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Analytical modeling of Dpp wt profile and tkv clones in Drosophila wing imaginal discs

Morphogen concentration gradients in developing organisms or tissues provide positional information which can induce patterning and space-dependent cell fates [1]. A well known example is Decapentaplegic (Dpp), involved in the patterning of *Drosophila* wing imaginal discs, which forms a concentration gradient along the Anterior-Posterior axis [2].

In a recent work [3], we developed and compared to experimental data a 1D analytical model describing the Dpp steady state gradient profile and tkv mutant clone effects. In this model, we identify three distinct Dpp components: external Dpp, Tkv-bound Dpp and internalized Dpp. We assume that the external Dpp diffuses from a finite-size production region and can bind to the Tkv receptors. The bound Dpp can unbind or be internalized. The internalized Dpp can be degraded or transported cell by cell by transcytosis. We consider that transcytosis is receptormediated and we model it in a pure diffusive way. Assuming a large number of free receptors allows for the linearization of the corresponding differential equations, from which we obtain simple analytical expressions for each Dpp component.

In the tkv clonal regions, the number of receptors as well as the receptor-mediated transcytosis are affected. We consider loss-of-function (LOF) experiments, with no receptors inside the clone, and gain-of-function (GOF) experiments, with a n-fold increase of receptors.

An extensive qualitative analysis of LOF experiments and quantitative data extraction from the GOF images allows to (i) constrain the parameters space and find a set of optimal parameters (ii) understand which of the external diffusion or transcytosis is the dominating mechanism in the Dpp gradient formation (iii) obtain the relative abundance of external, Tkv-bound and internalized Dpp. All the experimental data and theoretical results are reported in [3].

References

- [1] L. Wolpert L Positional information and the spatial pattern of cellular differentiation J. Theor. Biol. **25**(1) 1–47
- [2] E. V. Entchev et al. Gradient formation of the TGF-beta homolog Dpp Cell 103(6) 981–991
 [3] G. Schwank, S. Dalessi et al. Formation of the long range Dpp morphogen gradient Manuscript submitted