MAR09-2008-000226

Abstract for an Invited Paper
for the MAR09 Meeting of
the American Physical Society

Beller Lectureship Talk: Active response of biological cells to mechanical stress

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Forces exerted by and on adherent cells are important for many physiological processes such as wound healing and tissue formation. In addition, recent experiments have shown that stem cell differentiation is controlled, at least in part, by the elasticity of the surrounding matrix. We present a simple and generic theoretical model for the active response of biological cells to mechanical stress. The theory includes cell activity and mechanical forces as well as random forces as factors that determine the polarizability that relates cell orientation to stress. This allows us to explain the puzzling observation of parallel (or sometimes random) alignment of cells for static and quasi-static stresses and of nearly perpendicular alignment for dynamically varying stresses. In addition, we predict the response of the cellular orientation to a sinusoidally varying applied stress as a function of frequency and compare the theory with recent experiments. The dependence of the cell orientation angle on the Poisson ratio of the surrounding material distinguishes cells whose activity is controlled by stress from those controlled by strain. We have extended the theory to generalize the treatment of elastic inclusions in solids to "living" inclusions (cells) whose active polarizability, analogous to the polarizability of non-living matter, results in the feedback of cellular forces that develop in response to matrix stresses. We use this to explain recent observations of the non-monotonic dependence of stress-fiber polarization in stem cells on matrix rigidity. These findings provide a mechanical correlate for the existence of an optimal substrate elasticity for cell differentiation and function.

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