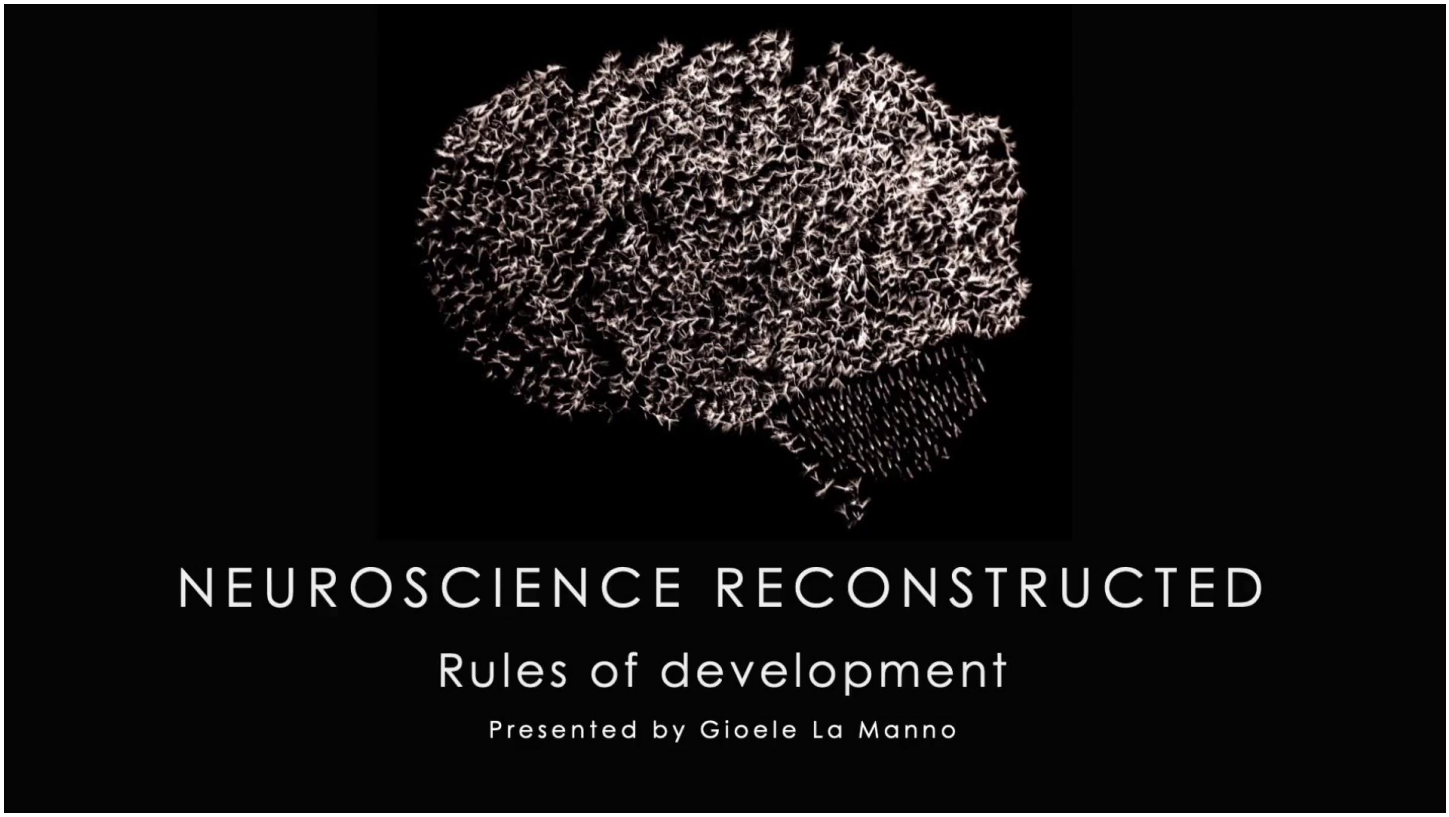

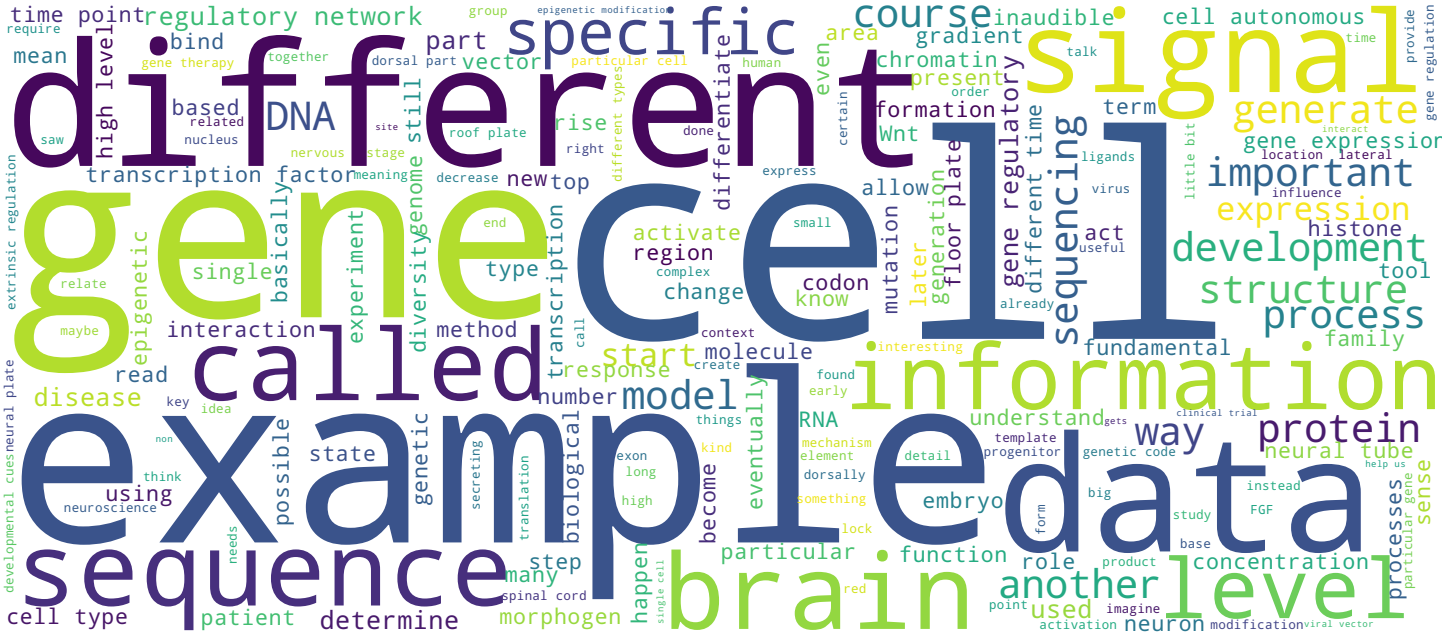

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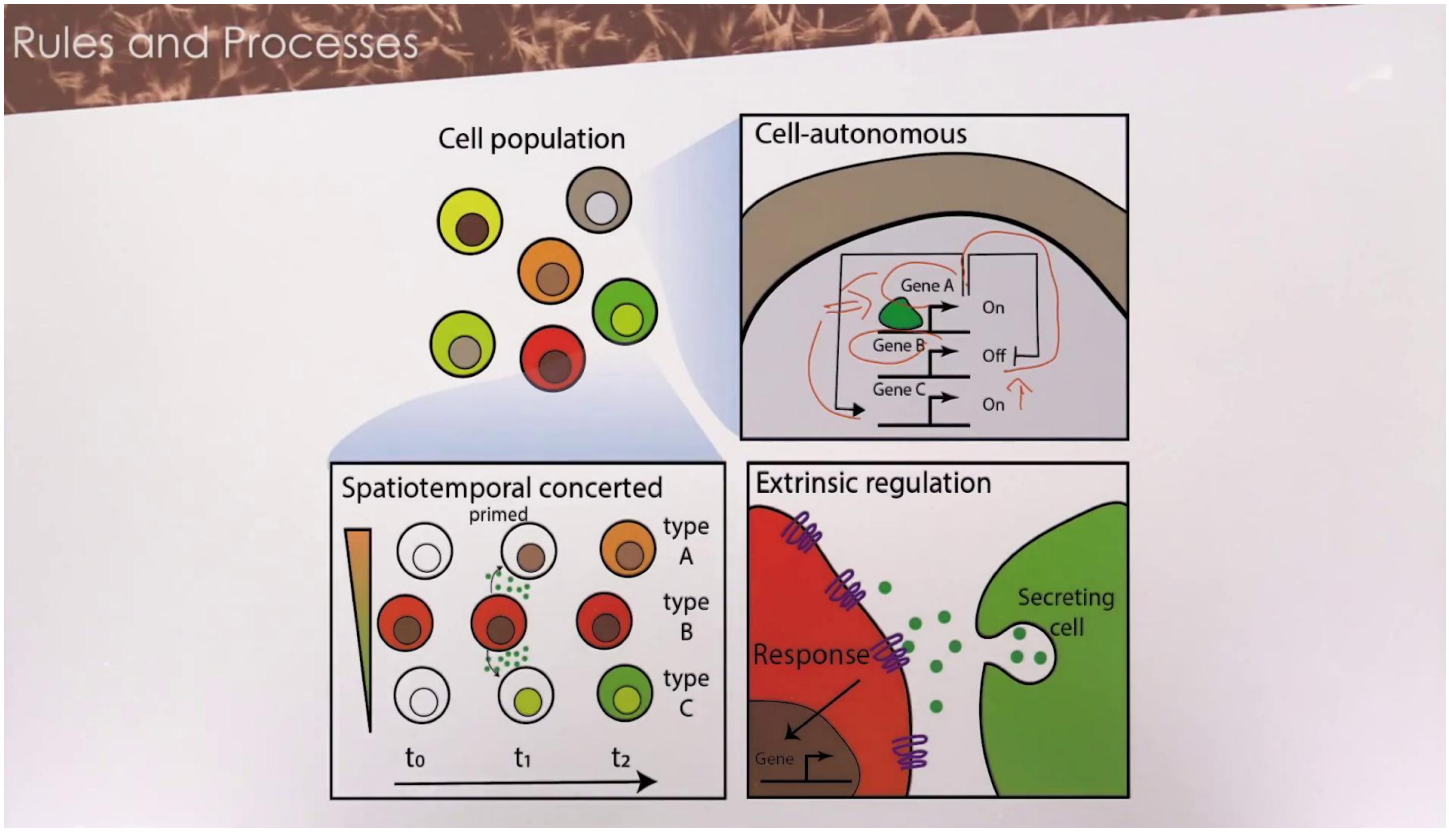
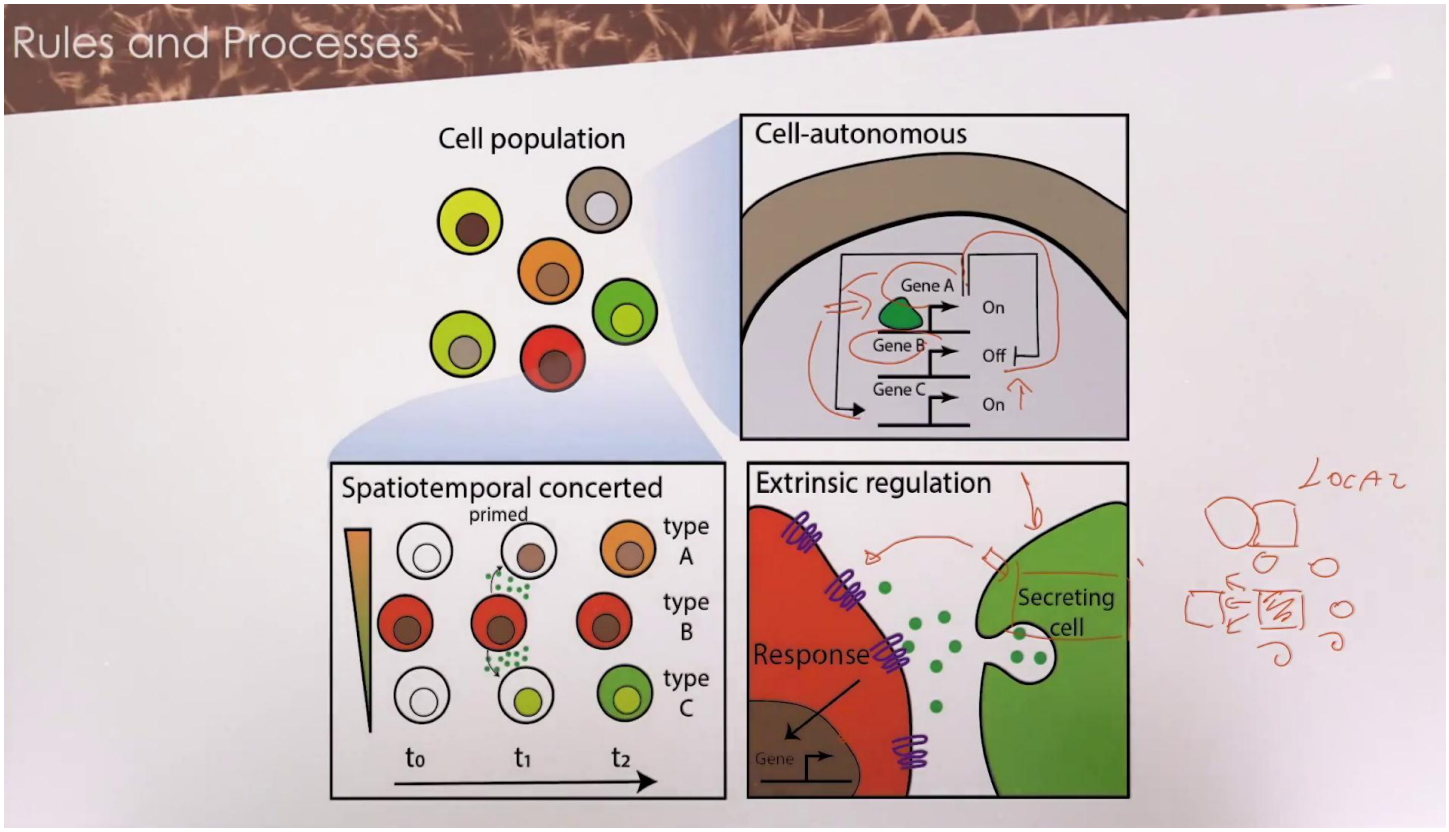


To better understand the complexity of this process, it's useful to use a set of rules in pillars of development. It will help us to at least conceptually deconstruct different process that at the cellular level happening are all at the same time, cells interacting, cells changing their expression. One fundamental way that elemental biologists think about this process is try to dissect them in cell-autonomous, extrinsic regulation, and then processes that happen spatiotemporally at the level of the cell population as a whole. Cell-autonomous process, for example, gene regulation operated by gene regulatory networks, process happen within a cell, they relate with the activity of particular transcription factor to again activate or inhibit other genes. What you see here, for example, is a very simple example of what... For example, Gene A can have an inhibiting activity on Gene B, while Gene A at the same time activate gene C. This will give rise to a certain set of changes. If this cell has a very high level of gene A, then this mechanism will kick in and we'll see later a very high level, for example, of Gene C as well. This process is happening within the cell.

Notes

Summary

0m 05s

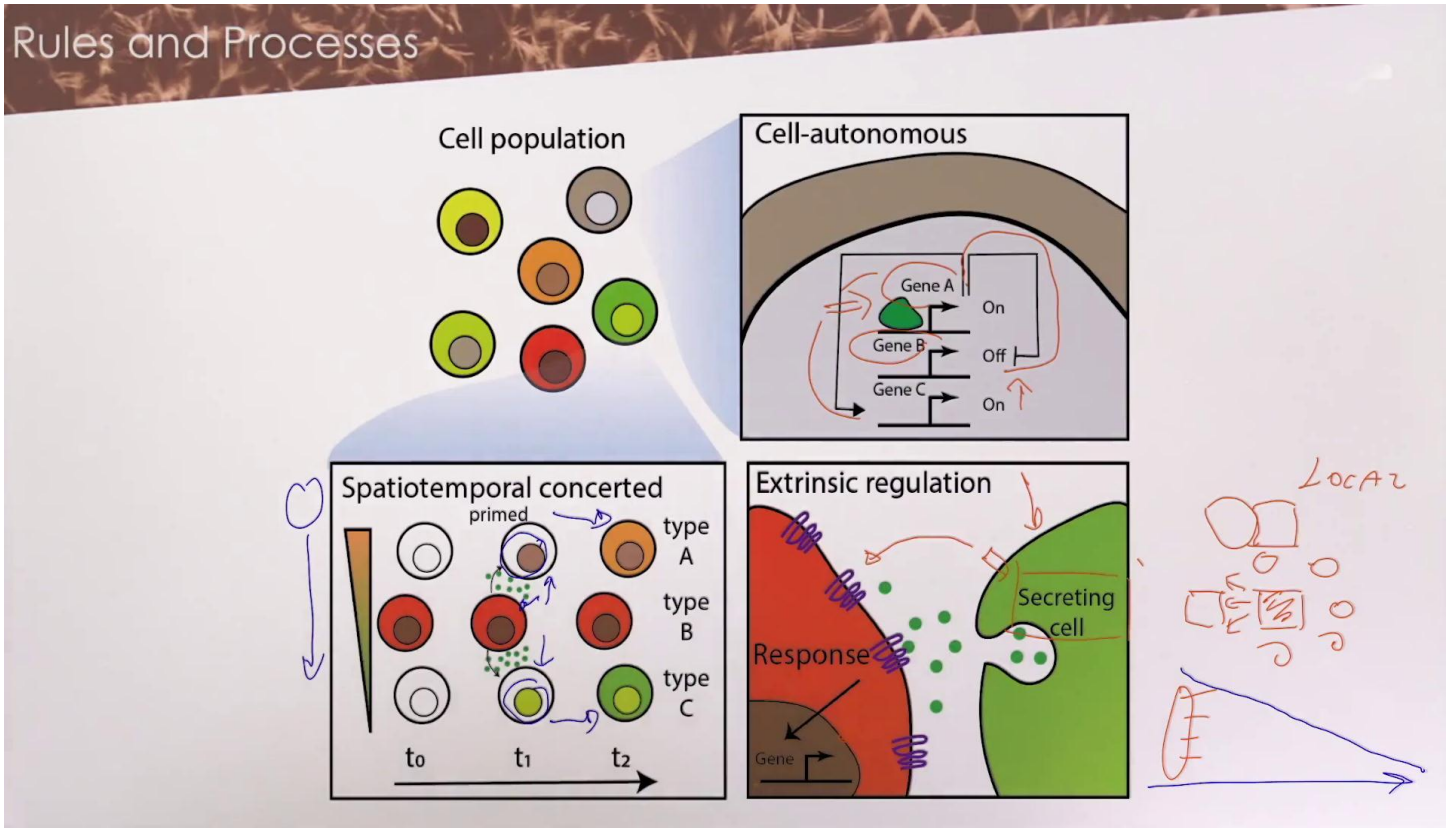


They're wired in in the genetic code, and they can be thought as cell-autonomous. Of course, this is complementary to interaction between cells. Extrinsic regulation mechanisms. Particular kind of cells can at some point start to express a set of morphogens, soluble molecules and ligands, or even membrane exposed protein that can interact with specific proteins in another cell called receptors that can bind to those ligands and activate cascades of a signal transduction. Eventually, this will activate, by phosphorylation of transcription factor, and determine activation of downstream genes. This means that as the response of the signal that the particular cell here in green has sent to its surrounding, we get a response. The signals or morphogens can act very locally sometimes. They do require, for example, the contact of two cells that needs to be found in proximity to act. Those, we can call them local. They can act at a short length and determined by signals that are, for example, short-lived, and they can only activate cells that are in a relatively limited proximity around the secreting cell. Finally, there are signals that generate really a gradient.

Notes

Summary

1m 32s

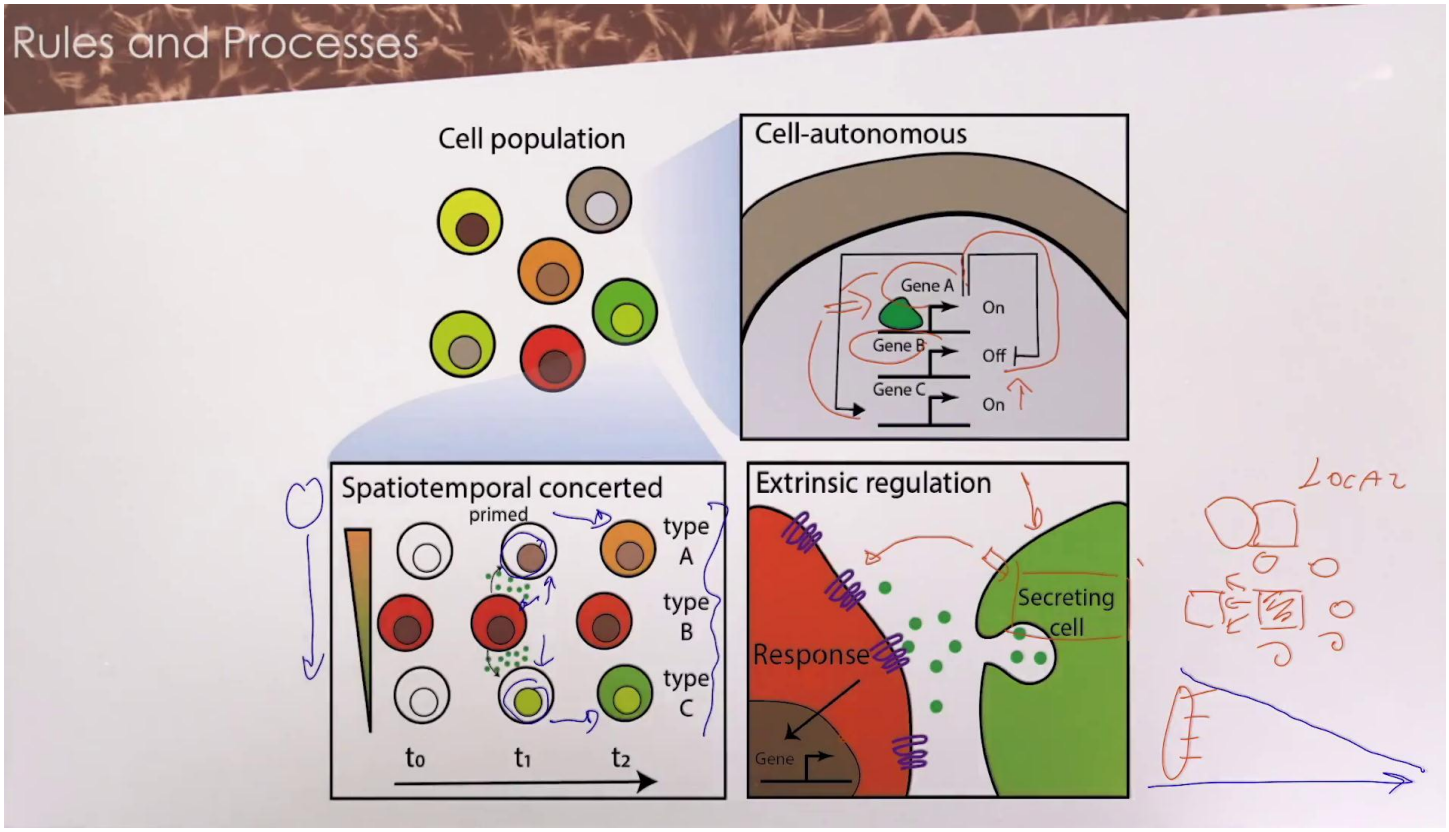


For example, it could be a group of cells that is secreting a particular morphogen. Then the concentration of this molecule will decrease progressively with increasing distance from the cell. This gradient of concentration reconstitute information that can be used by other cells to take this information as a positional cue to know where they are in the body plan. Finally, interactions between cells. Interaction between cells can play a role in a complex way spatiotemporally. This, for example, a basic example of things that can happen during development and during brain development. There can be, first, an establishment of a gradient. For example, there is a particular cell, say here, that generated and has been secreting a morphogen in this direction. This can generate an induction activity on cells. Cells that sense the signal very strongly, for example, is indicated here by the different colour of the nucleus, will activate different genes, for example will activate or not the particular gene. This can determine the cells to be primed. For now, for example, there is maybe not a big immediate change, but later on the cells may be triggered by this cell in red to differentiate by the same signal, can behave differently, determining, for example, that the generation of different cell types.

Notes

Summary

3m 15s

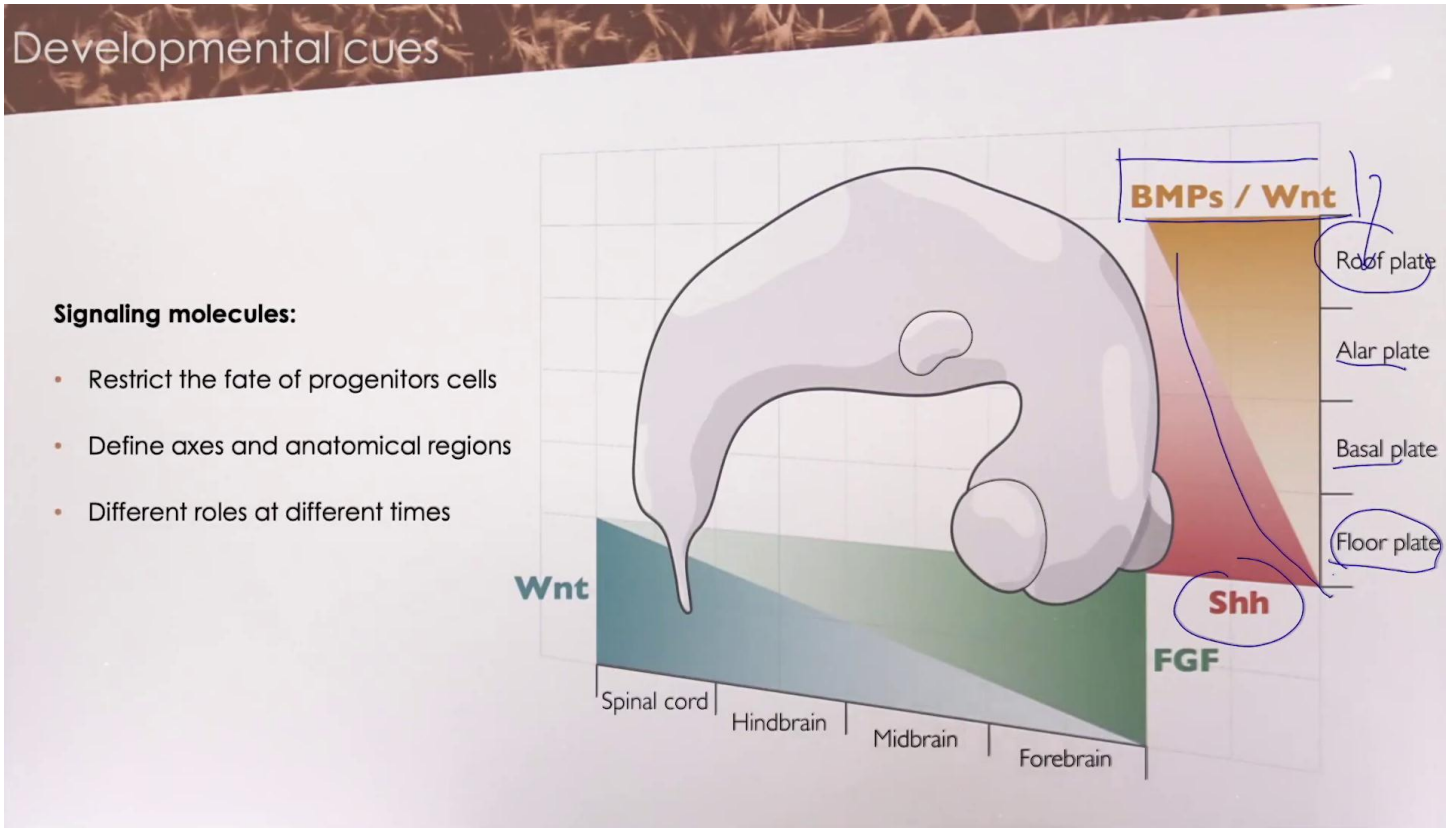


Again, processes like these are spatiotemporally concerted in nature because they take the combined information from the past that has generated changes in the cell, and from the present, immediate signals and triggers to then determine the formation of diversity. Like in this case, the generation of different types of cells.

Notes

Summary

4m 51s

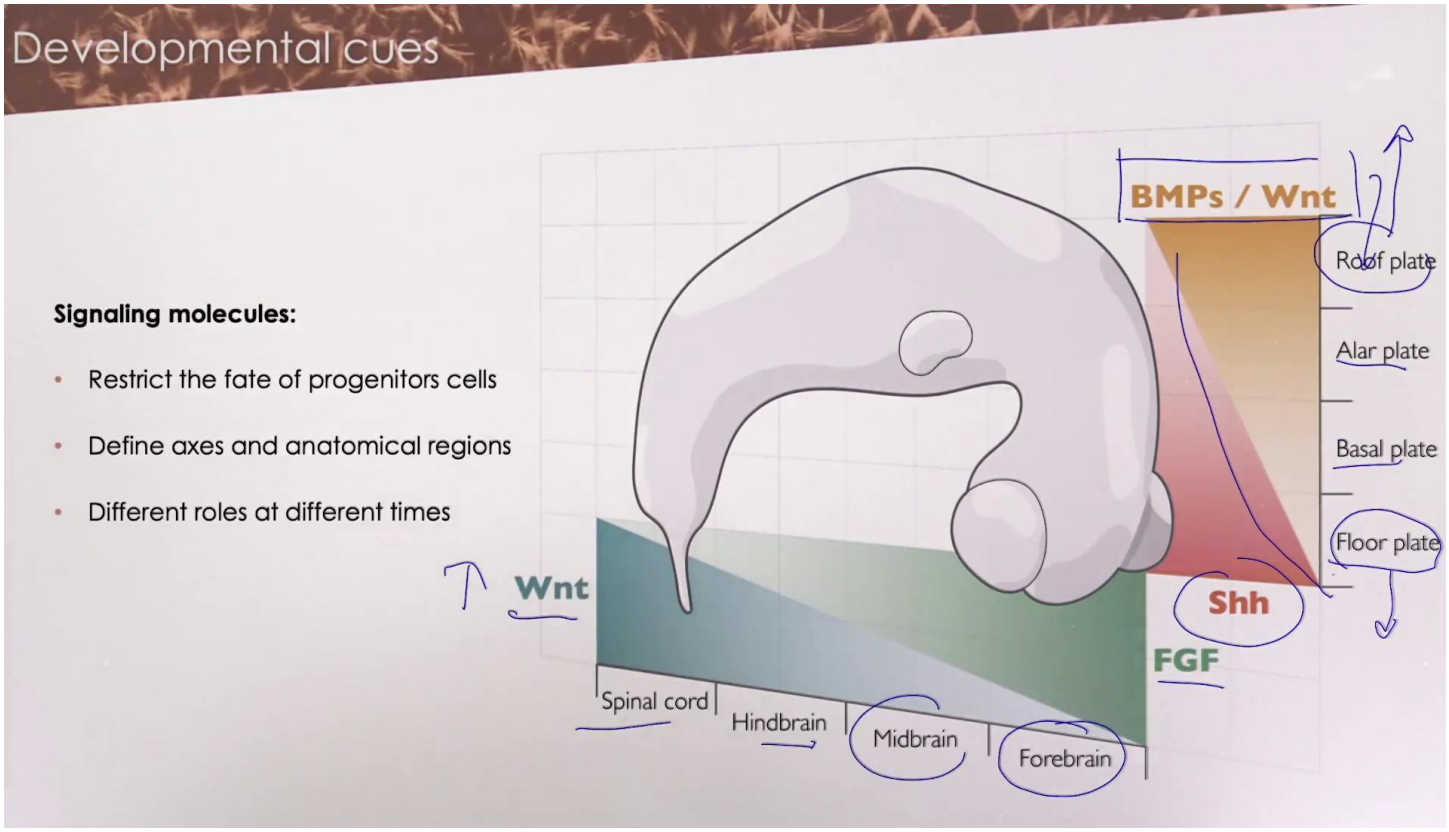


Those developmental cues and morphogens that we talked about in the previous slide have a fundamental role in restricting the fate of progenitors cells. In very early stages of development, they do it by first defining access. For example, the cells present in the embryo dorsally can express genes of the family of BMP and Wnts. Those will be secreted, and it generate the gradient that decrease from the dorsal part of the embryo to the ventral part. Cells at the base, we're going to see cells in the [inaudible 00:05:57], we're going to see that they express sonic hedgehog signals that again will decrease in concentration going upwards towards the dorsal part of the embryo and will determine Wnt formed cells that surround the signal that they need to specify in specific fates that are ventral to the brain. The neural tube, for example, thanks to this gradient, can encode an intrinsic regionalisation. Cells that are more ventral, they get a lot of sonic, they will be called progenitors of the floor plate. More laterally, and moving also more lateral in dorsally, we're going to have basal and alar plate. And then on the top, so to more dorsally on the neural tube, we have the generation of the roof plates progenitors.

Notes

Summary

5m 17s

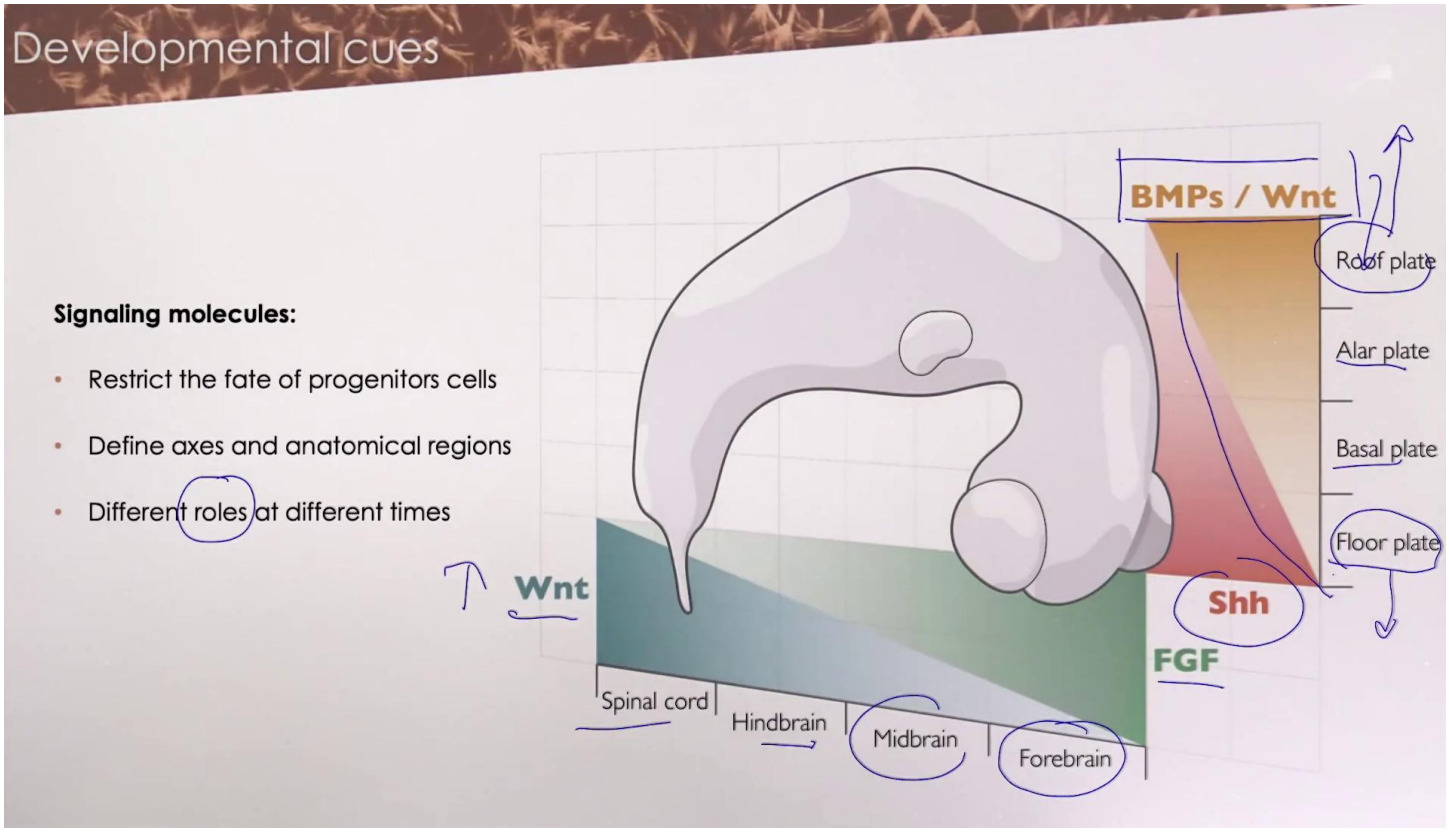


The cells will lock in in a state. Thanks to their gene regulatory network, they will lock in in a state that they will not be able to change later on. They have information that is cell-autonomous, and they will know that their final fate will be only a subset of possible neurones. Floor plate cells will give rise to a specific family of neurones. For example, dopaminergic neurones is one of those. A roof plate, for example, [inaudible 00:07:22] that will generate the only particular family of, for example, gabaergic neurones. Developmental cues and morphogens can overlap in complex patterns, giving different information to the cells about their location. On your right, you see here, for example, BMPs, Wnts, and Sonic give information on dorsal-ventral axis, but at the same time, Wnts and members of the family of Wnts and FGF can give an information about the anterior-posterior patterning. For example, cells that have been exposed to a concentration of FGF, particular members of the family of FGF, and instead of Wnt, they will be spatially specified and then differentiate the specific cells of the forebrain, midbrain, or hindbrain. Or even more caudally, spinal cord.

Notes

Summary

6m 48s



Finally, it's important to mention the different time points the same morphogen can be reused for different purposes. At different time point, the same morphogen might have very different roles and we need to... There is a time dependency of the meaning of a signal. In this way, cells can reuse the same gene, the same signal to specify different meanings at different time points. For example, very early, we have Wnt, just a particular induction role, but if we go very late in development, the same Wnt signalling molecule might specify and determine the activation of another gene regulatory network.

Notes

Summary

8m 12s