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

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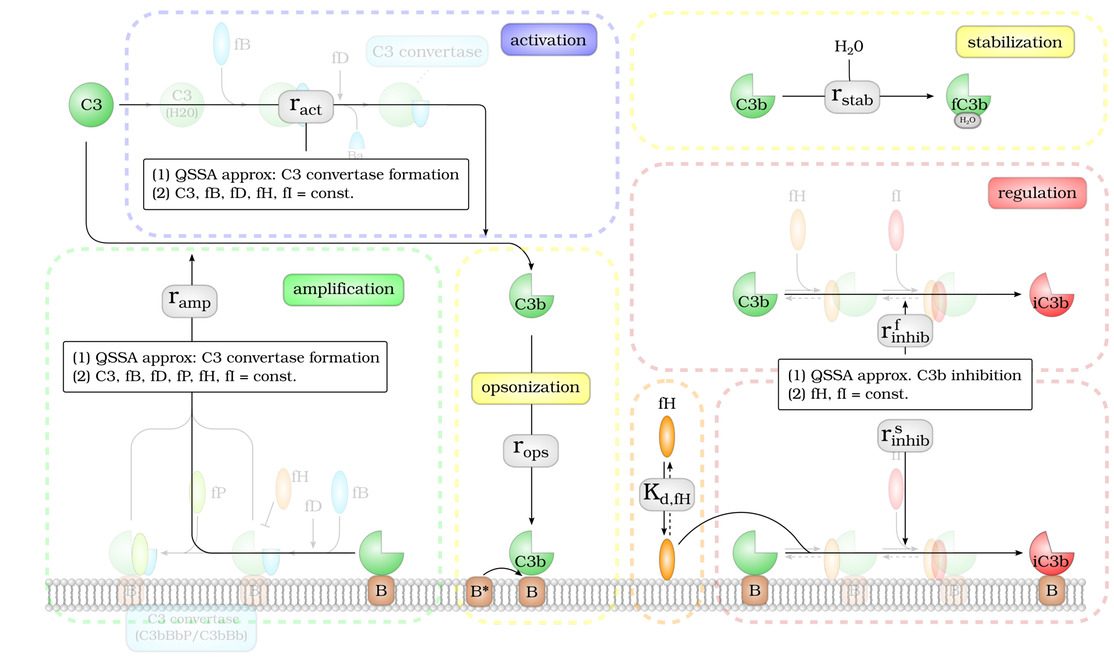
## complement system

The complement system is a key factor in host defence and its main task is to recognize and opsonize invading microorganisms as well as attracting phagocytes to the site of infection. It comprises 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

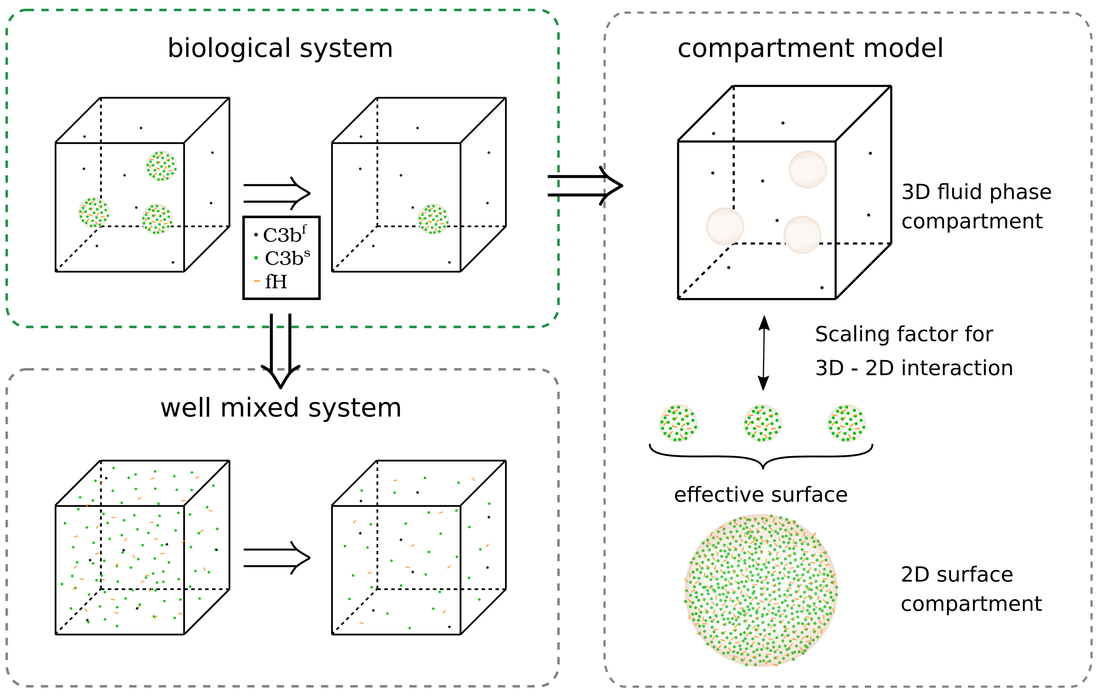
$$\frac{d}{dt}C3b^f = r_{act} + r_{amp}(fH^s, C3b^s) \cdot C3b^s - r_{ops} \cdot B^*(fH^s, C3b^s) \cdot C3b^f - r_{stab} \cdot C3b^f - r^f_{inhib} \cdot C3b^f$$

$$\frac{d}{dt}C3b^s = r_{ops} \cdot B^*(fH^s, C3b^s) \cdot C3b^f - r^s_{inhib}(fH^s, C3b^s) \cdot C3b^s$$

$$\frac{d}{dt}iC3b^s = r^s_{inhib}(fH^s, C3b^s) \cdot C3b^s - \mu_{iC3b^s} \cdot iC3b^s$$

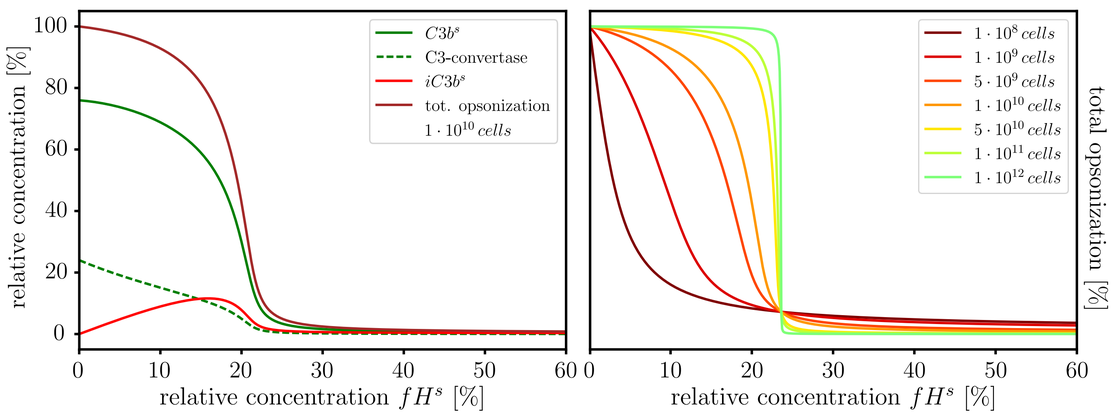
## adding spatial information to the model

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



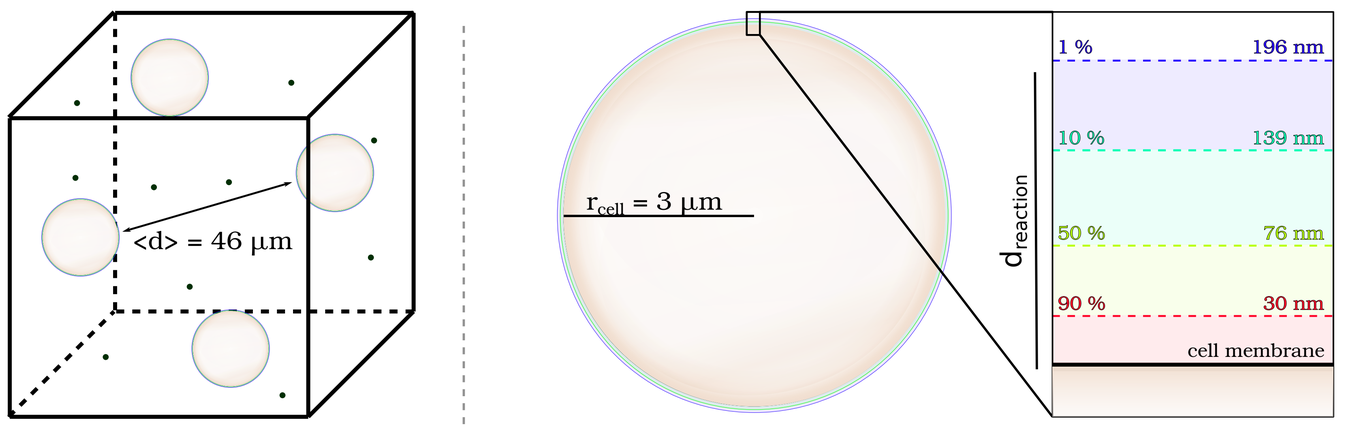

## **model II:** compartment model of cell interaction

- well representation of surface bound molecules
- concentraion 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 ($t_{1/2}$ = 60µs)
- 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 modelled individually
- compartment model: - 3D compartment includinng 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

| | determine reaction rates | determine driving processes | predictions |
|---|---|---|---|
| model I: well mixed system | ✗ | ✗ | ✗ |
| model II: two compartment model | (✓) | ✓ | ✓ |
| 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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