Title of the dataset

Figures and videos supporting the paper: 2D morpho sensitivity

Files and descriptions

The files in this online resource correspond to a single simulation with mean parameter values in the paper *"Sensitivity of a two-dimensional biomorphoelastic model for post-burn contraction".* Within this paper, we consider a two-dimensional morphoelastic model that predicts contraction in scars. This paper is a follow-up for our previous sensitivity analysis in 1D. We study the model's sensitivity. The following videos show the evolution of the model's variables in case of mean parameter values.

Moving_mesh.avi: In this video, we show how the triangulation mesh moves. The boundary of the initial wound is white. Around the boundary, the mesh is dense. We see that the mesh contracts until day 61 after which is retracts and converge after a year.

Fibroblasts_N.avi: In this video, we show how the fibroblast distribution changes during the wound healing. The red color means that the fibroblast cell density is in equilibrium, while the color blue means that there are no cells present. We see that in the first 100 days, the cell density next to the boundary outside the wound decreases as cells differentiate to myofibroblasts. After 100 days, cells migrate towards to scar and proliferate, and we see the cell density increasing inside the white scar boundary as the scar retracts. After one year, the cell density is not yet in equilibrium.

Myofibroblasts_M.avi: In this video, we show how the myofibroblast distribution changes during the wound healing. The blue color means that there are no cells present. We see that, shortly after the simulation starts, the cell density increases inside the wound. There is a high peak of myofibroblasts near the white wound boundary, and further, inside the wound, the cell density increases. The cells move toward the center of the scar and disappear around the white boundary as the scar retracts initially. Later, the cells disappear in the whole are as the scar retracts further. After one year, there are no cells present anymore.

Signaling molecules_c.avi: In this video, we show how the signaling molecule density changes during the wound healing. The dark blue color means there are no molecules present, and the lighter blue color means some molecules are (initially) present. We see the density increasing in the center of the wound rapidly, peaking on day 61. Then, the molecules gradually disappear and during this whole period, there are no molecules around the white scar boundary. The molecules vanished on day 100.

Collagen_rho.avi: In this video, we show how the collagen density changes during the wound healing. The light blue color means that the collagen density is in equilibrium, while the dark blue color means there is no collagen present. We see the density increasing gradually during wound healing with a high peak of collagen around the wound's boundary inside the wound and a little bit outside the wound. When the scar retracts, the peak in collagen shifts to the center of the scar, where is decreases gradually. The collagen density is not yet in equilibrium after one year, but almost.

Velocity_v1.avi: In this video, we show how the displacement velocity density v_1 changes during the wound healing. The yellow color means that the velocity is zero. Soon after the wound healing starts, the velocity on the left side of the wound increases, and it decreases on the right side of the

wound, peaking on the left and right edge corners. There is a clear symmetry line in y = 0. We see the density changing after 21 days. The peaks far outside the white boundary move toward the boundary, crossing it around day 42, after which the density moves toward equilibrium inside the scar. When the scar retracts, we see this phenomenon in this video as the density changes sign. The density increases on the right outside corner of the scar, peaking inside the scar around day 108, after it moves to equilibrium, relaxing the scar. The scar relaxes within one year.

Velocity_v2.avi: In this video, we show how the displacement velocity density v_2 changes during the wound healing. The description of what we see is similar to the above video, but then not for left and right sides, but for above and below sides.

Displacement_u.avi: In this video, we show how the displacement u changes during the wound healing. The green color means that the displacement is zero. Soon after the wound healing starts, the displacement on the left side of the wound increases, and it decreases on the right side of the wound, peaking on the left and right edge corners. There is a clear symmetry line in y = 0. We see the density peaking on day 61, after which is changes gradually to equilibrium. The peaks far outside the white boundary move toward the boundary, crossing it around day 85, after which the density moves toward equilibrium inside the scar. The scar shows little displacement after one year.

Displacement_v.avi: In this video, we show how the displacement v changes during the wound healing. The description of what we see is similar to the above video, but then not for left and right sides, but for above and below sides.

The following figures are shown in the paper.

Init_FB.fig: This Matlab figure corresponds to Figure 1 in the paper. This is an example of the initial fibroblast density. We also show the initial mesh and the wound boundary (in white). The color bar shows the number of cells per cm^3. Hence, on the wound boundary left-hand-side, there are 2000 cells/cm^3, and on the right-hand-side, there are 10000 cells/cm^3.

Example_RSA_density.fig: This Matlab figure corresponds to Figure 2a in the paper. This is an example of the evolution of the relative surface area (RSA). The figures shows that the RSA drops to about 65% (35% contraction) in 62 days, after which it increases to about 85% (day 150), to a final RSA of 87.6%.

Example_timestep.fig: This Matlab figure corresponds to Figure 2b in the paper. This is an example of the evolution of the time step during a simulation. The figure shows shows that the initial timestep of 0.1 day increases to the maximum of dt = 0.5 day within five days, after which it stays 0.5 days until the RSA increases. The timestep increases until the RSA increases too rapidly. Subsequently, the time step is reduced to obtain convergence in the inner Picard iteration loop. Once the second derivative of the RSA decreases, the time step reaches dt = 2 days, which stays constant until the RSA does not change more than 0.1% between time iterations. Then the timestep increases towards 18 days.

Example_mesh_quality.fig: This Matlab figure corresponds to Figure 2c in the paper. This is an example of the evolution of the mesh quality during a simulation. The figure shows that the mesh quality initially increases when the mesh moves. In this example, when the mesh contracts at the highest rate, the mesh quality starts decreasing. No remeshing is needed; hence the mesh quality increases when the mesh slowly moves toward maximum contraction (day 48 to 62) and keeps

increasing when the mesh retracts. When the retraction speed increases (day 70), the mesh quality decreases a little, however, remeshing is not needed, and the quality starts increasing again (day 76) until (some) triangles move in wrong positions as the retraction speed is increasing (day 88). Again, no remeshing is needed despite the decrease in quality, and subsequently, the mesh quality starts increasing rapidly again as the timestep increases (day 95 to 102). The rest shows that the mesh quality keeps increasing slower and decreasing slightly while the retraction speed slows down (day 124). In this example, the simulation did not need any remeshing.

Effects_of_nu_on_RSA.fig: This Matlab figure corresponds to Figure 3 in the paper. It is not the same figure but shows the effects on the relative surface area when the Poisson's ratio (nu) changes. We see that the scar contracts more for lower Poisson's ratios, where the lowest ratio of nu = 0.46 shows an extreme contraction of 84%. In the corresponding figure in the paper, we see that the boundary of the wound is very bumpy.

The following figures present the effect of the variations on the parameters on both the post-burn contraction and the discomfort that a patient might experience.

RSAmin.fig: This Matlab figure corresponds to Figure 4a in the paper. It shows the effects on the minimum of the RSA. We see that the most influencing parameters on decreasing the maximum contraction are the proliferation enhancement factor r_F^{max}, the generated stress per unit cell density xi, the equilibrium fibroblast distribution (N with a bar), the myofibroblast apoptosis rate δ_M, the (myo)fibroblast proliferation rate r_F, and the contraction inhibition constant R. Increasing values for δ_M, r_F and R, and decreasing values for r_F^{max}, xi and *N with a bar* result in less contraction.

RSAday.fig: This Matlab figure corresponds to Figure 4b in the paper. It shows the effects on the day when the RSA reaches the minimum. We see that te above results in maximal contraction on a later day. In addition, increasing values for the equilibrium collagen concentration results in maximal contraction on an earlier day.
The reduction in contraction because of increasing values for δ_M and R is not counter-intuitive because myofibroblast pull on the skin, and that R reduces the effect. The effect of the reduction in equilibrium collagen concentration is most prominent for the day of maximum contraction: a decrease of 25% delays this day by 40 days relative to the base simulation.

RSA365.fig: This Matlab figure corresponds to Figure 4c in the paper. It shows the effects on the RSA on day 365. We see that the signaling molecule secretion rate k_c and decay rate δ_c, the equilibrium collagen concentration *rho with a bar*, and the rate of morphoelastic change *zeta* can influence decreasing the contraction after one year the most. Increasing values for *rho with a bar* and δ_c, and decreasing the values for k_c and *zeta* results in less remaining contraction after scar maturation. If fewer signaling molecules are available to enhance the proliferation of (myo)fibroblasts and myofibroblast differentiation, then the tissue is influenced less according to the morphoelastic change. Further, an increase in collagen concentration results in stiffer tissue that resists contraction and acts as a buffer for effective strain.

SEDmax.fig: This Matlab figure corresponds to Figure 4d in the paper. It shows the effects on the maximum of the total strain energy (called SED in the paper, which was better to call TSE, but here we will still call it SED).
SEDday.fig: This Matlab figure corresponds to Figure 4e in the paper. It shows the effects on the day when the SED reaches the maximum.

We see that decreasing the maximal contraction by targeting r_F^{max}, xi, *N with a bar*, δ_M, and R results in less maximal discomfort, on a later day. An increase in the equilibrium collagen concentration

results in maximum discomfort on an earlier day.

RSA_NM.fig: This Matlab figure corresponds to Figure 5a in the paper. It shows the effects of the different proliferation rates on the RSA.
SED_NM.fig: This Matlab figure corresponds to Figure 5b in the paper. It shows the effects of the different proliferation rates on the SED.

These plots clearly show that we need to decrease the myofibroblast proliferation rate, in contrast to what the original model with equal proliferation rates shows. The advice to increase the proliferation rate means to increase the fibroblast proliferation rate, implying that the *fibroblast proliferation rate* is more sensitive than the *myofibroblast proliferation rate* in contrast to the result found before. Further, **RSA_NM.fig** shows that decreasing the myofibroblast proliferation rate by 25% results in a more extended retraction period, which is also seen in the clinic. In addition, **SED_NM.fig** shows that the decreased myofibroblast proliferation rate results in an extended period of persistent discomfort correlated with slower retraction.

Methodology

We used the finite element method and implemented the equations in Matlab. This way, we were able to produce the videos.

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