The Application of Neural Networks to Predict Skin Evolution After Burn Trauma

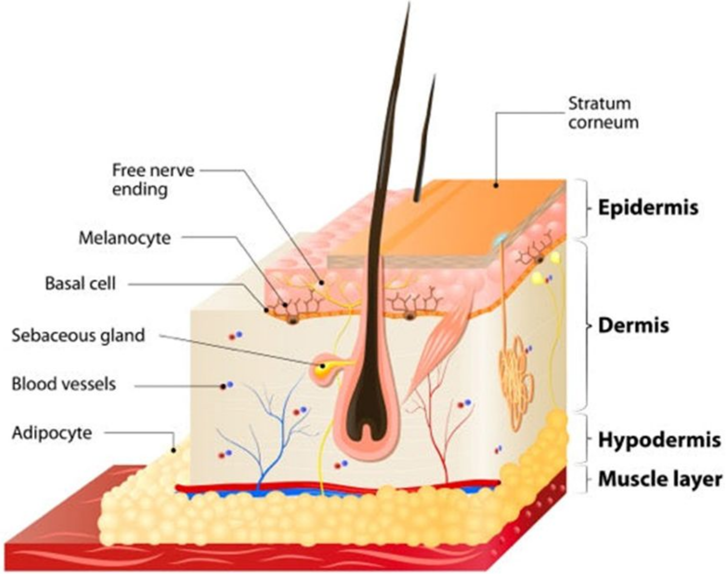
Literature Presentation

Selma Husanovic

Contents

Biological Background

Skin Consists of Three Layers

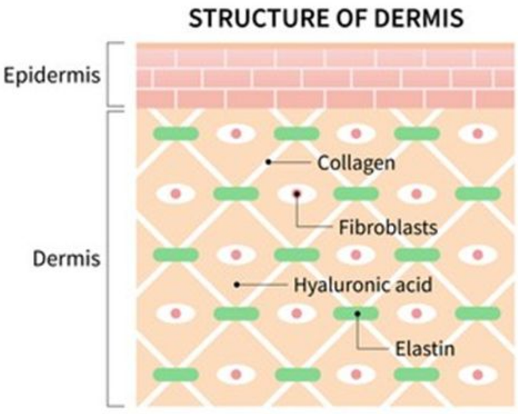


- Wounds to the epidermis are superficial and heal quickly, without scarring
- Wounds that affect the dermis are more complex, as the damaged dermis needs to be regenerated
- The focus is on the latter

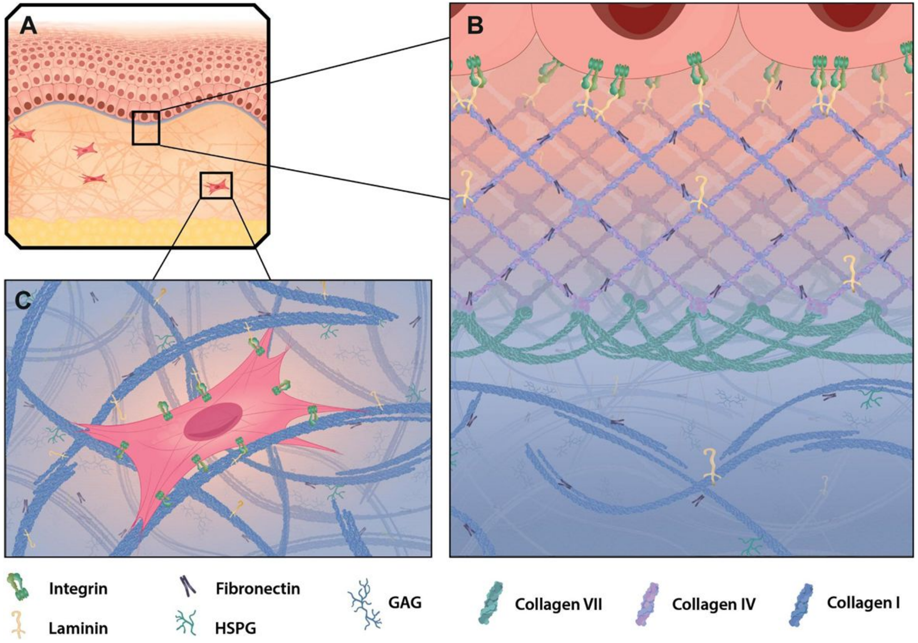
Gholizadeh, Z., Yousefi, R., & Asadi, S. (2020). The Role of Mutations on Genes KRT5, POFUT1 & POGLUT1, in Dowling-Degos Syndrome. International Journal of Innovative Research in Medical Science (IJIRMS), 5(08).

The Dermis Consists of

- Water
- Cells: **fibroblasts** being the most common ones
- ECM: 3D network of molecules that surrounds and supports the cells. Consist mostly out of **collagen** proteins



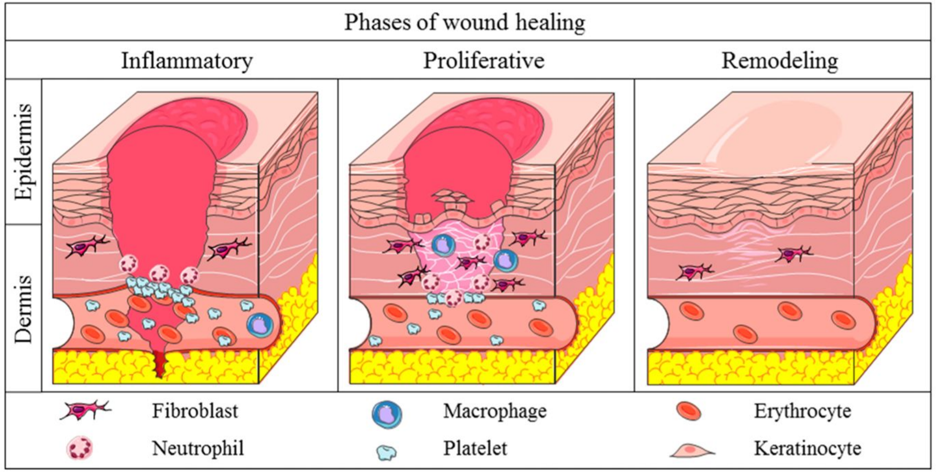
Extracellular Matrix (ECM)



- Acts as a scaffold for cells, such that they can migrate and perform their functioning
- Contains **signalling molecules**

Pfisterer, K., Shaw, L. E., Symmank, D., & Weninger, W. (2021). The extracellular matrix in skin inflammation and infection. Frontiers in cell and developmental biology, 9, 682414.

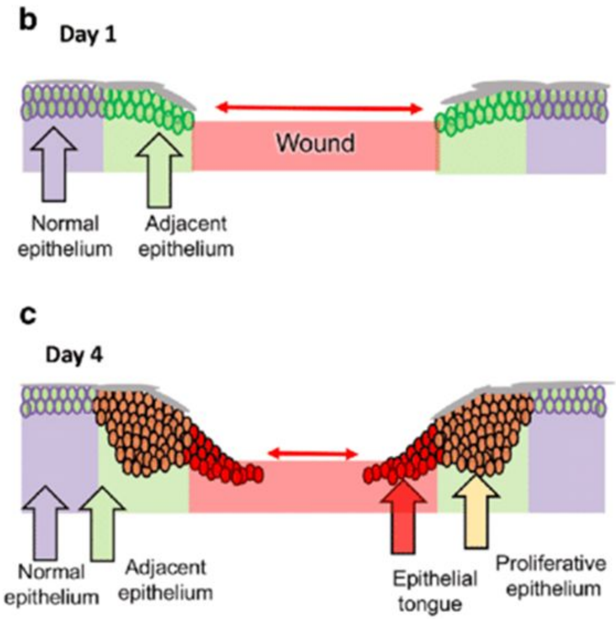
Wound Healing (ECM is damaged)

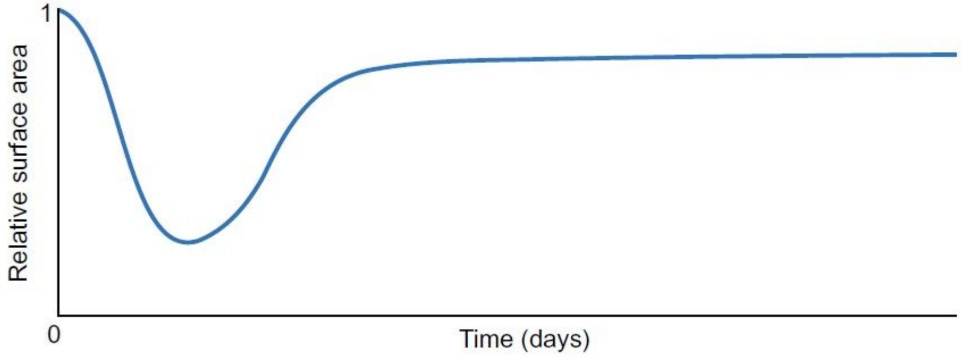


Ribatti, D., Benagiano, V., & Guidolin, D. (2023). Overlapping between Wound Healing Occurring in Tumor Growth and in Central Nervous System Neurodegenerative Diseases. Brain Sciences, 13(3), 398.

- Fibrin cloth is made, acting as temporary ECM
- Pathogens are removed
- Fibroblasts come in and deposit new ECM
- Signalling molecules: fibroblasts -> myofibroblasts
- Myofibroblasts pull on the ECM
- New ECM undergoes reorganisation

Contraction





Nascimento-Filho, C. H., Silveira, E. J., Goloni-Bertollo, E. M., de Souza, L. B., Squarize, C. H., & Castilho, R. M. (2020). Skin wound healing triggers epigenetic modifications of histone H4. Journal of Translational Medicine, 18(1), 1-11.

Egberts, G., Vermolen, F., & van Zuijlen, P. (2023). Stability of a two-dimensional biomorphoelastic model for post-burn contraction. Journal of Mathematical Biology, 86(4), 59.

Mechanical Background

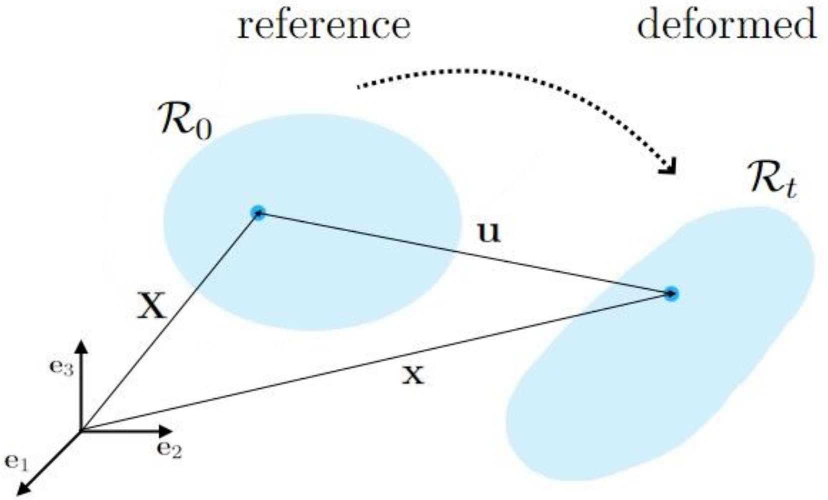
Description of Motion

Lagrangian / Material Description:

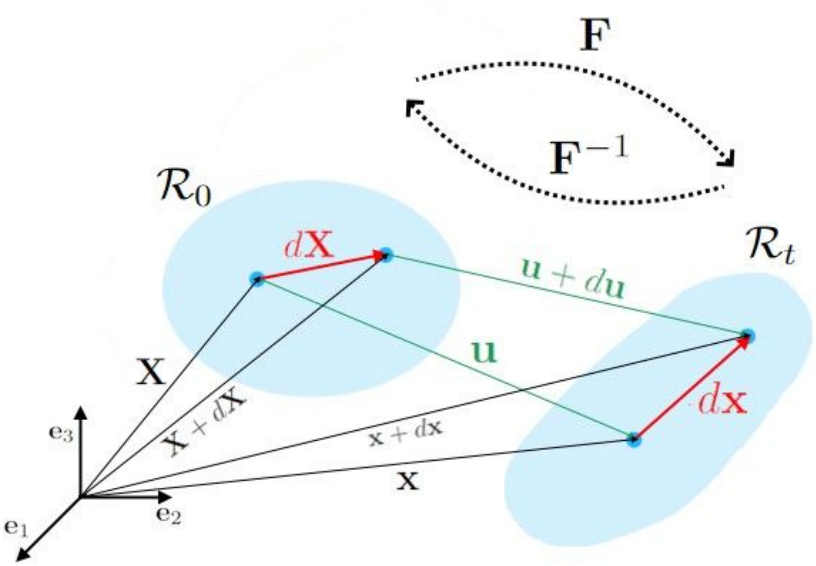
$$\mathbf{x} = \mathbf{f}(\mathbf{X}, t)$$

Eulerian / Spatial Description:

$$\mathbf{X} = \mathbf{f}^{-1}(\mathbf{x}, t)$$



Deformation Gradient Tensor



- Fundamental measure of deformation
- Maps line elements in reference configuration to line elements in current configuration

$$d\mathbf{x} = \mathbf{F}\, d\mathbf{X}$$

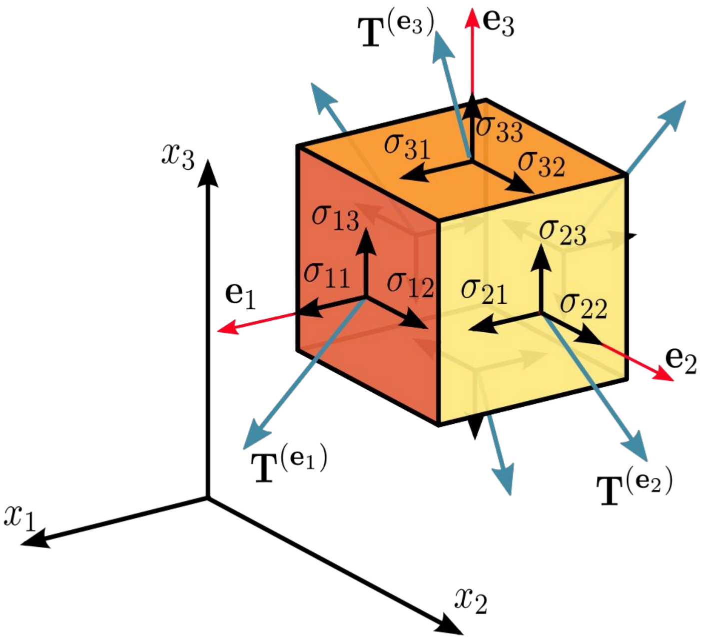
Strain tensor

- Strain is a measure of deformation of a body with respect to a reference configuration
- Presence of a stress will generally lead to strain

$$\boldsymbol{\varepsilon} = \frac{1}{2}\left[\nabla\mathbf{u} + (\nabla\mathbf{u})^T\right]$$

$$\boldsymbol{\varepsilon} = \begin{pmatrix} \varepsilon_{11} & \varepsilon_{12} & \varepsilon_{13} \\ \varepsilon_{21} & \varepsilon_{22} & \varepsilon_{23} \\ \varepsilon_{31} & \varepsilon_{32} & \varepsilon_{33} \end{pmatrix}$$

Stress tensor



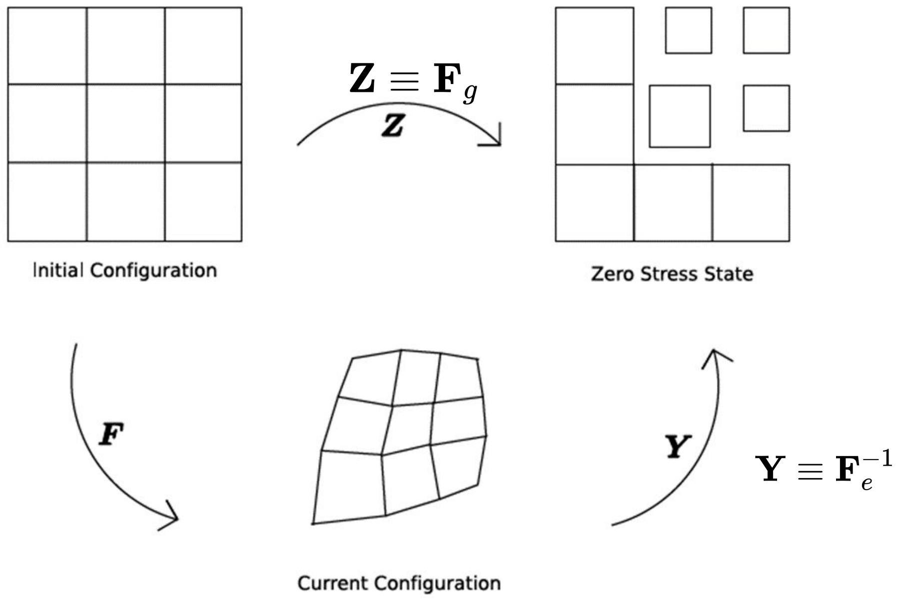
File:Components stress tensor cartesian.svg. (2022, March 16). Wikimedia Commons. Retrieved 21:10, October 24, 2023 from https://commons.wikimedia.org/w/index.php?title=File:Components_stress_tensor_cartesian.svg&oldid=639858293.

- Stress expresses the internal forces that neighbouring material particles exert on each other
- This can be as a reaction to external forces on the surface

$$\boldsymbol{\sigma} = \begin{pmatrix} \sigma_{11} & \sigma_{12} & \sigma_{13} \\ \sigma_{21} & \sigma_{22} & \sigma_{23} \\ \sigma_{31} & \sigma_{32} & \sigma_{33} \end{pmatrix}$$

Morphoelastic Model for Burn Injuries

Morphoelasticity



Decomposition:

$$\mathbf{F} = \frac{\partial \mathbf{x}}{\partial \mathbf{X}} = \frac{\partial \mathbf{x}}{\partial \boldsymbol{\chi}} \frac{\partial \boldsymbol{\chi}}{\partial \mathbf{X}} = \mathbf{F}_e \mathbf{F}_g$$

Hall, C. L. (2008). Modelling of some biological materials using continuum mechanics (Doctoral dissertation, Queensland University of Technology).

Mathematical Model

$$\frac{\mathrm{D}z_i}{\mathrm{D}t} + z_i(\nabla \cdot \mathbf{v}) = -\nabla \cdot \mathbf{J}_i + R_i,$$

conservation of cell density / concentration

$$\rho_t\left(\frac{\mathrm{D}\mathbf{v}}{\mathrm{D}t} + \mathbf{v}(\nabla \cdot \mathbf{v})\right) = \nabla \cdot \boldsymbol{\sigma} + \mathbf{f},$$

conservation of linear momentum

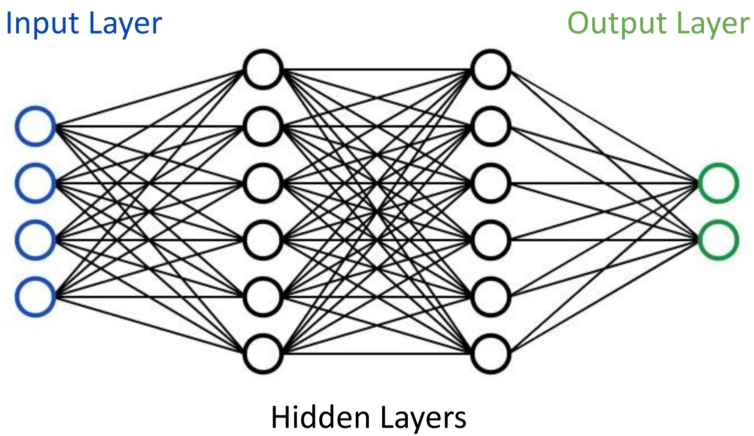
$$\frac{\mathrm{D}\boldsymbol{\varepsilon}}{\mathrm{D}t} + \boldsymbol{\varepsilon}\,\mathrm{skw}(\nabla\mathbf{v}) - \mathrm{skw}(\nabla\mathbf{v})\,\boldsymbol{\varepsilon} + (\mathrm{tr}\,(\boldsymbol{\varepsilon}) - 1)\,\mathrm{sym}(\nabla\mathbf{v}) = -\mathbf{G}.$$

evolution equation of strain, morphoelasticity of dermal layer

Biological Constituents				Mechanical Components			
N	fibroblasts	c	signalling molecule	$\mathbf{u}$	displacement	$\boldsymbol{\varepsilon}$	strain
M	myo-fibroblasts	ρ	collagen	$\mathbf{v}$	velocity		

Machine Learning Background

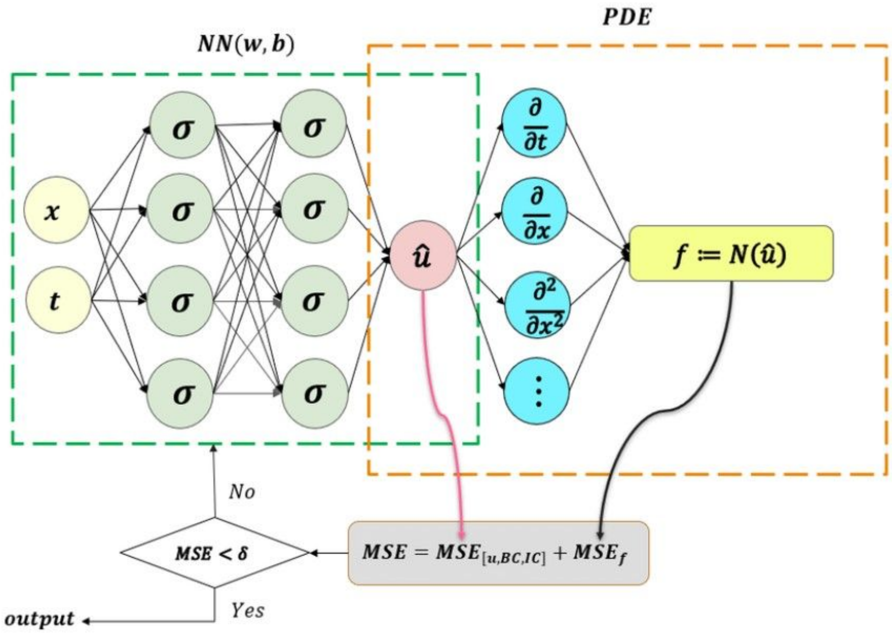
Neural Networks (NNs)



- Layers of interconnected nodes (neurons)
- Each neuron receives input. Inputs are weighted, summed and passed through an activation function to produce the neuron's output
- NN minimises a loss function by adjusting weights and biases during training

Nuzzi, R., Boscia, G., Marolo, P., & Ricardi, F. (2021). The impact of artificial intelligence and deep learning in eye diseases: a review. Frontiers in Medicine, 8, 710329.

Physics Informed Neural Networks (PINNs)



Use the physical prior knowledge (PDEs) to constrain the NN's space of admissible solutions

$$u_t + \mathcal{N}[u; \lambda] = 0, \; x \in \Omega, t \in [0, T]$$

$$f := u_t + \mathcal{N}[u; \lambda]$$

$$MSE = MSE_u + MSE_f$$

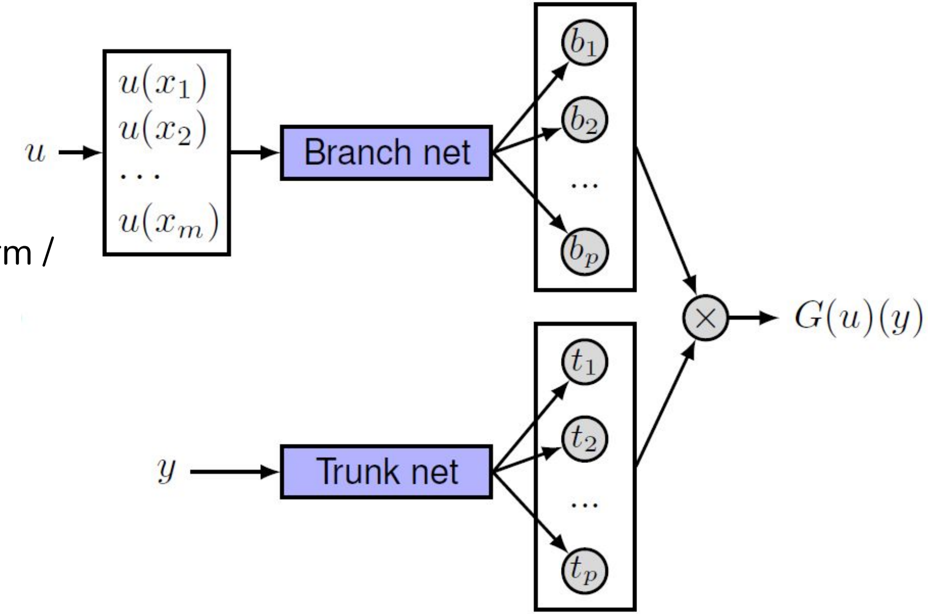
$$MSE_u = \frac{1}{N_u} \sum_{i=1}^{N_u} |u(t_u^i, x_u^i) - u^i|^2,$$

$$MSE_f = \frac{1}{N_f} \sum_{i=1}^{N_f} |f(t_f^i, x_f^i)|^2.$$

Guo, Y., Cao, X., Liu, B., & Gao, M. (2020). Solving partial differential equations using deep learning and physical constraints. Applied Sciences, 10(17), 5917.

Deep Operator Networks (DeepONets)

- Learns maps between function spaces: solution operator of PDE
- There is some input parameter u the solution depends on. Could be forcing term / source term / IC / coefficient / domain geometry
- Learn the map between u and the whole spatio-temporal solution



Lu, L., Jin, P., & Karniadakis, G. E. (2019). Deeponet: Learning nonlinear operators for identifying differential equations based on the universal approximation theorem of operators. arXiv preprint arXiv:1910.03193.

What Has Been Done?

ML for Wound Healing

- 1D model: simple feedforward NN with 25 parameters as inputs and RSAW, displacement vector and strain energy as output
- Same for 2D model
- Fixed wound shape (rotated square in 2D) and data generated using the FEM model
- Hybrid model: NN as surrogate for computationally expensive step in FEM for solving 1D problem

Direction of Research

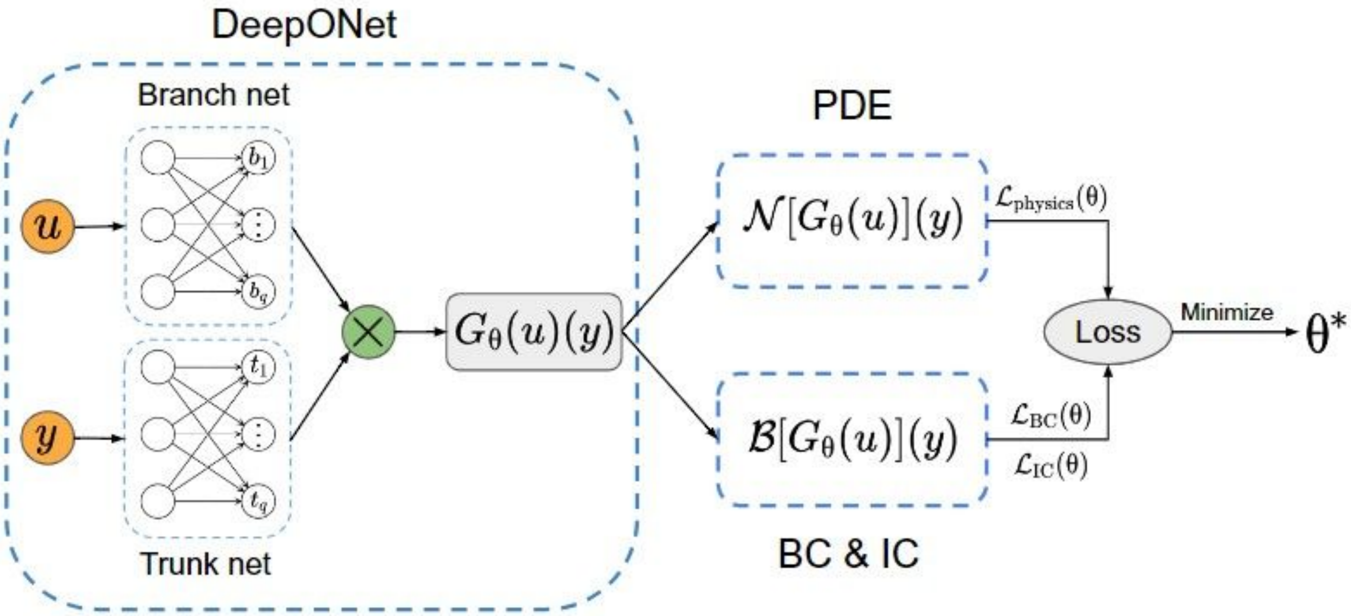
Research Question

Can a neural network be trained to predict the entire time evolution of skin contraction, given only the initial geometry of the wound as input?

For this we would incorporate:

- DeepONet
- PINNs setup in the loss function
- Data using the finite element simulation

Physics Informed DeepONets



Wang, S., Wang, H., & Perdikaris, P. (2021). Learning the solution operator of parametric partial differential equations with physics-informed DeepONets. Science advances, 7(40), eabi8605.

Approach

- Start simple
- Given one material parameter, we want to predict the displacement of the wound at fixed time T
- If this is feasible using the proposed set-up, use two material parameters
- Consider the input to the branch net to be a continuous function
- Consider the input to the branch net to be discrete (image of the wound)

Thank you for your attention!

Complete Model

$$\frac{\mathrm{D}N}{\mathrm{D}t} + N(\nabla\cdot\mathbf{v}) = -\nabla\cdot(-D_F F\nabla N + \chi_F N\nabla c) + r_F\left(1+\frac{r_F^{\max} c}{a_c^I + c}\right)(1-\kappa_F F)N^{1+q} - k_F c N - \delta_N N,$$

$$\frac{\mathrm{D}M}{\mathrm{D}t} + M(\nabla\cdot\mathbf{v}) = -\nabla\cdot(-D_F F\nabla M + \chi_F M\nabla c) + r_F\left(\frac{(1+r_F^{\max})c}{a_c^I + c}\right)(1-\kappa_F F)M^{1+q} - k_F c M - \delta_M M,$$

$$\frac{\mathrm{D}c}{\mathrm{D}t} + c(\nabla\cdot\mathbf{v}) = -\nabla\cdot(-D_c\nabla c) + \frac{k_c(N+\eta^I M)c}{a_c^{II}+c} - \delta_c\frac{(N+\eta^{II}M)\rho}{1+a_c^{III}c}c,$$

$$\frac{\mathrm{D}\rho}{\mathrm{D}t} + \rho(\nabla\cdot\mathbf{v}) = k_\rho\left(1+\frac{k_\rho^{\max} c}{a_c^{IV}+c}\right)(N+\eta M) - \delta_\rho\frac{(N+\eta^{II}M)\rho}{1+a_c^{III}c}\rho,$$

$$\rho_t\left(\frac{\mathrm{D}\mathbf{v}}{\mathrm{D}t} + \mathbf{v}(\nabla\cdot\mathbf{v})\right) = \nabla\cdot\left(\mu_1\operatorname{sym}(\nabla\mathbf{v}) + \mu_2[\operatorname{tr}(\operatorname{sym}(\nabla\mathbf{v}))\mathbf{I}] + \frac{E\sqrt{\rho}}{1+\nu}\left(\boldsymbol{\varepsilon} + \operatorname{tr}(\boldsymbol{\varepsilon})\frac{\nu}{1-2\nu}\mathbf{I}\right)\right) + \nabla\cdot\left(\xi M\left(\frac{\rho}{R^2+\rho^2}\right)\mathbf{I}\right),$$

$$\frac{\mathrm{D}\boldsymbol{\varepsilon}}{\mathrm{D}t} + \boldsymbol{\varepsilon}\operatorname{skw}(\nabla\mathbf{v}) - \operatorname{skw}(\nabla\mathbf{v})\boldsymbol{\varepsilon} + (\operatorname{tr}(\boldsymbol{\varepsilon})-1)\operatorname{sym}(\nabla\mathbf{v}) = -\xi\left(\frac{(N+\eta^{II}M)c}{1+a_c^{III}c}\right)\boldsymbol{\varepsilon}.$$