Virtual phagocytosis assays reveal strain-specific differences in the microscopic parameters of the interaction between alveolar macrophages and two A. fumigatus strains

Reduce noise

Enhance contrast



Quantification &

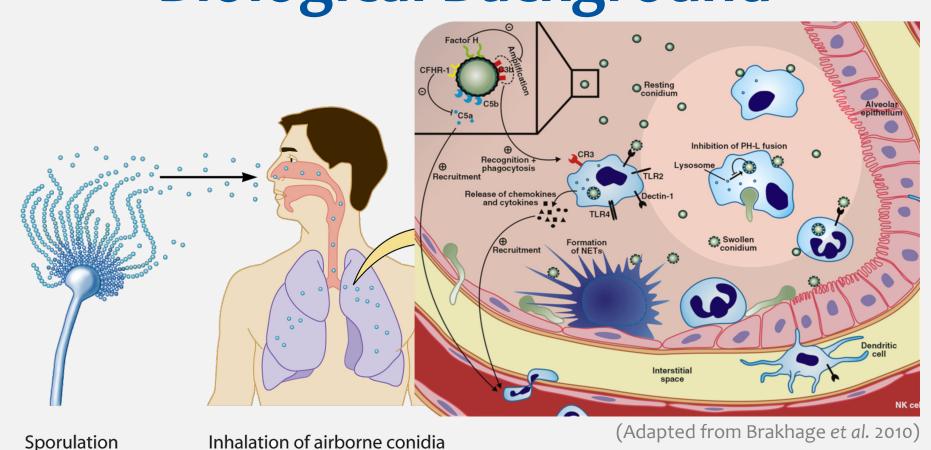
Phagocytosis Measures



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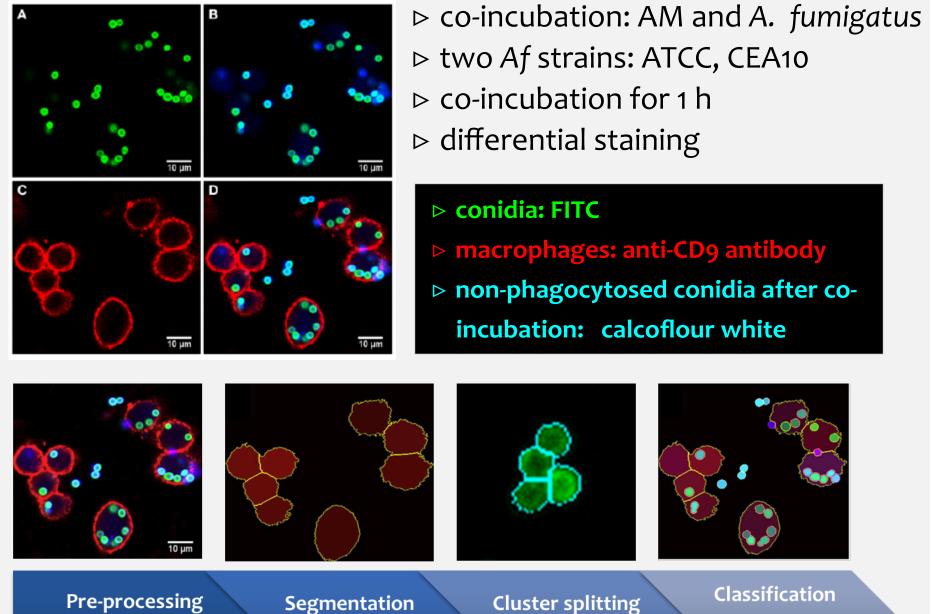
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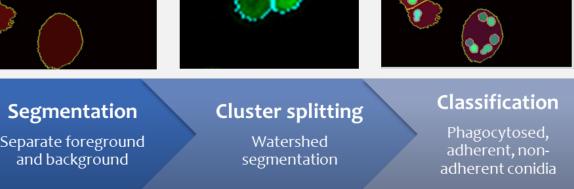
Biological Background

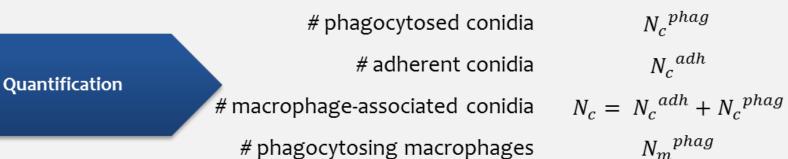


Aspergillus fumigatus is a ubiquitious human-pathogenic fungus. It distributes its small spores (conidia), with a diameter of 2 - 3 µm, via the air. Thus, every human individual inhales several hundred conidia per day. The resident immune cells in the lung - the alveolar macrophages (AM) - phagocytose these conidia and thereby are major players against this pathogen. However, in immunocompromised patients the clearance of the conidia is disturbed leading to severe infections with mortality rates ranging from 30 - 90%. Therefore, it is very important to better understand the host-pathogen interaction of A. fumigatus and AM.

Experiments and Image Analysis







N_c^{phag}

 N_m^{phag}

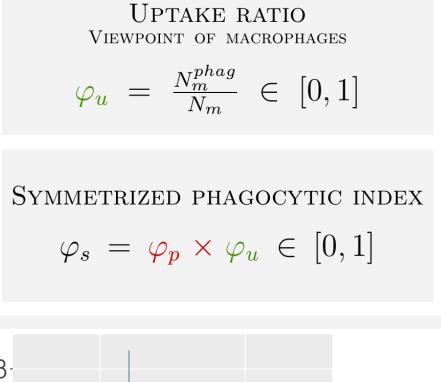
olue 0.4

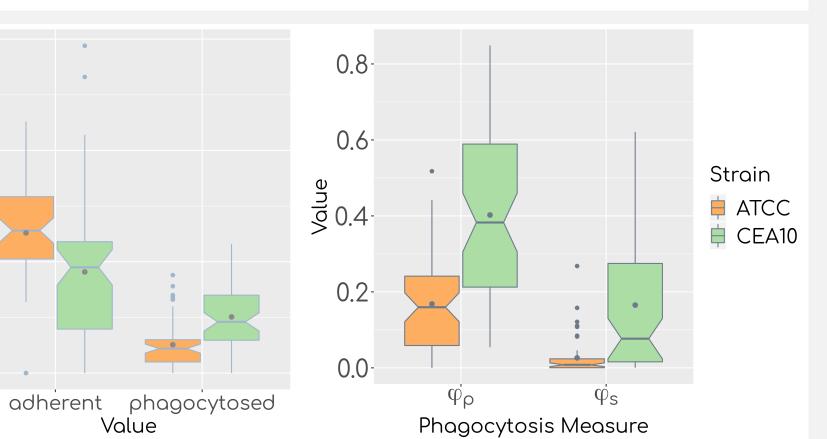
PHAGOCYTOSIS RATIO

 $\varphi_p = \frac{N_c^{phag}}{N_c^{phag} + N_c^{adh}} \in [0, 1]$

PHAGOCYTIC INDEX

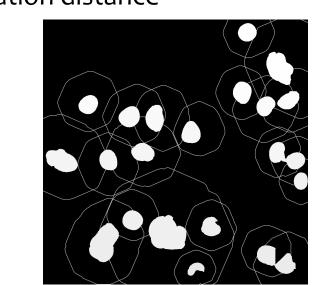
 $\varphi_i = \frac{N_c^{phag}}{N_m} \times \varphi_u \in [0, \text{MOI}]$

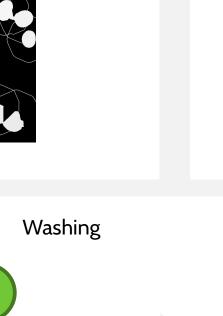


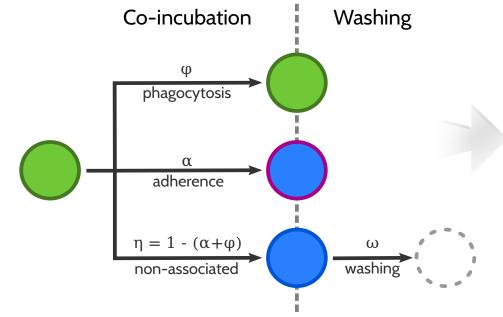


Model & Simulation



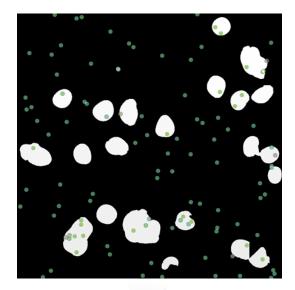


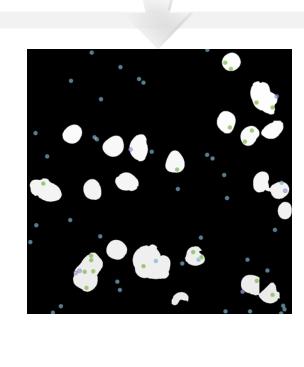






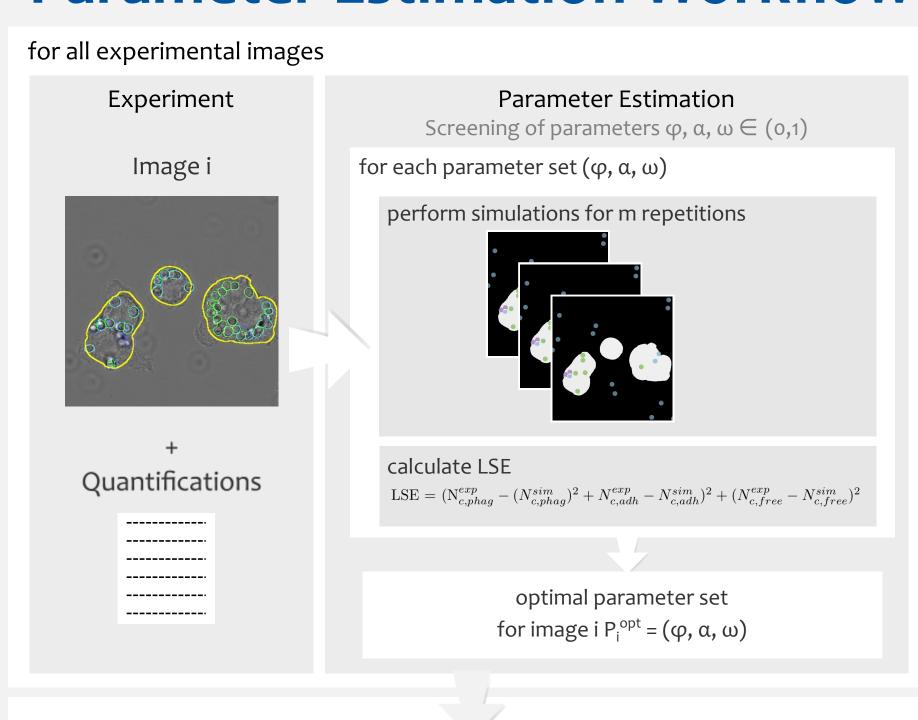
Distribution of cells:







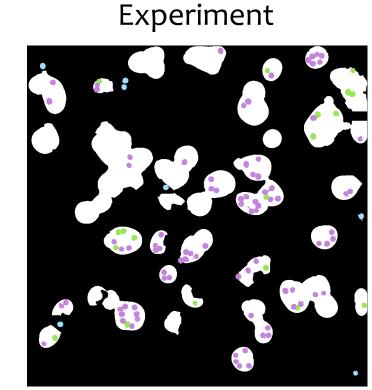
Parameter Estimation Workflow

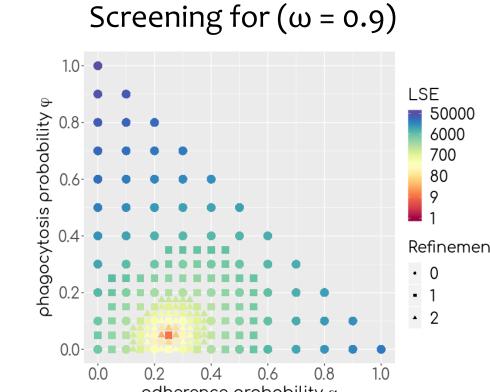


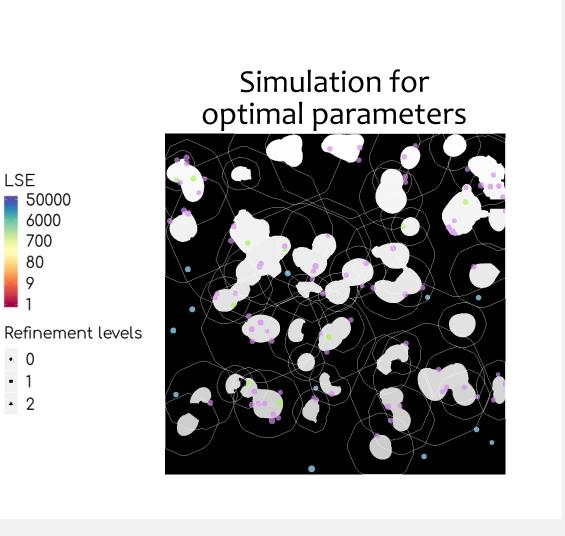
calculate average Parameter set over all P_i opt

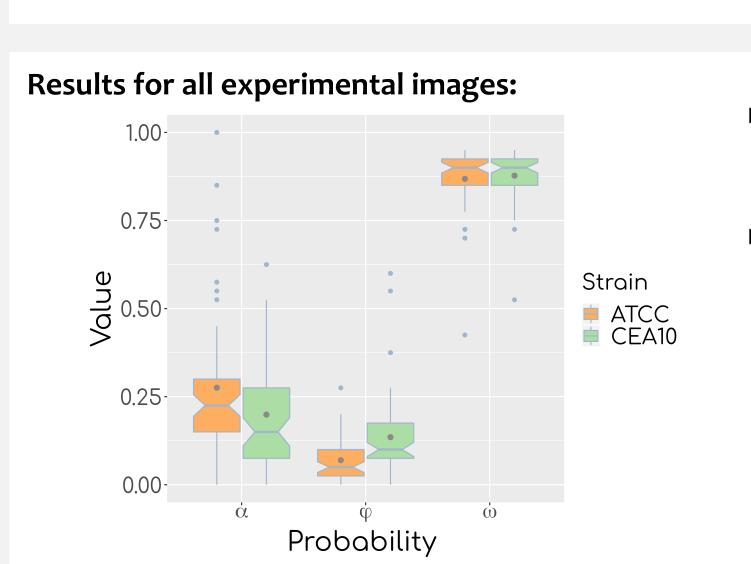
Estimation of Microscopic Parameters

Example: Screening for one image









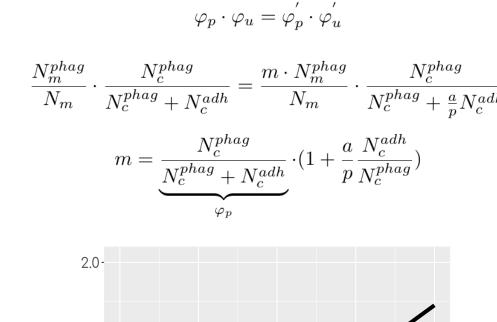
- ▶ higher adherence probability and lower phagocytotsis probability for ATCC compared to CEA10

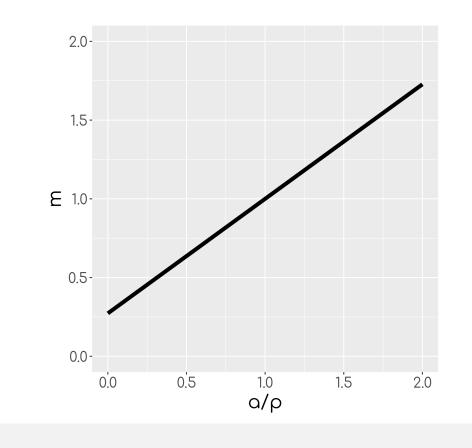
Outlook:

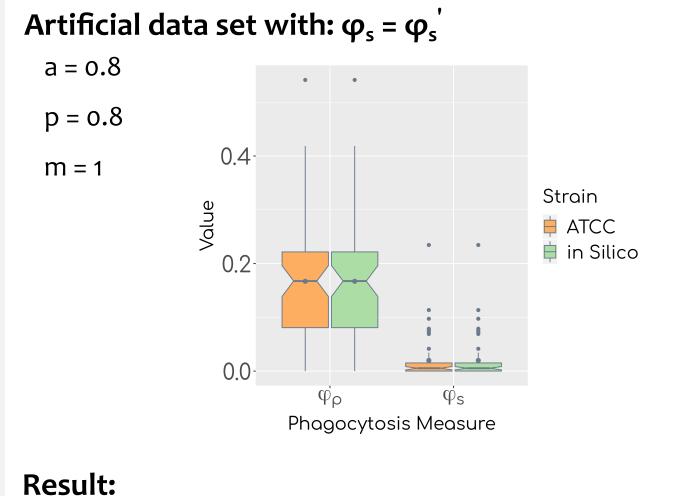
- ▷ estimation of migration distance
- ▶ fitting of model to probability distribution that a macrophage contains a certain number of adherent and phagocytosed conidia

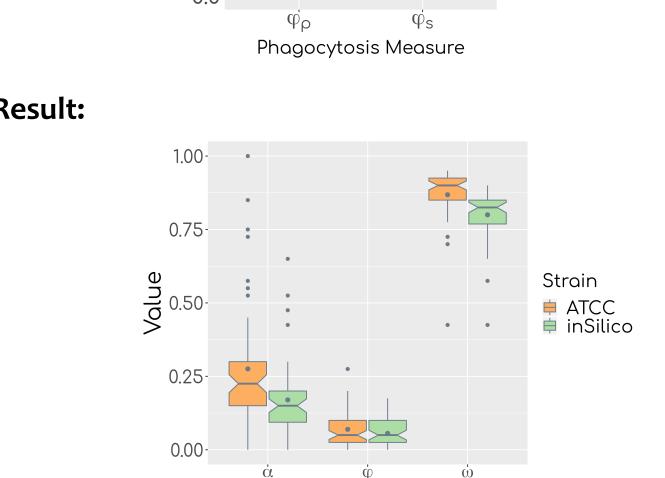
Resolve Ambiguities of Phagocytosis Measures

Assumption: Two indepenendt experiment with $\varphi_p = \varphi_p'$ possible for p = a > 0 $\varphi_{s}=\varphi_{s}^{'}$









Probability

Outlook:

- ▷ generation of artificial macrophage images

References:

Cseresnyes Z*, Kraibooj K*, Figge MT, *authors contributed equally (2018) Hessian-based quantitative image analysis of host-pathogen confrontation assays. Cytometry A 93(3), 346-356.

Kraibooj K*, Schoeler H*, Svensson C-M, Brakhage AA, Figge MT (2015) Automated quantification of the phagocytosis of Aspergillus fumigatus conidia by a novel image analysis algorithm. Frontiers in Microbiology 6(549), *authors contributed equally.

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