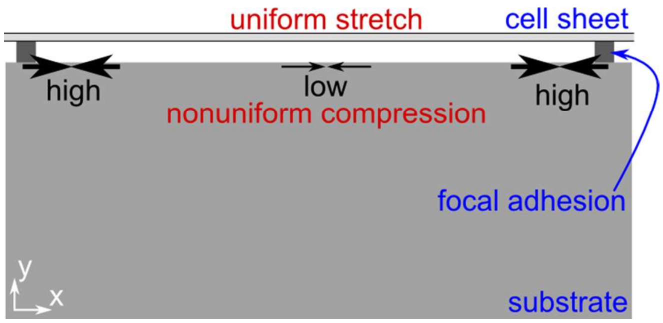
Soft Matter

Comment on "Intracellular stresses in patterned cell assemblies" by M. Moussus et al., Soft Matter, 2014, 10, 2414

Journal:	*Soft Matter*
Manuscript ID:	SM-CMT-03-2014-000597.R1
Article Type:	Comment
Date Submitted by the Author:	22-Apr-2014

Complete List of Authors:	Tambe, Dhananjay; Harvard School of Public Health, Department of Environmental Health Butler, James; Harvard School of Public Health, Department of Environmental Health Fredberg, Jeffrey; Harvard School of Public Health, Department of Environmental Health



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(Article type **COMMENT**)

Dhananjay T. Tambe, James P. Butler, Jeffrey J. Fredberg

To quantify intercellular stresses in a cell sheet, Moussus *et al.*[1] have recently proposed an approach which, under appropriate circumstances, may lead to significant simplification of the calculations required for stress recovery. Central to their approach is the assumption that the displacement fields of the substrate and the cells are continuous across the cell/substrate boundary. The purpose of this comment is to assess the validity and to highlight the implications of the displacement continuity assumption.

In a multicellular collective, the mechanical stresses that each cell exerts on its neighbors can now be quantified with several techniques[2-5]. Among these is Monolayer Stress Microscopy (MSM) where local mechanical stresses are quantified as two dimensional tensors. As such, MSM provides estimates of both anisotropic normal as well as shear components[5]. The MSM approach is based on the fact that stresses are continuous across the cell/substrate boundary, which follows from a simple argument concerning balance of forces. However, MSM requires an intermediate calculation of stresses at the cell/substrate boundary; these stresses are calculated through an inverse Boussinesq formulation in Fourier space[6]. To eliminate the intermediate stress calculations, Moussus *et al.*[1] assume that surface displacements of the substrate match those in the cell sheet itself; i.e. the displacement field is continuous at the cell/substrate boundary. In addition, the Moussus et al. approach requires that the elastic modulus of the cell sheet to be spatially uniform and quantitatively known (which is not a major concern with MSM[7]).

These observations then lead to the question of the extent to which, or under what circumstances, the condition of displacement continuity is satisfied in a real cell sheet. We argue that continuity is not likely to be satisfied. First, cell/substrate interactions are commonly understood to be effected through focal adhesions; at these sites, displacement continuity is assured through adhesion, but continuity elsewhere remains unknown. Second, away from the focal adhesion, substrate strains are highly non-uniform but cell sheet strains are expected to be relatively uniform (Fig 1)[7,8]. By construction, therefore, displacement continuity promotes intercellular stresses that are highly

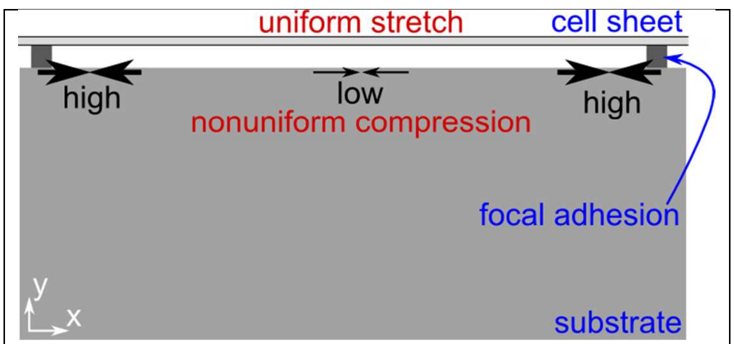

Figure 1. Strain field in the cell sheet and the substrate are discontinuous. *The cell sheet and the substrate are in contact at discrete points called focal adhesion, with nonuniform stresses in the substrate, but uniform stress in the cell sheet. The assumption of displacement continuity would lead to nonuniform stress recovery in the cell sheet.*

non-uniform.

We conclude that since MSM depends solely on stress continuity, it may represent more faithfully the intercellular stress distribution, without the introduction of spurious heterogeneities associated with the assumption of displacement continuity. In certain circumstances the approach of Moussus et al. might be valid, and, indeed, represent an advance, but those circumstances have not yet been validated. Given its robustness in accounting for the cell/substrate interaction, MSM remains the more appropriate approach.

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