July 16, 2009

Mathematical Models of Axon Guidance: Towards the Understanding of a Key Process in Development

Giovanni Naldi

University of Milan

ABSTRACT OF THE TALK

In the embryo, undifferentiated sets of cells form organized patterns following pathways marked by chemical cues. At this small scale, cues are represented by single molecules, displaced from their release location by diffusion. Diffusion is the movement of matter from areas with higher concentrations (near the source) to areas of lower concentrations. Cells crawl along the positive gradient, towards the direction of increasing chemical signal, from the periphery to the source. This establishes the controlled flow of material needed to build structured tissues. Cells work out the right direction sensing the chemical cues released in the environment, filtering out noise. In this worh we focus on the axon growth phenomena in neural development.

To understand this mechanism, it is essential to dig into the process of gradient sensing. Cells try to detect very small differences in molecule concentration across their tiny diameter. With this respect, they behave like an instrument that counts molecules in its surroundings and is allowed only a limited number of probings. The study of the measurement errors of such an instrument can explain the shape of the trajectories.

Moreover, we know that repeating the measure can reduce uncertainty, but it requires more time. A mathematical model of the measuring process and of the subsequent cell motion sheds light on the balance between the unevenness of trajectories and the time span of the motion in different conditions. This analysis can explain why neurons grow more slowly when the

surrounding environment is more complex, for example when they have to perform sharp turns like when they approach the developing spinal cord.

The model also suggests that some sort of amplification of the signal must occur inside the cell. This effect stems from a cascade of intracellular biochemical reactions that are only partially known to biologists. Mathematics can predict the magnitude of the amplification needed to separate a weak, but coherent signal, from the background noise and explain how even a couple of molecules in more in a certain direction can make the difference for life.

This is a joint work with P. Causin, G. Aletti, M. Gozzo (University of Milano, Italy), A. Zaghetto (Dulbecco Telethon Institute CNR-ITB, Italy), and G. Merlo (University of Torino, Italy)."