From Conidial Germination to Hyphal Growth: A Spatial Model of *Aspergillus niger*
Thesis Proposal MSc Computational Science

Boyan Mihaylov

October 2024

Abstract

The development of fungal organisms from spores to mycelial colonies is driven by complex biochemical pathways through multiple stages of structural transformation. While research endeavours have focused on these stages separately, general models which consolidate system knowledge to simulate fungal growth from spores to mycelia are not abundant. The objective of the current proposal is to bridge this gap by modelling the filamentous fungi of the genus *Aspergilli* - ubiquitous species in the human environment and important components in industrial biosynthesis. Studying their spatial development under different germination conditions could enable accurate predictions in industrial, medical or microecological applications.

1 Research Context

Aspergillus spp. have been studied through 2D[7] and 3D[10] imaging with regard to their conidial germination and subsequent hyphal growth. It has thus been established that nutrient medium[8], spore sizes and density[7] and the interaction with competitor spores[9] affect the incidence and time of germination of conidia cultures. The latter measurements are correlated with the lag and density of hyphal extension[6], adding to the effect of inoculum consistency on the morphology of the resulting mycelium[12]. To obtain a broader understanding of fungal development, it is necessary to construct a spatial model which consistently links germination to hyphal extension.

2 Research Methods

The proposed framework aims to represent spatial and morphological phenomena spanning from microscopic scale (single conidia and agglomerates thereof) to mesoscopic scale (free fillaments and hyphal pellets), starting with the well-studied model species *Aspergillus niger* and potentially exploring the applicabil-

ity of the model to other species such as *Aureobasidium pullulans*. Two primary sources of data are outlined so far:

- microscopic imagery of *Aspergillus* spp. germination up to early hyphal extension, obtained from an oCelloscope[5] system with extracted statistical data, used in the context of Ijadpanahsaravi et al. (2022)[7] and Ijadpanahsaravi et al. (2023)[9];

- synchrotron radiation-based microcomputed tomography data of the pellets of a hyperbranching *A. niger* mutant.

Relevant metrics from the first set describe the incidence, time and heterogeneity of germination and have been obtained by fitting a statistical model[4] to observed data. Despite the good fit of the model, it is not explained by closely related biological mechanisms[3], which opens a lateral research question whether modelling the spatial interactions between conidia (e.g. competition for the diffusive supply of resources[13] and carbon sensing[11]) can produce equivalent results. More importantly, the germination data can be used to model the distribution from which the germination times of conidia are drawn.

The imagery from this research also includes the early extension of germ tubes into hyphal filaments. For its specific purpose, overlapping hyphae have been removed from the set to avoid measurement ambiguities. However, the observed object overlaps can be revisited in search of more general statistics, e.g. related to hyphal densities.

The second data set represents the other extreme of the model scope - three-dimensional developed pellets of branching hyphae, starting from submerged agglomerates of conidia. It can therefore be used to verify the final morphology of the simulated mycelia, e.g. through volume, density, fractal dimension and curvature comparisons.

As a starting point, an agent-based model can encode the inherent heterogeneities of conidia[1] in static individual agents, which interact based on proximity and expand spatially through hyphal growth. The mechanisms of conidial agglomeration inform the initial spore distribution and should therefore be investigated. If evidence in literature establishes that the diffusive transport of molecules plays an important role in the process, the model can be re-formulated to incorporate lattice-based PDE techniques.

3 Significance of Research

Fungi of the genus *Aspergillus* are extensively used in fermentation for the food industry and in the industrial production of citric acid, enzymes and other biological molecules[2]. Concurrently, they are food spoilers and producers of harmful mycotoxins. Understanding their life-cycle and predicting the extents of their developmental stages therefore enables more advanced control over their effects.

4 Tentative Timeline

A tentative overview of some key milestones includes:

1. Submission of Thesis Proposal - by 21.10.2024;

2. Literature review (carbon signalling during germination, spore agglomeration, mechanics of hyphal growth) - by 01.12.2024;

3. Minimal model completion and data access setup - by 17.01.2025;

4. Verification and correction of model - by 28.02.2025;

5. Analysis of model results - by 28.03.2025;

6. Expansion of model (application to other species, incorporation of other mechanisms) - by 25.04.2025;

7. Documentation (writing of Thesis) - by 30.05.2025.

References

[1] R. Bleichrodt et al. "Cell Wall Composition Heterogeneity between Single Cells in Aspergillus fumigatus Leads to Heterogeneous Behavior during Antifungal Treatment and Phagocytosis". In: *mBio* 11 (2020). URL: https://api.semanticscholar.org/CorpusID:218617331.

[2] Timothy C. Cairns, Corrado Nai, and Vera Meyer. "How a fungus shapes biotechnology: 100 years of Aspergillus niger research". In: *Fungal Biology and Biotechnology* 5 (2018). URL: https://api.semanticscholar.org/CorpusID:44079887.

[3] Philippe Dantigny, Audrey Guilmart, and Maurice Bensoussan. "Predictive mycology: some definitions". In: *Cryptogamie Mycologie* 24 (2003), pp. 377–383. URL: https://api.semanticscholar.org/CorpusID:88848997.

[4] Philippe Dantigny et al. "A new model for germination of fungi." In: *International journal of food microbiology* 146 2 (2011), pp. 176–81. URL: https://api.semanticscholar.org/CorpusID:38620666.

[5] Marlene Fredborg et al. "Real-Time Optical Antimicrobial Susceptibility Testing". In: *Journal of Clinical Microbiology* 51 (2013), pp. 2047–2053. URL: https://api.semanticscholar.org/CorpusID:23926444.

[6] Maria Gougouli and Konstantinos P. Koutsoumanis. "Relation between germination and mycelium growth of individual fungal spores." In: *International journal of food microbiology* 161 3 (2013), pp. 231–9. URL: https://api.semanticscholar.org/CorpusID:7014604.

[7] Maryam Ijadpanahsaravi, Wieke R. Teertstra, and Han A. B. Wösten. "Inter- and intra-species heterogeneity in germination of Aspergillus conidia". In: *Antonie Van Leeuwenhoek* 115 (2022), pp. 1151–1164. URL: `https://api.semanticscholar.org/CorpusID:250697351`.

[8] Maryam Ijadpanahsaravi et al. "Minimal nutrient requirements for induction of germination of Aspergillus niger conidia." In: *Fungal biology* 125 3 (2020), pp. 231–238. URL: `https://api.semanticscholar.org/CorpusID:229474784`.

[9] Maryam Ijadpanahsaravi et al. "The impact of inter- and intra-species spore density on germination of the food spoilage fungus Aspergillus niger." In: *International journal of food microbiology* 410 (2023), p. 110495. URL: `https://api.semanticscholar.org/CorpusID:265268197`.

[10] Henri Müller et al. "Synchrotron radiation-based microcomputed tomography for three-dimensional growth analysis of Aspergillus niger pellets". In: *Biotechnology and Bioengineering* 120 (2023), pp. 3244–3260. URL: `https://api.semanticscholar.org/CorpusID:259993568`.

[11] Nir Osherov and Gregory S. May. "Conidial germination in Aspergillus nidulans requires RAS signaling and protein synthesis." In: *Genetics* 155 2 (2000), pp. 647–56. URL: `https://api.semanticscholar.org/CorpusID:15056931`.

[12] Maria Papagianni and Michael Mattey. "Morphological development of Aspergillus niger in submerged citric acid fermentation as a function of the spore inoculum level. Application of neural network and cluster analysis for characterization of mycelial morphology". In: *Microbial Cell Factories* 5 (2006), pp. 3–3. URL: `https://api.semanticscholar.org/CorpusID:263970456`.

[13] Anthony P. J. Trinci and Christine Whittaker. "Self-inhibition of spore germination in aspergillus nidulans". In: *Transactions of The British Mycological Society* 51 (1968), pp. 594–596. URL: `https://api.semanticscholar.org/CorpusID:83539867`.