TISSUE INTERFACE COMPUTATIONAL MODELLING

A discussion instigated by Reg Harris and completed in October 2015

Reg Harris I’m interested in the challenges of understanding/modelling what happens at the interface between biological tissues [or between biological tissue and nonbiologic implants, I suppose]. I recall that [in a recent discussion] we touched on the articular chondro-osteo region as example.

The scope of skelGEN\textsuperscript{1} includes bone, cartilage and tendons. I can see, or at least think I can see, that modelling the bone-cartilage interface, with its cytological, mechanobiological, physicochemical [etc] properties and behaviour will definitely be possible. Part of my 'sense' of this comes from the idea that the compact bone on one side of the interface, the interface \textit{per se}, and the cartilage on the outside constitute a reasonably stable [I don't mean closed] 'slow-moving' system in which it should be possible to place boundaries/outer/inner limits on the model[s] and to nourish them with new data as necessary [viz as a result of peculiarities of individual patients in the clinic].....and that if there had to be three models, one for each zone, they’d sync together easily within those boundaries.

I might be making a meal of this when it's all a doddle, and there may be better ways of expressing what I'm saying. Anyway, if you can bear with me.....

I have some difficulty visualising the modelling of tendon. The fact that skelGEN doesn't include muscle suggests, to me, that defining the boundaries for tendon models will be a bit harder. The interface.....bad term, a better one would be region.....between tendon and muscle is quite complicated. There is no right-cylinder type of interface where one might imagine building a clearly defined, finite model i.e. 'the tendon model stops here and the muscle model starts here'. Rather the region, correctly called the myotendinous junction or MTJ, appears to be characterised by an ensemble of specialised cells bridging the two tissues, possibly including finger-like sarcolemmal projections into the tendinous tissue; energy systems that transduce contractile forces from mechanically compliant muscle to the bone 'lever'; energy storage cross-talk between the two tissues; etc. So I'm thinking any model developed for tendon would need to be sort of open-ended, with 'hooks' that allow the various aspects of muscle behaviour to be incorporated as part of the 'super-system', which it is.

Cameron Brown\textsuperscript{2} It is indeed a difficult problem to model the interfaces (between different tissues, different regions of the same tissue, and scaffold-tissue interfaces), which is partly why we are trying to start with structure and build everything else on top of that. We already have mechanostuctural feedback and can call in biological/biochemical feedbacks and control the time scales on which they operate. One of the main things I am looking to do within the scope of skelGEN is to link into the CellML language to make use of what has already been developed (and those that are currently being developed).

This is going to require a reasonable amount of development, and some external funding to support it. I think the skelGEN project gives us a really nice basis from which to leverage these funds so we can certainly pursue it.

Yang Liu\textsuperscript{3} I assume we are discussing the tissue transition region between muscles and tendon, tendon and bone. Just as you said you can't draw a clear line as the boundary of the two type tissues, the anisotropic

\textsuperscript{1} An EU-sponsored four-country four-year project under IRSES [International Research Staff Exchange Scheme] to advance understanding and commercial translation of skeletal regeneration mechanisms

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structure represents gradually faded of one type of tissue as another type of tissue become more dominant across the transition zone and it is just this nature that make the tissue engineering of physiologically-representative organ (more than two type of tissue) more difficult.

Bram Sengers It all depends on the underlying question the model is meant to answer. For example, the bone-tendon interface would not significantly affect the predictions of a whole body biomechanical model, so if the transition is very local then one could choose to simply ignore this for that purpose. However load transfer between bone-tendon would be crucial for integration and repair, so in that case the interface would definitely need to be accounted for.

The way to model the interface at the macroscopic tissue scale (cm) would be to describe the variation in the mechanical properties as a continuous function of the position. So you would have stiff bone on one end and more flexible tendon on the other. What happens in between will lie somewhere in the middle. The exact dependency will indeed depend on the tissue constituents and their organisation at the microscopic scale.

As it may be difficult to find such local parameters, a multi-scale approach may be beneficial. For example, micro-scale models (e.g. based on histology) may help to inform how the macroscopic mechanical properties depend on the local tissue organisation and the fractions of the different tissue constituents.

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