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THE CELLULAR CONTROL OF BONE FORMATION: A CONTINUOUS MODEL OF MATRIX DEPOSITION AND OSTEOCYTE GENERATION

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Introduction. The formation of new bone involves both the deposition of bone matrix by osteoblasts and the formation of a network of cells embedded within it, called osteocytes. Osteocytes derive from osteoblasts that become buried in bone matrix during bone deposition. There has been a growing interest in osteocytes in recent years with the realisation that these cells are essential to the detection of micro-damage in bone, and that they participate in the orchestration of local bone renewal [1]. However, the generation of osteocytes is a complex process that remains incompletely understood. Whilst osteoblast burial determines the density of osteocytes, the expanding network of osteocytes regulates in turn osteoblast burial [1, 2].

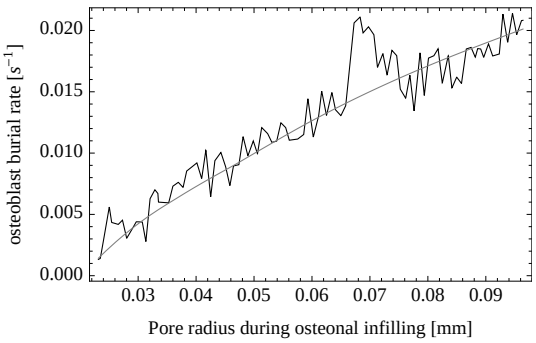
In this contribution, a continuous model of matrix deposition and osteocyte generation is proposed to elucidate the interplays between rate of new bone formation, rate of burial, and curvature of the bone substrate in determining (i) the density of osteocytes in the new bone matrix; (ii) the evolution of the surface density of osteoblasts; and (iii) the evolution of the bone interface through the secretory action of the osteoblasts and the control of osteocytes. This continuous model allows to determine how some of the bone formation dynamic processes occurring at the bone deposition front become 'imprinted' in the bone matrix.

Model. The generation of osteocytes and the evolution of the osteoblast surface density are described at the continuous level, by considering material balance equations in which source and sink terms are defined as biochemical reaction rates involving local cell densities. The governing equation for the osteocyte volumetric density is singular at the moving bone deposition front since osteocytes are only created at this front.

The evolution of the bone interface is described by a propagating interface equation and solved numerically by a level set method. The local rate of bone surface propagation

depends on the population of osteoblasts. Osteoblasts may locally concentrate or dilute with the locally contracting or expanding bone surface depending on the surface curvature.

Results. The governing equation for osteocyte density can be solved independently for osteocyte density. This reveals that the density of osteocytes generated at the moving deposition front depends solely on the ratio of the instantaneous burial rate and matrix secretion rate. It is remarkably independent of osteoblast density and substrate curvature. Consequently, burial rate can be estimated from osteocyte density and matrix secretion rate only. Using experimental data on osteocyte lacuna density from synchrotron-radiation microCT scans of cortical bone samples from a 20 year old male, burial rate is found to decrease during osteonal infilling (see Figure). Burial rate correlates positively with the density of osteocytes close to the deposition front, and negatively with the total number of osteocytes present underneath.



Osteoblast density increases in concavities of the bone surface due to the locally contracting surface. Thus concavities tend to refill faster than other regions of the surface. This effect, however, does not prevent the formation of singularities of the interface ('shock waves'), unless osteoblast diffusion is included.

Conclusions. Matrix deposition commonly occurs on substrates of complex curvatures with a varying osteoblast population. Whilst this can affect strongly the evolution of the bone interface, near uniform osteocyte distribution can still be expected in such tissues.

Marotti hypothesised that osteocytes promote osteoblast burial when they become covered with sufficient new matrix [2]. The positive correlation between burial rate and osteocyte density near the front is inconsistent with this hypothesis. However, our results suggest that such a control of osteoblast burial could emanate as a collective signal from a larger group of osteocytes.

REFERENCES

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