

# Applications of multisource data-based dynamic modeling to cell-cell signaling and infectious disease spreading

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#### Stellingen

#### Behorende bij het proefschrift

## Applications of multisource data-based dynamic modeling to cell-cell signaling and infectious disease spreading

- 1. Notch ligands can self-associate to form a homo-dimer that mediates the cis-inhibition of Notch while the ligand monomer mediates the trans-activation of Notch. (Chapter 2)
- 2. Increasing the expression of Notch ligand Dll4 in endothelial cells induces synchronized dynamics of Notch signaling in adjacent cells. This phenomenon can be attributed to lateral induction of Dll4 mediated by Dll4-Notch signaling between cells. (Chapter 3)
- 3. The hetero-dimerization of Notch ligands Dll4 and Jag1, together with the asymmetric affinity of Dll4 and Jag1 for Notch1 during trans-activation explains the opposing effects of Dll4 and Jag1 on angiogenesis. (Chapter 4)
- 4. Multi-cellular network formation in vasculogenesis can be caused by the attraction between dispersed cells and the repulsion between cells that are in direct contact. Notch1 signaling affects vasculogenesis by changing the strength of cell-cell attraction. (Chapter 5)
- 5. Timely control of air pollutant emission can improve regional air quality and reduce the risk of respiratory infection in the population. (Chapter 6)
- 6. The strict mobility restrictions between cities can be lifted, and the movement from cities with a higher risk of infection to cities with a lower risk of infection will not trigger a second outbreak of the epidemic, provided that the sum of the growth rate of new infections in each city remains negative. (Chapter 7)
- 7. The oligomerization of Notch ligands gives rise to new types of ligands that may exhibit different affinities for Notch than the ligand monomers, both in trans-activation and cisinhibition. This represents a general mechanism through which the simple Notch signaling pathway becomes complex.
- 8. Due to the flexibility to mimic experimentation, mathematical modeling is suitable for studies that require simulations of experiments that are currently difficult to perform in reality.
- 9. A stalk cell itself will not compete for the tip position in angiogenic sprouting, but multiscale feedback allows it to. By losing contact with surrounding tip cells, a stalk cell may differentiate into a tip cell due to a lack of Dll4-Notch1 signaling, thereby changing its position in the vessel.
- 10. Creating a database that quantifies the connectedness of cities around the world via transportation networks is critical to predicting and preventing global pandemics.
- 11. Completing a PhD demands more than just interest and enthusiasm; candidates should strengthen their resilience to cope with failure by building a good family and social network.