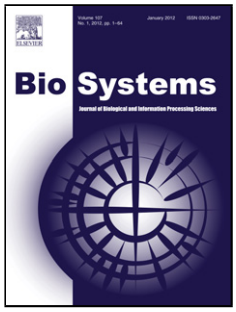

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Aggregating, Polarizing, Networking – The Evolution of Cell Adhesion Codes

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Abstract

Adhesion is a central mechanism in the development of multicellular life. It underlies cell movement, communication and differentiation. Remarkably, the presence of only three classes of interconnected molecules is sufficient to establish functional adhesive interactions between cells: Extracellular Matrix components (ECMs); Cell Adhesion Molecules (CAMs); and cytoskeleton microfilaments. In the present work, we shall dissect the nature and the dynamical interactions between these three classes of molecules as they appear in evolution, to postulate that their organization into an organic code *sensu* Barbieri[1] parallels the development of multicellularity. Adhesion codes are based on the use of CAMs as adaptors that establish arbitrary, yet specific, correspondences between the extracellular world presented by the ECM, and intracellular world, as shaped by the cytoskeleton. We review the literature to show that these three classes of molecules have very remote evolutionary origins, and were progressively co-opted for adhesive functions, being eventually articulated in the triadic structure that is a signature feature of organic codes. We draw on the published data for the description of molecular and structural novelties that allow for the elaboration of increasingly complex: molecular structures at cell level, *i.e.* the ECM, the cell junctions, the synapses; cell structures at tissue level, *i.e.* biofilms and filaments, the epithelium, the endothelium; and cell behaviors at cell, tissue and systems level, *i.e.* aggregating, polarizing, and networking. We additionally correlate the come into being of new structural and functional patterns of adhesion with some

[1] we can prove that an organic code exists if we find three things: (1) two independent worlds of molecules, (2) a potentially unlimited number of arbitrary connections between them implemented by adaptors, and (3) a selection of the adaptors (a set of coding rules) that ensures a specific mapping (Barbieri, 2003)