

A reaction-diffusion model for the activity of stem cell-specific transcription factors in *Arabidopsis* roots

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Stem cells are one of the fundamental features characterizing complex multicellular organisms. They are distinguished by their capacity for self-renewal, providing precursors of more specialized cell types to build the organism during development, and constitute a reservoir for tissue regeneration upon situations of damage or stress. To these ends, the size of stem cell niches is tightly regulated. Through mathematical modelling and experiments we study the spatial activity of two transcription factors involved in the division of cells within the root stem cell niche of the model plant *Arabidopsis thaliana*, and disclose the mechanisms by which their spatial activity is achieved.

The identity these cells is controlled by both positional signalling and local cues between neighbouring cells, many regulations of which are yet to be uncovered. BRAVO and WOX5 are two transcription factors specifically expressed in the stem cell niche of the primary root, and are known for their role as repressors of stem cell division [1][2]. By combining experimental analysis and mathematical modelling, we recently disclosed regulatory interactions between the two factors, finding that they interplay in a circuit involving the activation of BRAVO by WOX5 and the formation of a transcriptional complex [3]. While WOX5 is only expressed in a small group of cells (called the quiescent center), the expression of BRAVO covers both the quiescent center and part of the vasculature (Figure 1). Interestingly, in loss of function mutants of BRAVO (*bravo-2*), the activity of the BRAVO promoter expands shootwards (Figure 1). This means that in wild-type roots, BRAVO confines its own expression to the stem cell niche, in a mechanism that requires WOX5. Our aim here is to uncover the details behind these mechanisms of self-confinement.

To explain the spatial patterns observed in roots, we introduce a modelling framework based on reaction-diffusion equations, where the regulatory interactions between BRAVO and WOX5, together with diffusion of WOX5, are taken into account. The equations describing these interactions have the form [4]:

$$\frac{dB(x,t)}{dt} = P_B(B,W) - \lambda BW - d_B B$$

$$\frac{dW(x,t)}{dt} = P_W(B,W) - \lambda BW - d_W W + \nabla [D_W(x)\nabla W]$$

Where P_B and P_W are regulatory functions controlling the production of each factor, λBW represents the irreversible formation of an immobile complex, and $d_B B$, $d_W W$ represent protein degradation. The equations are implemented in a realistic root layout through the explicit spatial dependence of the diffusion coefficient $D_W(x)$, making the system spatially heterogeneous. In particular, $D_W(x)$ takes different values depending on whether the spatial position belongs to the interior of a cell or to the cell wall, thus incorporating the natural boundaries already present in the cellular structure of the root. With this model, we are able

to recapitulate the spatial patterns of promoter activities in wild-type and mutant plants (Figure 1).

Altogether, our results propose a mechanism to drive self-confined expression based on the attenuation of a diffusible activator. In the case of BRAVO, attenuation happens through the formation of a complex with WOX5, which prevents its movement and subsequent activation of BRAVO. We expect our results to shed light on the regulatory principles underlying the maintenance of stem cell populations not only in plants, but in multicellular organisms on the whole.

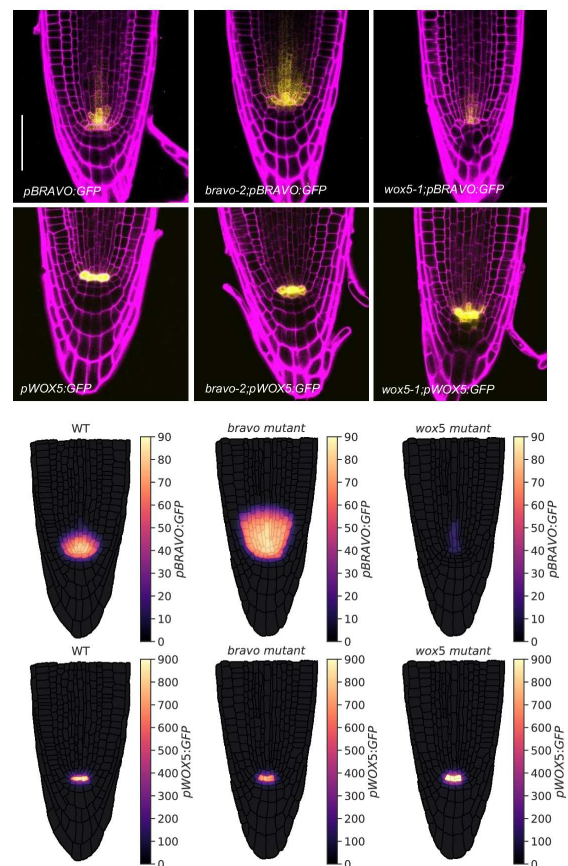


Fig. 1. Promoter activity of BRAVO and WOX5 in the *Arabidopsis* stem cell niche. Comparison between experiments (Top) and simulations in a realistic root layout. Images taken and adapted from [3][4].

[1] J. Vilarrasa-Blasi *et al*, *Dev. Cell.* **30** (1) 36-47 (2014).

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