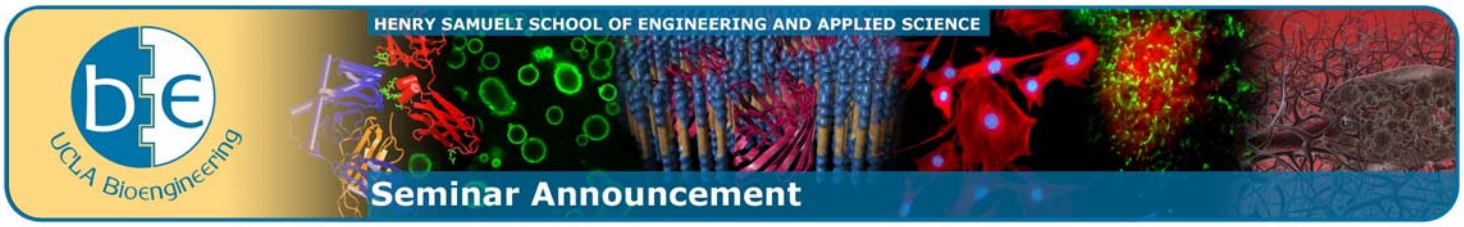

"Pattern Formation in Physiology and Pathophysiology"

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2101 Engineering V

ABSTRACT:

Morphogenesis, the formation of spatial patterns, is an integral part of embryological development, and is also important in the formation of pathological patterns later in life. The mechanisms by which patterns form are poorly understood. Our group uses mathematical models and computer simulation to understand the biochemical and spatial processes that create particular kinds of pattern.

These mathematical models use Partial Differential Equations (PDEs) to describe the diffusion and reaction of *morphogens*, proteins that act as activators or inhibitors of cell movement and/or commitment. Their biological and biochemical interactions, together with physical diffusion processes, can account for a number of physiologically important patterns.

For example, in atherosclerotic calcification, calcified lesions form 'focally,' that is, as localized spots. Bone morphogenetic protein (BMP), a potent chemotactic agent and inducer of commitment to bone phenotype, is known to be active in these calcifying lesions, along with several inhibitors of BMP, such as matrix GLA protein (MGP). Using a PDE model of BMP and MGP, we showed that 'stripe' and 'spot' patterns could be explained. Understanding how the spatial mechanisms produce the pattern also enabled us to make interventions to alter the patterns. Other potential examples of BMP-driven spatial patterns include the transition from cortical to trabecular bone, and the formation of other types of localized lesions, such as on the skin.

A number of morphogens are now known to be physiologically active, including FGF, EGF, retinoic acid, squint and others. How they interact spatially to produce observed normal and pathological patterns is an exciting area of research.

BIOGRAPHY :

Education

BA, Cornell University, Ithaca, NY (1966) (Mathematics, Philosophy)
PhD, Harvard University, Cambridge, MA (1975) (Philosophy, Mathematics)

Selected Publications

Garfinkel, A. *Forms of Explanation*. New Haven: Yale University Press, 1981 (Paperback edition, 1990).
A. Garfinkel, M.L. Spano, W.L. Ditto and J.N. Weiss. Controlling cardiac chaos. *Science* 1992
P Krogstad, C Uittenbogaart, R Dickover, YJ Bryson, S Plaeger and A Garfinkel. Primary HIV infection of infants: the effects of somatic growth on lymphocyte and virus dynamics. *Clinical Immunology* 1999
A Garfinkel, *et al*. Preventing ventricular fibrillation by flattening cardiac restitution. *Proc Natl Acad Sci USA* 2000
Garfinkel, A., Tintut, Y., Petrasek, D., Bostrom, K., and Demer, L.L. Pattern formation by vascular mesenchymal cells. *Proc Natl Acad Sci USA* 2004
Sato D, Xie LH, Sovari AA, Tran DX, Morita N, Xie F, Karagueuzian H, Garfinkel A, Weiss JN, Qu Z. Synchronization of chaotic early afterdepolarizations in the genesis of cardiac arrhythmias. *Proc Natl Acad Sci U S A.* 2009

Patents

US Patent #5342401 - Real time cardiac arrhythmia stabilizing system
US Patent #5447520 - Real time stabilizing system for pulsating activity