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The diffusive vesicle supply center model for tip growth in fungal hyphae

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Abstract

We propose the *diffusive vesicle supply center model* for tip growth in fungal hyphae. The model is based on the three-dimensional vesicle supply center (VSC) model [Gierz, G., Bartnicki-García, S., 2001. A three-dimensional model of fungal morphogenesis based on the vesicle supply center concept: J. Theor. Biol. 208, 151–164], but incorporates two aspects of a more realistic vesicle delivery mechanism: vesicle diffusion from the VSC and a finite rate constant for vesicle fusion with the cell membrane. We develop a framework to describe tip growth for a general class of models based on the vesicle supply center concept. Combining this with a method for calculating the steady state distribution of diffusive vesicles we iteratively solve for stationary cell shapes. These show a blunter tip than predicted by the original VSC model, which we attribute to increased forward-directed vesicle delivery via diffusion. The predicted distance between the VSC and the utmost tip of the cell is set by the ratio between the diffusion constant and the rate constant for vesicle exocytosis. Combined with the cell radius, these define the only dimensionless parameter for our model.
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1. Introduction

1.1. Tip growth

Tip growth, also called apical growth, is an extremely polarized form of cell growth that leads to a narrow tubular extension of the cell. This phenomenon presents a beautiful example of morphogenesis that has captured the imagination of experimentalists and theorists alike. For a recent overview, see Geitmann et al. (2001) and references therein. Cells exhibiting tip growth are found in root hairs in plants as well as in the kingdoms of the protista and monera, but we will focus on the prominent example of fungal hyphae. These hyphae are cylindrical cell structures with a radius between 1 and 10 μm. Their growth speeds vary widely from one fungal species to another, but average around 1 μm/min. The length of an individual hypha can reach many times its diameter, giving it its distinct thread-like appearance.

The cytoplasm of fungal hyphae is separated from the outside world by a cell envelope consisting of two layers. The inner one is the plasma membrane. The outer layer is a stiff cell wall made of a network of polysaccharides and proteins that are interlinked by hydrogen- and covalent bonds. The growth process requires new material to be inserted into both the plasma membrane and the cell wall. This material is delivered through exocytosis of vesicles. As these vesicles fuse with the plasma membrane, they thereby increase its surface area, and simultaneously deposit their contents into the cell wall. In fact, the delicate balance between the

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amount of materials delivered to the inner and outer cell wall is maintained by the reverse process of endocytosis as demonstrated by Read and Hickey (2001).

An additional, intriguing aspect of hyphal growth is the presence of the *Spitzenkörper*, a characteristic cellular complex that is observed exclusively in growing tips. It appears to be surrounded by a high concentration of vesicles, suggesting that it plays an important role in directing growth. This view is supported by experiments, which show that the direction of growth can be controlled by displacing the *Spitzenkörper* (Bartnicki-García, 2002).

1.2. VSC model

Based on the putative role of the *Spitzenkörper* in growing hyphae, Bartnicki-García et al. (1989) proposed the *Vesicle Supply Center* (VSC) model. It postulates that vesicles mediating cell growth are created in the Golgi bodies and first transported to the *Spitzenkörper*, which acts as an organizing center. From there the vesicles are released to ultimately fuse with the plasma membrane.

The mathematical abstraction of the *Spitzenkörper* is a point-like object called the vesicle supply center. For the analysis it is not important how the vesicles are transported from the Golgi bodies to the VSC, as long as there is a steady stream of vesicles being released from it (indeed, if the VSC *produced* the vesicles, the model would remain unchanged). In the VSC model these vesicles are released randomly in all directions and move in straight lines from the VSC to the cell envelope. Once a vesicle hits the plasma membrane, it fuses with the membrane and externalizes its contents, causing a local expansion of the cell envelope.

The VSC model was originally introduced in a two-dimensional formulation (Bartnicki-García et al., 1989). It was elaborated through analytical calculations as well as numerical simulations to determine the cell shape, yielding approximately realistic results. Furthermore, the simulations, refined by Reynaga-Peña et al. (1997), could qualitatively reproduce non-steady state phenomena such as tip formation, growth reorientation and branching. It was only in 2001 that the original model was consistently extended to three dimensions (Gierz and Bartnicki-García, 2001).

Whilst appealing through its conceptual simplicity, the features of the original VSC model imply a somewhat hidden assumption, not often made explicit, which makes it distinctly unphysical. The problem arises from the notion of an isotropic vesicle delivery. More precisely, the model assumes the amount of wall material delivered to the cell envelope to be the same for any solid angle, as seen from the VSC. This is a natural starting point, which was undoubtedly chosen for its simplicity. However, when attempting to justify such a vesicle delivery pattern, the hypothesis of isotropic delivery sets in fact serious requirements on the inner workings of the cell.

To this end, the simplest explanation for an isotropic distribution profile would be an isotropic release from the VSC, followed by ballistic motion of the vesicles through the cytoplasm and instantaneous exocytosis at the cell wall. However, this must be rejected since, in absence of external forces, the sub-micrometer sized vesicles undergo essentially thermal motion, as already pointed out by Koch (1994). The vesicles will therefore *not* move in straight lines, but follow random walk-like trajectories.

An alternative explanation would therefore require guided vesicle transport, presumably through an intricate distribution network that would have to deliver vesicles in exactly the right proportions to the right locations. We have not been able to find evidence in the literature for the presence of such a distribution network. But even if it did exist, a relatively large proportion of material would have to be deposited towards the base of the cell in order to achieve isotropic vesicle delivery. This would therefore require active vesicle transport over large distances from the VSC, making isotropic delivery again an unlikely hypothesis.

1.3. Diffusive VSC model

In the light of the above analysis, we propose to study tip growth letting the vesicles diffuse freely after their release from the vesicle supply center. This assumption improves on the original VSC model in several ways. Primarily it avoids the physical impossibility of ballistic vesicle motion. Secondly, we shall show that it naturally leads to a forward-centered vesicle absorption profile with nearly no material being deposited near the base of the cell. Finally, diffusion allows for a finite vesicle exocytosis rate to be incorporated into the model in a natural way, through the boundary conditions. The latter advantages remain valid even if both diffusion and active directed transport were to play a role. The vesicle absorption profiles predicted, based on diffusive vesicles, are therefore a better starting point for further refinement than the isotropic distribution.

Before developing the details of a model based on diffusion, it is appropriate to justify its relevance by some simple order-of-magnitude estimates. The effective diffusion constant of the vesicles can be estimated from the Einstein relation $D = k_B T/(6\pi\eta a)$. Assuming the vesicle size a to be roughly 50 nm (Markham, 1995) and the viscosity η equal to that of water yields a diffusion constant of about $4\,\mu m^2/s$. Taking into account the fact that the cytoplasm is more viscous than water we estimate $D \approx 1\,\mu m^2/s$. This implies that vesicles will take only a few seconds to travel from the VSC to the cell