

Mathematical model of the factor H mediated self and non-self discrimination by the complement system

A. Tille, T. Lehnert, M.T. Figge

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Alexander Tille^{1,2}, Teresa Lehnert¹ and Marc Thilo Figge^{1,3}

¹ Applied Systems Biology, Leibniz Institute for Natural Product Research and Infection Biology - Hans-Knöll-Institute, Jena, Germany
² Friedrich-Schiller University Jena, Germany

complement system
The complement system is a key factor in host defence and its main task is to recognize and eliminate binding mechanisms as well as attracting phagocytes to the site of attack. It contains a set of plasma proteins that get activated via biochemical reactions on distinct pathways. To protect host cells from opsonization a tight regulation mechanism is needed.

key molecules

- opsonin C3b: - forms a molecular complex, that activates new C3b molecules
- regulator factor H (fH): - plasma protein that can be bound to surfaces
 - accelerates decay of C3b amplification complex
 - mediates C3b degradation

aims of the mathematical model

- determine reaction rate by fitting model to experimental data
- determine driving processes of the opsonization mechanism
- predict opsonization level based on concentration of surface bound factor H

model I: well mixed system

$$\frac{d}{dt} C3b^I = r_{act} + r_{amp}(fH^*, C3b^*) \cdot C3b^I - r_{stab} \cdot C3b^I - r_{inhb} \cdot C3b^I$$

$$= r_{ops} \cdot B^*(fH^*, C3b^*) \cdot C3b^I - r_{inhb}(fH^*, C3b^*) \cdot C3b^I$$

$$\frac{d}{dt} C3b^* = r_{inhb}(fH^*, C3b^*) \cdot C3b^* - \mu_{C3b^*} \cdot iC3b^*$$

adding spatial information to the model

- false interpretation of the concentration of surface molecules in well mixed model
- need to include spatial information into the model

model II: compartment model of cell interaction

- cell representation of surface bound molecules
- concentration of surface bound molecules in relative units in order to compensate scaling of cell size and numbers
- bimolecular reaction rates on surfaces are not comparable to experimental results due to mismatching units

model III: modeling a single cell

- short lifetime of active C3b molecules in liquid ($t_{1/2} = 60\mu s$)
- mean interparticle distance much larger than the distance a C3b molecule can travel
- amplification on a cell is a local phenomenon and each cell will be modeled individually
- compartment model: - 3D compartment including the interaction volume defined by $d_{reaction}$
- 2D surface compartment

drawback: - mode depends on artificially introduced parameter $d_{reaction}$
- spatial distribution of C3b molecules not well represented

solution: - combination of ODE and PDE to describe spatial distribution in liquid
- much more complex steady state solution → solve radial Poisson equation

summary and outlook

	determining reaction rates	driving processes	predictions
model I: well mixed system	X	X	X
model II: two compartment model	(V)	✓	✓
model III: single cell	✓	✓	✓

Model II and model III can be used to correctly describe the concentration of surface-bound molecules. Experiments will be used to determine which model better describes the biological system. In particular, the question whether the interaction of cells plays a role must be clarified.

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CONTACT
alexander.tille@leibniz-hki.de
Research Group
Applied Systems Biology

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