David Moore’s World of Cyberfungi

Neighbour-Sensing Documentation

The mathematical models presented in these web pages are described in much more detail in the following publications.

PDF files can be downloaded from our website at http://www.davidmoore.org.uk/CyberWEB/Cyber08.htm

Branching in fungal hyphae and fungal tissues: growing mycelia in a desktop computer

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Abstract: In mycelial fungi the formation of hyphal branches is the only way in which the number of growing points can be increased. Cross walls always form at right angles to the long axis of a hypha, and nuclear division is not necessarily linked to cell division. Consequently, no matter how many nuclear divisions occur and no matter how many cross walls are formed there will be no increase in the number of hyphal tips unless a branch arises. Evidently, for the fungi, hyphal branch formation is the equivalent of cell division in animals, plants and protists. The position of origin of a branch, and its direction and rate of growth are the crucial formative events in the development of fungal tissues and organs. Kinetic analyses have shown that fungal filamentous growth can be interpreted on the basis of a regular cell cycle, and encourage the view that a mathematical description of fungal growth might be generalised into predictive simulations of tissue formation. An important point to emphasise is that all kinetic analyses published to date deal exclusively with physical influences on growth and branching kinetics (like temperature, nutrients, etc.). In this chapter we extrapolate from the kinetics so derived to deduce how the biological control events might affect the growth vector of the hyphal apex to produce the patterns of growth and branching that characterise fungal tissues and organs. This chapter presents: (i) a review of the published mathematical models that attempt to describe fungal growth and branching; (ii) a review of the cell biology of fungal growth and branching, particularly as it relates to the construction of fungal tissues; and (iii) a section in which simulated growth patterns are developed as interactive three-dimensional computer visualisations in what we call the Neighbour-Sensing model of hyphal growth. Experiments with this computer model demonstrate that geometrical form of the mycelium emerges as a consequence of the operation of specific locally-effective hyphal tip interactions. It is not necessary to impose complex spatial controls over development of the mycelium to achieve particular morphologies.

Original reference:

Moore, D., McNulty, L.J. & Meškauskas, A. (2006). Branching in fungal hyphae and fungal tissues: growing mycelia in a desktop computer. In *Branching Morphogenesis*, ed. J. Davies. Austin, TX: Landes Bioscience Publishing/Eurekah.com. Chapter 4, pp. 75-90.

Concerted regulation of all hyphal tips generates fungal fruit body structures: experiments with computer visualisations produced by a new mathematical model of hyphal growth

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Abstract: Filamentous hyphal growth is inherently suited to kinetic analysis, and in many respects the fungal mycelium can be viewed as a very mechanical biological system, which lends itself to mathematical modelling. The mathematics of hyphal tip extension growth are well established. However, even though a hyphal growth equation can be written with confidence, and we have a good understanding of the effects of tropisms on growth, it is not easy to form a mental picture of the behaviour of large populations of hyphal tips. What is required, and what we believe we have produced, is a mathematical model that is sufficiently sophisticated to produce a realistic visualisation of fungal hyphal growth. This provides us with a cyberfungus that can be used for experimentation on the theoretical rules that might govern hyphal patterning, hyphal interactions, and tissue formation and organ development by actually visualising the virtual hyphal growth patterns that result from different regulatory scenarios. From a series of model experiments the most significant observation is that complex fungal fruit body shapes can be simulated by applying the same regulatory functions to all of the growth points active in a structure at any specific time. No global control of fruit body geometry is necessary. No localised regulation is necessary. The shape of the fruit body emerges from the concerted response of the entire population of hyphal tips, in the same way, to the same signals.

Original reference:

Meškauskas, A., McNulty, L. J. & Moore, D. (2004). Concerted regulation of all hyphal tips generates fungal fruit body structures: experiments with computer visualisations produced by a new mathematical model of hyphal growth. *Mycological Research*, **108**: 341-353. DOI: http://dx.doi.org/10.1017/S0953756204009670. CLICK HERE to download the full text.

Simulating colonial growth of fungi with the Neighbour-Sensing model of hyphal growth

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Abstract: The Neighbour-Sensing model brings together the basic essentials of hyphal growth kinetics into a vector-based mathematical model in which the growth vector of each virtual hyphal tip is calculated by reference to the surrounding virtual mycelium. The model predicts the growth pattern of many hyphae into three spatial dimensions and has been used to simulate complex fungal fruit body shapes. In this paper we show how the Neighbour-Sensing model can simulate growth in semi-solid substrata like agar or soil, enabling realistic simulation of mycelial colonies of filamentous fungi grown in 'Petri-dish style' experimental conditions. Newly implemented capabilities in the model include: a measurement and logging system within the program that maintains basic statistics about the mycelium it is simulating, this facilitates kinetic experimentation; inclusion of 'substrates' in the data space causing positive or negative tropisms for the growing mycelium; a horizontal plane tropism that provides a way of simulating colonies growing in or on a substratum like agar or soil by imposing a horizontal geometrical constraint on the data space the cyberhyphal tips can explore; three categories of hypha - standard hyphae are those that start the simulation, leading hyphae can emerge from the colony peripheral growth zone to take on a leading role, and secondary hyphae are branches that can arise late, far behind the peripheral growth zone, when mature hyphal segments resume branching to in-fill the older parts of the colony. We show how the model can be used to investigate hyphal growth kinetics in silico in experimental scenarios that would be difficult or impossible in vivo. We also show that the Neighbour-Sensing model can generate sufficiently realistic cord-like structures to encourage the belief that this model is now sufficiently advanced for parameters to be defined that simulate specific *in silico* cyberfungi. The potential utility of these cyberspecies is that they provide a means to model the morphogenetic effects of a variety of factors, from environmental and nutritional features to mutations, in experimentally realistic situations, offering a valuable addition to the experimental toolkit of all those interested in fungal growth and morphology.

Original reference:

Meškauskas, A., Fricker, M. D. & Moore, D. (2004). Simulating colonial growth of fungi with the Neighbour-Sensing model of hyphal growth. *Mycological Research,* **108**: 1241-1256. DOI: http://dx.doi.org/10.1017/S0953756204001261. CLICK HERE to download the full text.

Inspiration from microbes: from patterns to networks

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Abstract: Many relatively simple organisms, such as bacteria, cellular and acellular slime moulds and fungi, can self-organise to form patterns or complex developmental networks with a rich variety of structure andbehaviour. Many of these systems are intimately associated with nutrient acquisition or distribution, particularly under conditions where resources are limited and distributed patchily in time and/or space. It is postulated that emergent structures are likely to be efficient and resilient as they have been subject to many cycles of evolutionary selection pressure. In comparison to many biological networks, such as neural networks, genetic and biochemical pathways or food webs, microbes are also extremely accessible, and provide tractable experimental systems. In this Chapter, we briefly review areas where emphasis has been given to morphological representation of microbial structures and discuss areas of potential overlap with current developments in network theory.

Original reference:

Fricker, M. D., Bebber, D., Darrah, P. R., Tlalka, M., Watkinson, S. C., Boddy, L., Yiasoumis, L., Cartwright, H. M., Meškauskas, A., McNulty, L. J., Moore, D., Smith, D. M. D., Nakagaki, T., Lee, C. F. and Johnson, N. (2005). Inspiration from microbes: from patterns to networks. In: *Coping with Complexity*, Proceedings of the International Workshop on Complex Agent-based Dynamic Networks held at the Saïd Business School, University of Oxford, 5 - 7 October 2003.

A search for developmental gene sequences in the genomes of filamentous fungi

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Abstract: There is now a sufficient number of filamentous fungal genomes in the public databases to warrant at least initial comparisons with animal and plant genomes. Our interest lies in the control of multicellular morphogenesis, which is a feature of filamentous ascomycetes and basidiomycetes. Search of a representative collection of filamentous fungal genomes with gene sequences generally considered to be essential and highly conserved components of normal development in animals failed to reveal any homologies. We conclude that fungal and animal lineages diverged from their common opisthokont line well before the emergence of any multicellular arrangement, and that the unique cell biology of filamentous fungi has caused control of multicellular development in fungi to evolve in a radically different fashion from that in animals and plants.

Original reference:

Moore, D., Walsh, C. & Robson, G. D. (2005). A search for developmental gene sequences in the genomes of filamentous fungi. In *Applied Mycology and Biotechnology*, vol. 6, *Genes, Genomics and Bioinformatics*, D.K. Arora and R. Berka, Editors. Elsevier Science Annual Review Series, Elsevier Science. ISBN-10: 044451807X, ISBN-13: 978-0444518071. CLICK HERE to download the full text.

Using web agents for data mining of fungal genomes

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Abstract: We created an application called Sight, a Java™-based package that provides a user-friendly interface to generate and connect agents for automatic genomic data mining without requiring programming skills from the user. Sight was originally developed to automate analysis of the human genome and attempts to generate web agents for fungus-related Internet resources revealed that some of those resources use new methods of representing the information they report, and some servers returned multiple intermediate pages leading towards their response, which created difficulties for automated recovery of results. Consequently, it was not possible to use effectively the old version of Sight so this version of the application was adapted with a little additional programming, creating a new version for which these features of the fungal genome servers do not represent a problem. The new version of Sight (v. 3.0.0) that is tailored to servers carrying fungal databases is freely available for download from the project website at these URLs: http://bioinformatics.org/jSight/ and http://jsight.sourceforge.net/index_SF.htm.

Original reference:

Meškauskas, A. (2005). Using web agents for data mining of fungal genomes. In *Applied Mycology and Biotechnology*, vol. 6, *Genes, Genomics and Bioinformatics*, D.K. Arora and R. Berka, editors. Elsevier Science Annual Review Series, Elsevier Science.

A comprehensive comparative analysis of the occurrence of developmental sequences in fungal, plant and animal genomes

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Abstract: We report a fully comprehensive data-mining exercise, involving an estimated total of 590,000 similarity searches, using agents available on the Internet to search for homologies to polypeptide sequences assigned to the category ‘development’ in the Gene Ontology Consortium AmiGO database (www.godatabase.org). The results indicate that of 552 such developmental sequences only 78 are shared between all three kingdoms, 72 are shared only between fungi and animals, 58 sequences are shared between plants and fungi, and four sequences were common only to *Dictyostelium* and fungi. ***No sequences were strictly fungus specific***, but 68 occurred only in plants (Viridiplantae) and 239 occurred only in animals (Metazoa). Although some homology was indicated for a total of 219 fungal sequences, 143 (65 %) of the matches returned were assigned E-values of 0.05 and must be categorised as weak similarities at best. The majority of the highly similar matches found in this survey proved to be between sequences involved in basic cell metabolism or essential eukaryotic cell processes (enzymes in common metabolic pathways, transcription regulators, binding proteins, receptors and membrane proteins). What is lacking is crosskingdom similarity in the management processes that regulate multicellular development. ***The crown group of eukaryotic kingdoms control and regulate their developmental processes in very different ways***. Unfortunately, we know nothing about molecular control of multicellular fungal developmental biology.

Original reference:

Moore, D. & Meškauskas, A. (2006). A comprehensive comparative analysis of the occurrence of developmental sequences in fungal, plant and animal genomes. *Mycological Research*, **110**: 251-256. DOI: http://dx.doi.org/10.1016/j.mycres.2006.01.003. . CLICK HERE to download the full text.

Some of the background research is described in much more detail in the following publications (arranged in chronological order):

Moore, D. (1991). Perception and response to gravity in higher fungi - a critical appraisal. *New Phytologist*, **117**: 3-23. DOI: http://dx.doi.org/10.1111/j.1469-8137.1991.tb00940.x. CLICK HERE to download the full text.

Kher, K., Greening, J. P., Hatton, J. P., Novak-Frazer, L. A. & Moore, D. (1992). Kinetics and mechanics of gravitropism in *Coprinus cinereus*. *Mycological Research*, **96**: 817-824. DOI: http://dx.doi.org/10.1016/S0953-7562(09)81028-9. CLICK HERE to download the full text.

Hatton, J. P. & Moore, D. (1992). Kinetics of stem gravitropism in *Coprinus cinereus*: determination of presentation time and 'dosage-response' relationships using clinostats. *FEMS Microbiology Letters*, **100**: 81-86. DOI: http://dx.doi.org/10.1111/j.1574-6968.1992.tb14023.x. CLICK HERE to download the full text.

Greening, J. P., Holden, J. & Moore, D. (1993). Distribution of mechanical stress is not involved in regulating stem gravitropism in *Coprinus cinereus*. *Mycological Research*, **97**: 1001-1004. DOI: http://dx.doi.org/10.1016/S0953-7562(09)80869-1. CLICK HERE to download the full text.

Novak-Frazer, L. & Moore, D. (1993). Antagonists and inhibitors of calcium accumulation do not impair gravity perception though they adversely affect the gravitropic responses of *Coprinus cinereus* stipes. *Mycological Research*, **97**: 1113-1118. DOI: http://dx.doi.org/10.1016/S0953-7562(09)80512-1. CLICK HERE to download the full text.

Moore, D. Greening, J. P., Hatton, J. P. & Novak-Frazer, L. (1994). Gravitational biology of mushrooms: a flow-chart approach to characterising processes and mechanisms. *Microgravity Quarterly*, **4**: 21-24. CLICK HERE to download the full text.

Hatton, J. P. & Moore, D. (1994). Kinetics of stipe gravitropism in the mushroom fungus *Coprinus cinereus* under the conditions of microgravity simulation provided by clinostat treatment. *Microgravity Quarterly*, **4**: 101-106. CLICK HERE to download the full text.

Moore, D., Novak-Frazer, L., Hatton, J. P., Greening, J. P., Bourne, A. M. & Robson, G. D. (1994). Gravitropic reactions of the mushroom fruit body of *Coprinus cinereus*. In *Proceedings of the 5th European Symposium on Life Sciences Research in Space*, (ed. H. Oser & T. D. Guyenne), pp. 133-138. European Space Agency Publications Division, ESTEC: Noordwijk, The Netherlands. CLICK HERE to download the full text.

*Stočkus, A. (1994a). Basic assumptions and comparison of three gravitropic response models. *Advances in Space Research*, **14**: 145-148.

*Stočkus, A. (1994b). Diagravitropic response in primary plagiogravitropic corn roots. *Environmental and Experimental Botany*, **34:** 87-94.

*Stočkus, A. & Moore, D. (1996). Comparison of plant and fungal gravitropic responses using imitational modelling. *Plant, Cell & Environment*, **19**: 787-800. DOI: http://dx.doi.org/10.1111/j.1365-3040.1996.tb00416.x. CLICK HERE to download the full text.

Moore, D. (1996). Graviresponses in fungi. *Advances in Space Research*, **17** (6/7): 73-82. DOI: http://dx.doi.org/10.1016/0273-1177(95)00614-K. CLICK HERE to download the full text.

Greening, J. P. & Moore, D. (1996). Morphometric analysis of cell size patterning involved in gravitropic curvature of the stipe of *Coprinus cinereus*. *Advances in Space Research*, **17** (6/7): 83-86. DOI: http://dx.doi.org/10.1016/0273-1177(95)00615-L. CLICK HERE to download the full text.

Novak-Frazer, L. & Moore, D. (1996). The role of calcium accumulation and the cytoskeleton in the perception and response of *Coprinus cinereus* to gravity. *Advances in Space Research*, **17** (6/7): 87-90. DOI: http://dx.doi.org/10.1016/0273-1177(95)00616-M. CLICK HERE to download the full text.

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Moore, D. & *Stočkus, A. (1998). Comparing plant and fungal gravitropism using imitational models based on reiterative computation. *Advances in Space Research*, **21** (8/9): 1179-1182. DOI: http://dx.doi.org/10.1038/2091157b0. CLICK HERE to download the full text.

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Meškauskas, A., Moore, D. & Novak-Frazer, L. (1998). Mathematical modelling of morphogenesis in fungi. Spatial organization of the gravitropic response in the mushroom stem of *Coprinus cinereus. New Phytologist*, **140**: 111-123. DOI: http://dx.doi.org/10.1046/j.1469-8137.1998.00252.x. CLICK HERE to download the full text.

Meškauskas, A., Novak Frazer, L. & Moore, D. (1999). Mathematical modelling of morphogenesis in fungi: a key role for curvature compensation ('autotropism') in the local curvature distribution model. *New Phytologist*,

143: 387-399. DOI: http://dx.doi.org/10.1046/j.1469-8137.1999.00458.x. CLICK HERE to download the full text.

Meškauskas, A., Jurkoniene, S. & Moore, D. (1999). Spatial organization of the gravitropic response in plants: applicability of the revised local curvature distribution model to *Triticum aestivum* coleoptiles. *New Phytologist*, **143**: 401-407. DOI: http://dx.doi.org/10.1046/j.1469-8137.1999.00459.x. CLICK HERE to download the full text.

Moore, D., Reeve, M. A., Meškauskas, A., Sánchez, C. & Chiu, S W. (2000). Mushroom mechanics and mathematical models of mushroom morphogenesis. In: *Science and Cultivation of Edible Fungi, Mushroom Science XV*, **vol. 1** (L. J. L. D. Van Griensven, ed.), pp. 103-107. Balkema: Rotterdam. CLICK HERE to download the full text.

*Dr. Alvydas Stočkus was killed in an accident in February 1996.

If you have a more general interest in space life sciences, you may be interested in this book, which provides a critical review of the whole Space Life Sciences research field:

Moore, D., Bie, P. & Oser, H. (eds) (2012). ***Biological and Medical Research in Space; An Overview of Life Sciences Research in Microgravity***. Berlin: Springer-Verlag. 569 pp. ISBN-10: 3642646948, ISBN-13: 978-3642646942. Softcover reprint of the original 1996 edition. CLICK HERE to view Amazon page

The book provides an overview of the field as the initial exploratory research phase came to a close towards the end of the twentieth century. It comprises scientific reviews which have been prepared by recognized experts in Cell Biology, Human Physiology, Radiation Biology and Exobiology that together form the foundation for the in-depth experimental programmes which will become more accessible in the era of the International Space Station Alpha. Although the original was first published in 1996, the book was reprinted in 2012 and is ***still the only text available*** that thoroughly, and critically, reviews the microgravity research done in the 20th century.

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