Fly Magnetism: Planar cell polarity in the wing

Yoram Burak[1] and Boris I. Shraiman[1]

We propose a model for the formation of planar cell polarity in the *Drosophila* wing, based on the hypotheses that the two membrane proteins Frizzled and Van-Gogh form complexes across inter-cellular interfaces. We analyze the dynamics of cell polarity taking into account the stochastic nature of underlying reactions, make quantitative predictions for polarity amplitude and orientation and explore their experimental implications.

I. Introduction

Epithelia in diverse tissues acquire polarization within the two-dimensional layer of cells [1] – a phenomenon called planar cell polarity (PCP). In the developing wing of *Drosophila*, PCP determines the growth direction of small hairs that extend radially from cell boundaries. In a normal fly's wing, where cells are approximately hexagonal and form a honeycomb lattice, all of these hairs point in a particular orientation, towards the distal end of the wing.

A series of experiments from the past several years [2] show that several key proteins, including the membrane-bound proteins Frizzled (Fz) and Van-Gogh (Vang), localize asymmetrically on cell boundaries – defining a direction in the plane within each cell and forming a characteristic zig-zag pattern of protein localization on the lattice. Other experiments [3-4] show that PCP is not determined independently in each cell: an interaction between neighboring cells strongly tends to orient their polarization in the same direction – bringing up an analogy between PCP and models of ferromagnetism in statistical mechanics.

A model for PCP formation was recently proposed in Ref. [5], and was shown to reproduce several experimental findings. This model involves more than 40 parameters that were tuned to reproduce a set of mutant phenotypes. Here we propose a simpler and more general model, which does not attempt to incorporate all the molecular details (unknown at this stage,) but involves a smaller number of (phomenological) parameters and degrees of freedom. This approach makes it possible to address the model's behavior in parameter space (for example, is there long-range order in the steady state?) – and to investigate quite generally the necessary conditions on constraining molecular interactions.

We argue that bistability on each inter-cellular interface can arise generically under the assumption that Fz and Vang form complexes across these interfaces, provided that one complex polarity inhibits formation of the opposite one. To further obtain the characteristic zig-zag pattern on a honeycomb lattice, inhibition should act non-locally within each cell. We suggest a general possible mechanism for generating such a non-local interaction, involving a modification (e.g. phosphorylation) of a diffusible protein.

Acknowledgements: This research was supported in part by the National Science Foundation under Grant No. PHY05-51164.

[1]Kavli Institute for Theoretical Physics, UC Santa Barbara.

II. Results

A. Phase Diagram, Stochasticity, and Dynamics

With a realistic number of molecules in each cell we find that noise-driven fluctuations are sufficiently weak to maintain long-range order in the steady-state. However, this steady state is not necessarily reached within developmental time scales, and noise plays an important role in this respect.

Dynamics are characterized by an isotropic symmetry-breaking instability at long wavelength – which, together with the stochasticity of molecular reactions, yields quantitative predictions on the time development of polarity amplitude and orientation. For example, in the absence of a symmetry-breaking, orienting field, a disordered pattern of polarity must arise first – to be followed by much slower coarsening dynamics. This observation may explain the disordered patterns seen in Fat clones [4], where only short-range polarity correlations are observed.

B. Orienting field

Stochasticity also excludes the possibility that the global signal, choosing the distal direction in a normal fly, is localized at the edge of the wing. In contrast, we find that a weak bulk field is able to fully orient the wing within relevant time-scales. In addition we find that, very generally, a graded expression of Fz or Vang within the wing can act as an orienting field.

C. Experimental implications

Inducing a tunable external field via graded expression of Fz or Vang can be invaluable for quantifying the endogenous orienting signal and ultimately elucidating its molecular nature; and for probing the nature of Fat mutants. This is now becoming a realistic experimental goal [6].

Our results on the dynamics of polarity amplitude and orientation provide additional quantitative predictions that can be used to either falsify the model – or to validate its salient predictions.

References

[1] Adler PN (2002). *Dev. Cell* **2**, 525.
[2] Usui T et al. (1999). Cell 98, 585; Axelrod JD (2001), *Genes Dev*. **15**, 1182; Strutt DI (2001), *Mol. Cell* **7**, 367; Tree DRP et al. (2002), *Cell* **109**, 371; Bastock R et al. (2003), *Development* **130**, 3007.
[3] Vinson CR and Adler PN (1987), *Nature* 329, 549.
[4] Ma D et al. (2003), *Nature* **421**, 543.
[5] Amonlirdviman K et al. (2005), *Science* **307**, 423.
[6] Shimizu-Sato S et al. (2002), *Nature Biotech*. **20**, 1041.