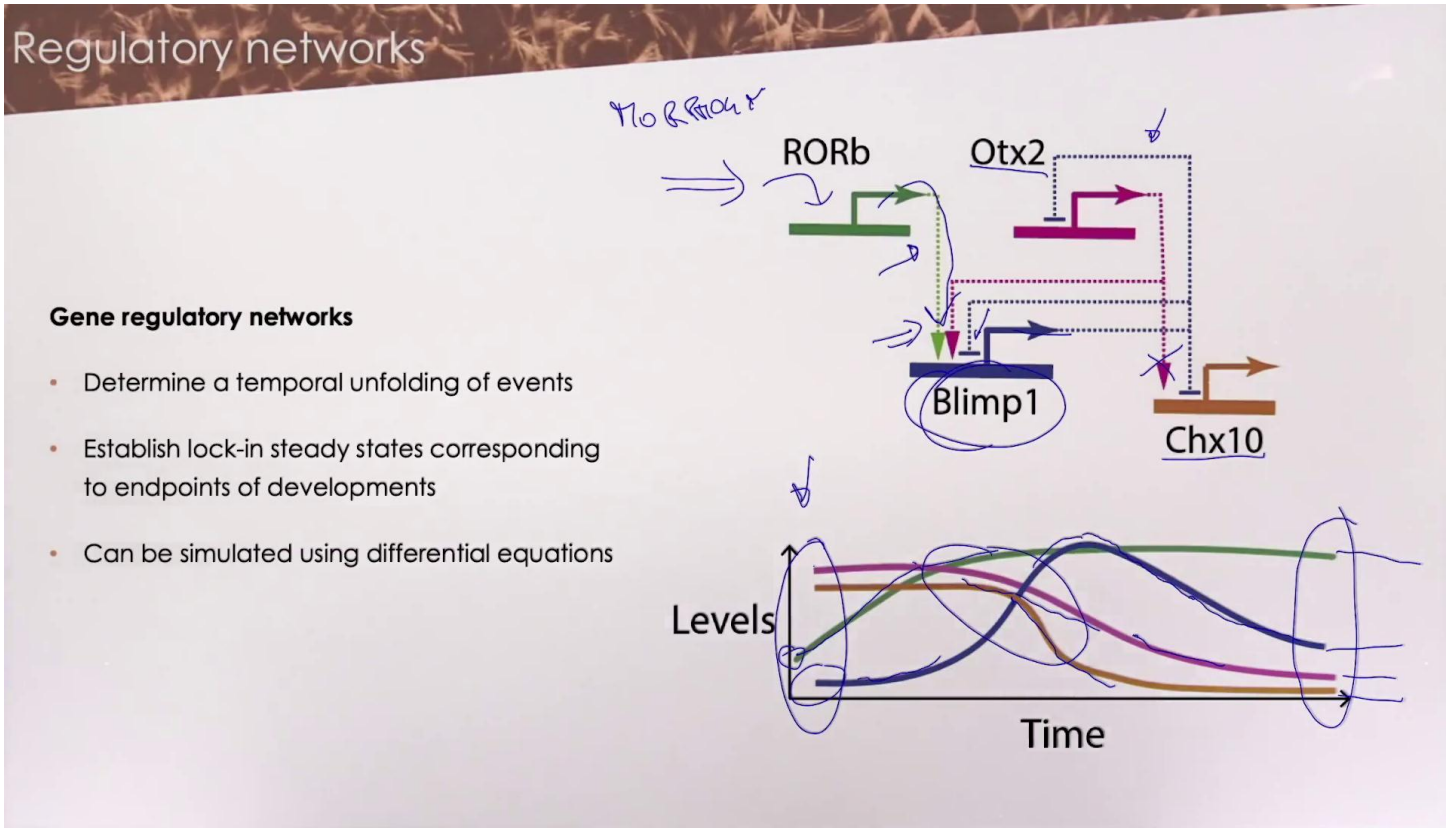


Blimp 1 will start to increase at the beginning slowly and proportionally to the increase to the absolute level of RORb. While Blimp expression increases, it's going to start acting, inhibiting both Chx10 and Otx2. This inhibition is going to translate in a reduction of gene expression that you see in this face of the plot. Otx2 starts to being expressed less. We see this level going down. Now when the levels of Otx are down, this fact is going to affect the level of Chx10 that is in turn also being inhibited by Blimp. This double effect of Blimp inhibition, Otx reduction will determine an even steeper decrease of Chx10, sorry, Chx10. Finally, when Blimp level are very high and considering that now Otx2 is basically extremely low, I have a very interesting situation where Blimp is self inhibiting itself. The presence of Blimp is reducing, is blocking its transcription. Otx2 is not presence anymore. The results of this is that now Blimp is going to actually reduce its transcription, its promoter, and its level. What we get at the end, we end up in a tractor state.

Notes

Summary

1m 39s

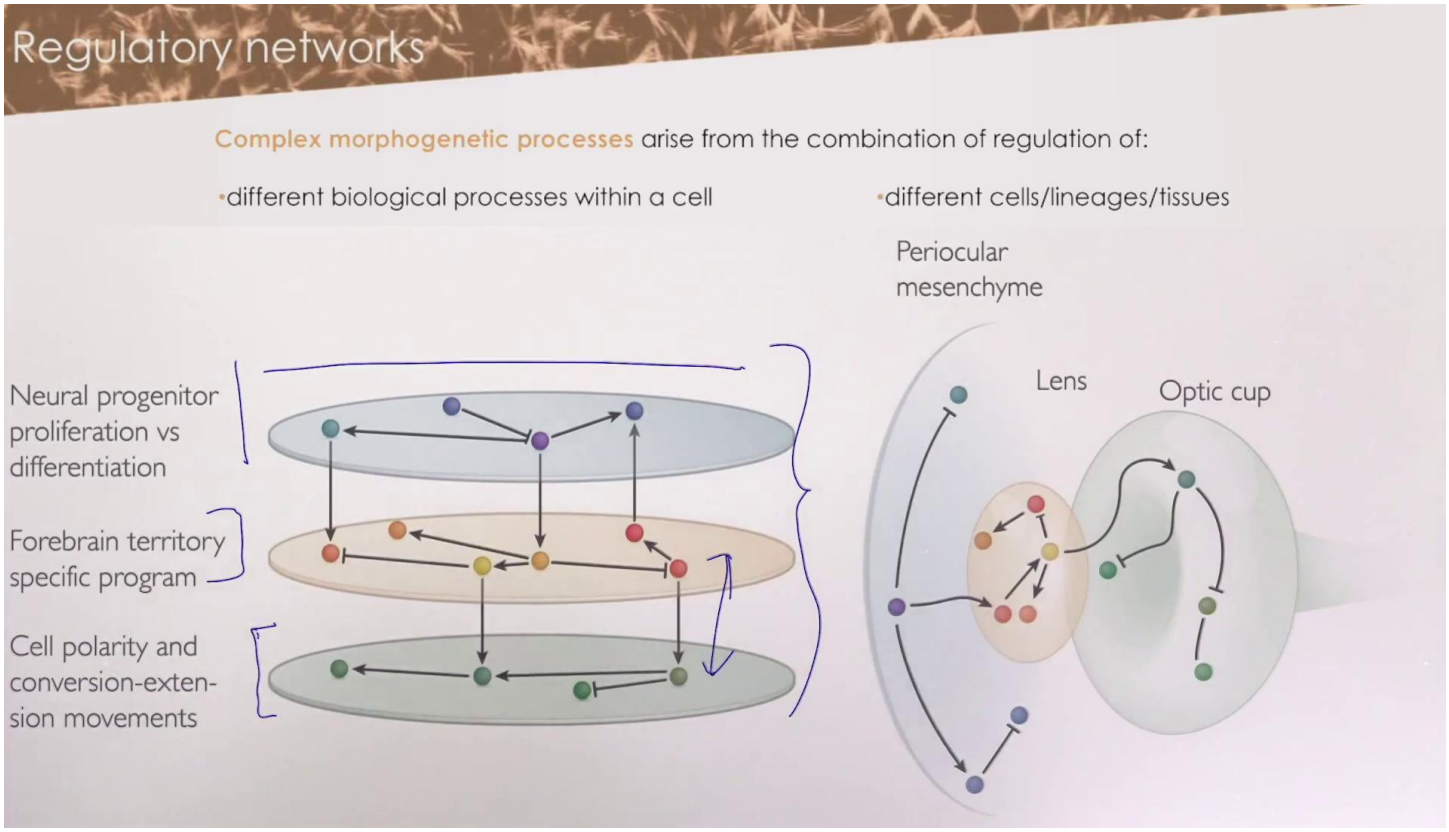


At this point in the future, the level of expression is going to be stable, and we have switched from initial configuration that was stable until we add this initial morphogen that was activating RORb, and we get towards the end, another steady state, another stable steady state at the end. We've seen, with this example, how gene regulatory network can determine temporal unfolding of events, and they can establish particular looking steady states. We were in one at the beginning, there was a change in input, and we ended up in a different steady state towards the end. Overall, this is particularly interesting and an interesting computational perspective because if we are to characterise first, if we get to characterise those interactions, we can then simulate by, for example, differential equation solver, these time courses just based on the knowledge and the activating and inhibiting activity of different transcription factor on downstream genes.

Notes

Summary

3m 10s

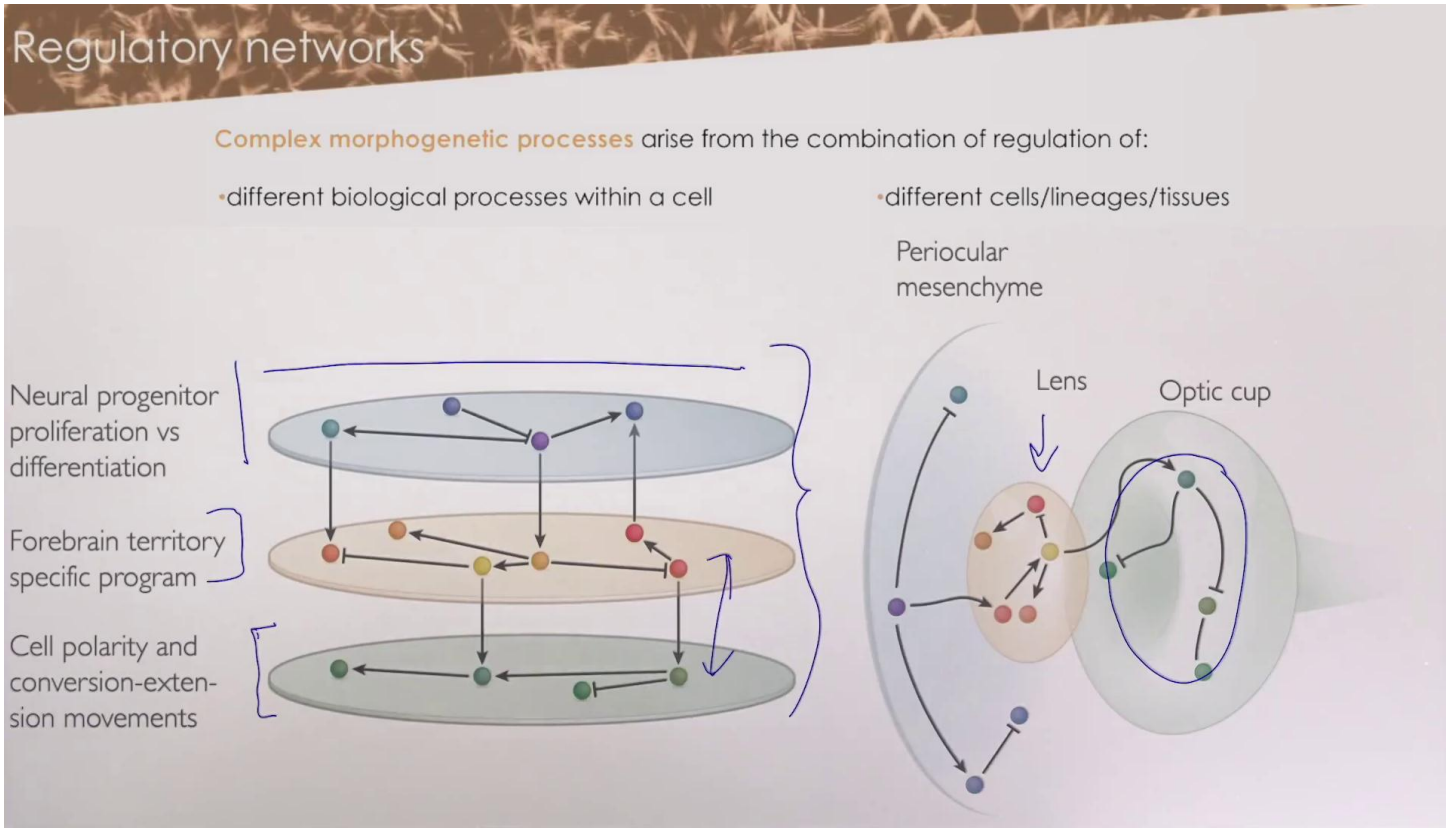


Typically, we can think of gene regulatory networks as regulating a particular function, particular differentiation path for a cell. For example, we can have a gene regulatory network here that is regulating neural progenitor proliferation versus differentiation decisions. We can have another one, for example, that is regulating and activating a steady state that is informing the cell that is specified to specific cell types for the forebrain territory. We can have even regulatory networks that activate downstream genes that relate to physiological activities and specific cellular functions, for example, establishment of cell polarity of the conversion of conversion-extension movement. But it's important to think about, even if some of those networks that have been characterised as partially segregated, so there are not many interactions between those networks, it's important to think about them as overlapping. A cell will not have only one of those networks activated, but every cell will be constituted by an overlap of those fundamental unit. That's the way we need to think about the crosstalk between those partial networks in a big gene regulatory network.

Notes

Summary

4m 19s



However, this autonomous aspect, if you want, so this is a different layer of regulation that happened within a cell, there are are not enough to give rise to the old complex developmental process. There needs to be also a level of interaction between different lineages and tissues. There will be gene regulatory networks that were, for example, encoding for a particular cell type, and they're characteristic of that cell type. But also very often, those gene regulatory networks will activate set of genes, for example, receptors, that make the cell type able to listen to specific signals from another one. For example, another cell type, say, in development of the [inaudible 00:06:32] here is depicted, can in the lens, for example, generate particular queues that are sent to nearby cells, for example, periocular mesenchyme. This is an example of different cells that relate to different structures and different cell types. They are autonomously regulated. This regulation give rise to ability of the cells to interact with other cells, and they form somehow a meta network of... That's the way we need to look at gene regulatory networks. At the autonomous level, they can crosstalk within cells through extrinsic signaling pathways and more morphogens, and they act at the complex pool of cells that is forming this particular structure of the embryo at a particular time point.

Notes

Summary

5m 49s