Modelling foundations of cyclically loaded biphasic tissues with multiplicative remodelling

Supplementary Material to “Mechanically induced structural changes during dynamic compression of engineered cartilaginous constructs can potentially explain increases in bulk mechanical properties”

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Supplement A: Cyclically loaded biphasic tissues

The “gel diffusion time”, the time it takes for a cylindrical biphasic material in unconfined compression to reach equilibrium, can be calculated from the aggregate modulus $H_A$, the sample radius $r_0$ and its hydraulic permeability $k$ as [1]:

$$\tau_g = \frac{r_0^2}{H_A k}$$

For articular cartilage with the approximate material parameters $H_A = 1$ MPa, $k = 1.0 \cdot 10^{-15}$ m$^4$N$^{-1}$s$^{-1}$ and the sample radius relevant for current tissue engineering studies $r_0 = 2$ mm we find a characteristic time constant of $\tau_g \approx 67$ min. For agarose with the same geometrical dimensions and the material parameters $H_A = 1.5$ kPa, $k = 6.61 \cdot 10^{-13}$ m$^4$N$^{-1}$s$^{-1}$ [2] we find $\tau_g \approx 67$ min as well. These rough estimates show a comparable order of magnitude for $\tau_g$ of the two materials.

During cyclic (harmonic) loading an initial transient phase in the dynamic response of a biphasic tissue is followed by a steady-state [3]. Consider a displacement controlled harmonic load $u_z(t) = u_m + u_a \sin \omega t$ applied to a biphasic tissue where $u_m$ is the offset compression (mean axial deformation) and $u_a$ the amplitude. The resulting lateral displacement $u_r$ and reaction

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Figure 1: Ramp-and-hold behaviour compared to cyclic loading. (a) Applied axial displacement relative to construct height over time normalised by the gel diffusion time; (b) resulting lateral displacement relative to sample radius over time normalised by the gel diffusion time.
force $F$ will be cyclical curves themselves with a mean corresponding to the value of $u_r$ or $F$ that would follow from step and hold test with $u_z(t) = u_m$. This has been confirmed by simulations with an exemplary parameter set, see Fig. 1.

**Supplement B: Remodelling of cyclically loaded tissues**

![Figure 2: Applied ($\lambda_a$) and mean ($\lambda_m$) deformation.](image)

Consider uniaxial remodelling of the recruitment stretch $\lambda_r$ towards a desired recruitment stretch $\lambda_0$ with the linear rate equation

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\dot{\lambda}_r = \frac{1}{\tau_r} (\lambda_0 - \lambda_r)
$$

and $\lambda_r(t = 0) = 1$. The specimen is loaded with a stretch $\lambda_a$ in form of a square wave alternating every second between $\lambda_t$ and $\lambda_c$, so that the mean deformation over time is equal to $\lambda_m = 0.5(\lambda_t + \lambda_c)$ (Fig. 2). With the characteristic time scale of loading $\tau_l$ we compare the transient evolution of the recruitment stretch for $\tau_r = 0.1\tau_l$, $\tau_r = \tau_l$, $\tau_r = 10\tau_l$ and $\tau_r = 100\tau_l$ for exemplary values of $\lambda_t = 1.3$, $\lambda_c = 0.4$ and hence $\lambda_m = 0.85$. Remodelling is driven either by the applied stretch – $\lambda_0 = \lambda_a$ – or by the mean stretch – $\lambda_0 = \lambda_m$.

Calculations show that for $\tau_r >> \tau_l$ remodelling can be approximated very well by remodelling with respect to the mean deformation rather than the actual current configuration (Figs. 3a to 3d). This approach allows for easier modelling and coarser time steps.

**Supplement C: Biphasic Materials at Equilibrium and Instantaneous Loading**

At equilibrium all hydraulic fluid pressurisation has decayed in a free draining porous medium ($p = 0$) so that the stress response equals that of a single phasic material with the constitutive relation of the solid matrix extended by the contribution of the osmotic pressure $\Delta \pi$. On the other hand, upon sudden loading the pore liquid is unable to escape the compressed matrix except for a thin boundary layer at free draining surfaces. The bulk material therefore behaves like a single phasic incompressible material [4].

Free swelling and the offset step were modelled as equilibrium loading. For the final dynamic load step, the parameter $D_2$ had to be modified to yield a nearly incompressible material (using $\nu = 0.495$). To maintain the current sample volume ratio $\tilde{J}$ at the point of transition $\tilde{t}$ an additional isotropic pressure term $-\tilde{p}I$ was added to the Cauchy stress tensor during the dynamic
Figure 3: Remodelling recruitment stretch for increasing remodelling time constants. Red curve with crosses: Remodelling with respect to current stretch ($\lambda_0 = \lambda_a$); blue curve with crosses: Remodelling with respect to mean stretch ($\lambda_0 = \lambda_m$); green curve: mean stretch $\lambda_m$.

Figure 4: (a) Volume ratio $J$ over applied compressive strain. (b) Reaction force over applied compressive strain. Lines represent results of biphasic models, the markers designate the single phasic approximation. Note, that the apparent strains for agarose and cartilage are different, as cartilage exhibits swelling and the compression in the bioreactor is applied with respect to day 0 (agarose) dimensions.

Load step (derived from $\psi_{I_3}^L + k = \psi_{I_3}^C$, and push forward $\tilde{p} = 2J^{-1}kI_3$)

$$\tilde{p} = \frac{4(D_2^{SL} - D_2^{DL}) \ln \tilde{J}^2}{J}$$  (3)
where $D_{2S}^L$ is the parameter value during the quasistatic load steps and $D_{2D}^{PL}$ the value during dynamic loading. All other material parameters were kept constant.

To test the accuracy of this approach we compared the volume ratio $J$ and the contact reaction force on the loading platen in a full biphasic model to the results of the single phasic approach. To cover the range of material properties of interest in this study we modelled an agarose sample and an isotropic cartilage sample ($C_1 = 0.11$ MPa, other material properties as in manuscript, no fibres). The boundary layer where the material does not behave quasi-incompressible was on the order of $< 5\%$ of the sample radius for agarose and $< 3\%$ of the sample radius for cartilage. Good quantitative agreement was found between both approaches. The volume ratio decreases during the equilibrium load step and stays nearly constant during the dynamic load step (Fig. 4a). The reaction force in the biphasic models increases more steeply with applied strain in the dynamic loading regimen as compared to the equilibrium load step due to fluid pressurisation (Fig. 4b). We conclude that under the present loading conditions the approximation of the biphasic medium as a compressible single phasic medium during the tare strain load step and an incompressible single phasic medium during the dynamic load step is sufficiently accurate.

References


