Hanifeh Khayyeri
Trinity Centre for Bioengineering, School of Engineering, Trinity College Dublin, Dublin, Ireland
e-mail: khayyerh@tcd.ie
Patrick J. Prendergast
Trinity Centre for Bioengineering, School of Engineering, Trinity College Dublin, Dublin, Ireland
e-mail: pprender@tcd.ie

Evolutionary simulation of the emergence of the mechano-regulated endochondral healing process

The ability of tissues to adapt to the mechanical environment is a remarkable feature of the skeleton. Several mechano-regulation theories have been proposed for describing how the mechanical environment modulates mesenchymal stem cell differentiation into bone, cartilage and fibrous tissue. Despite the biological complexity of the process, these theories have often been able to predict osseous healing through both membraneous and chondral healing, with reasonable success [1,2].

It is intriguing to wonder about the emergence of these healing processes, in particular the endochondral ossification process, in evolution and whether the ability of mechano-regulation has been involved in the emergence of new healing processes through natural selection. Early vertebrates, like cartilaginous fishes, could modulate their tissues to the mechanical environment and it is likely that evolution worked with adapting the skeletal tissues to the local conditions rather than involving major changes in cells or tissue types [3].

This study shows how the mechano-regulated endochondral ossification process could have emerged in evolution by being favoured in natural selection. The combination of a mechano-regulated tissue differentiation model [4] and a genetic algorithm for simulating evolutionary change [5], used in this investigation, was further able to capture inter-population variability in the mechano-regulated response and arrived at results that are in agreement with experimental studies of mechano-regulated differentiation and maintenance of bone [6,7].

References

[1] H. Isaksson *et al.*, 2006 *Corroboration of mechanoregulatory algorithms for tissue differentiation during fracture healing: Comparison with in vivo results* J. Orthop Res. **24** 898–907.
[2] H. Khayyeri *et al.*, 2009,*Corroboration of mechanobiological simulations of tissue differentiation in an in vivo bone chamber using a lattice-modeling approach* J. Orthop Res. **27** 1659–1666.
[3] B. K. Hall, 2005, *Bones and cartilage: developmental and evolutionary skeletal biology* San Diego, Elsevier Academic Press.
[4] P. J. Prendergast *et al.*, 1997, *Biophysical stimuli on cells during tissue differentiation at implant interfaces* J. Biomech. **30** 539–548.
[5] N. Nowlan and P. J. Prendergast, 2005, *Evolution of mechanoregulation of bone growth will lead to non-optimal bone phenotypes* J. Theor. Biol. **235** 408–418.
[6] E. F. Morgan *et al.*, 2010, *Correlations between local strains and tissue phenotypes in an experimental model of skeletal healing]* J. Biomech. **43** 2418–2424.
[7] U. Meyer *et al.,* 2001, *Tissue differentiation and cytokine synthesis during strain-related bone formation in distraction osteogenesis* Br. J. Oral Maxillofac. Surg. **39** 22–29.