

Solid- and fluid-like behaviour of biological tissues

Agnese Venezia¹, Matt Butler²

¹UCL Department of Biochemical Engineering, ²UCL Department of Mathematics



Introduction

The **extracellular matrix** (ECM) is an acellular polymer-like structure found around cells, composed primarily of collagen in animals and cellulose in plants.

Some of the functions of the ECM are structural support, intercellular signaling and tissue separation. These functions are carried out through chemical reactions, but also in virtue of the matrix's physical structure and mechanical properties [1,2].

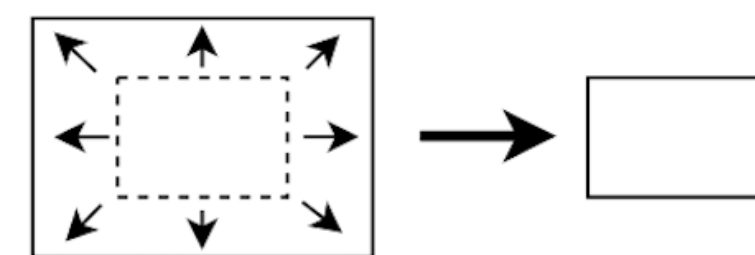
An important characteristic of the ECM is that it experiences a certain degree of **turnover**, physical replacement, of the collagen it contains.

We wish to create a mathematical model of the structure of the ECM to measure the effects of turnover on the matrix's mechanics.

Research question

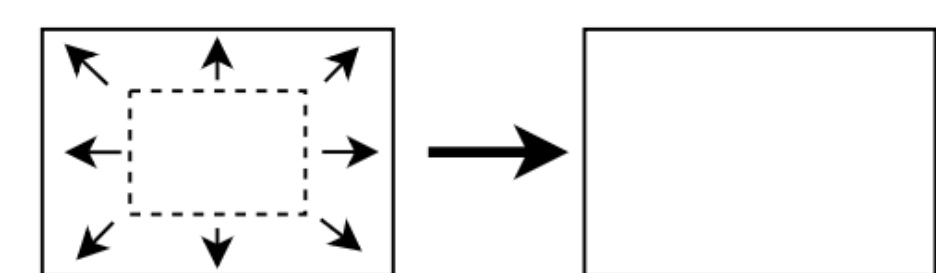
Does the ECM exhibit solid- and fluid-like behaviour when subjected to a stress or a strain?

SOLID-LIKE or elastic behaviour



An elastic material deforms when a force is applied on it, but it returns to its shape once the force is removed

FLUID-LIKE or viscous behaviour



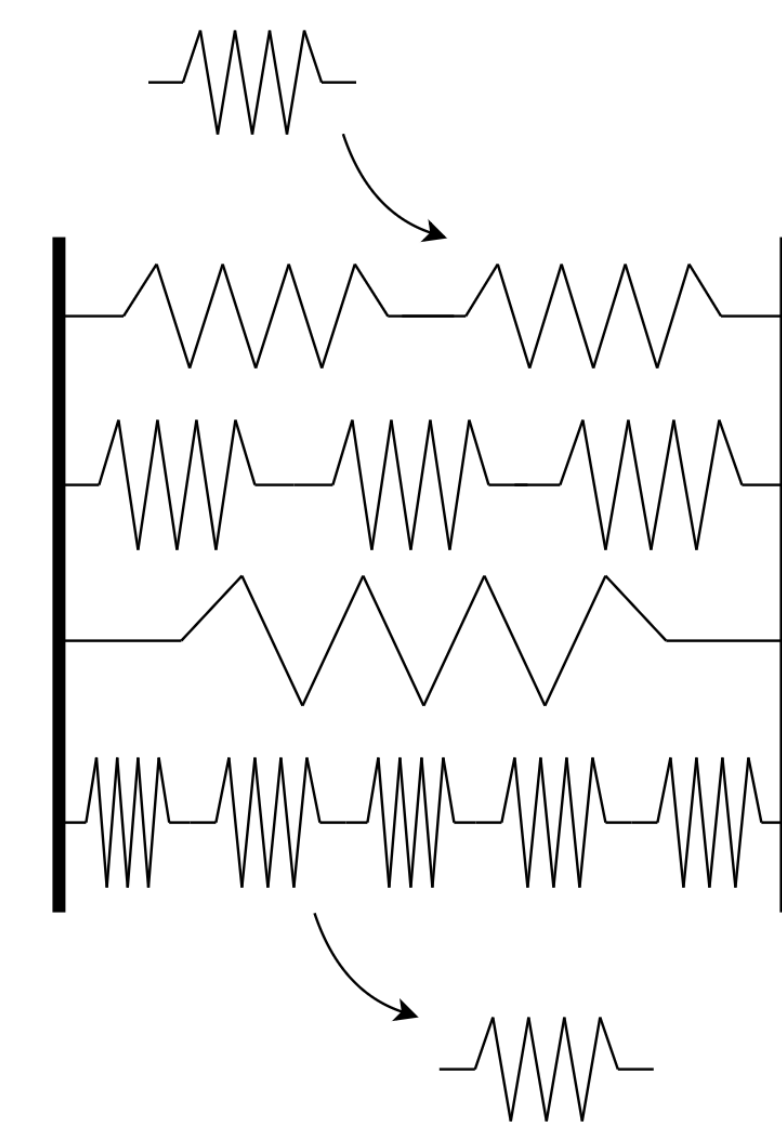
A viscous material deforms permanently when a force is applied on it.

Motivation

Our experimental collaborators wish to understand how turnover affects the mechanical properties of the ECM. Conducting these investigations in the laboratory would be challenging because it is extremely difficult to separate the ECM from the organism it is part of. Mathematical modelling is an alternative method of measuring the physical properties of the matrix.

Understanding the mechanics of the ECM is important because it could determine advances in research focusing on contexts such as cancer propagation, antibiotic resistance and wound repair [3,4].

Spring turnover model



The model of the ECM we have designed consists of chains of springs arranged in parallel with each other. Each chain contains a variable number of springs. Springs are purely elastic and mimic the collagen found in the ECM.

The springs are added to or removed from the system at given rates. This turnover is believed to generate a "viscous flow" in the ECM.

Numerical solver

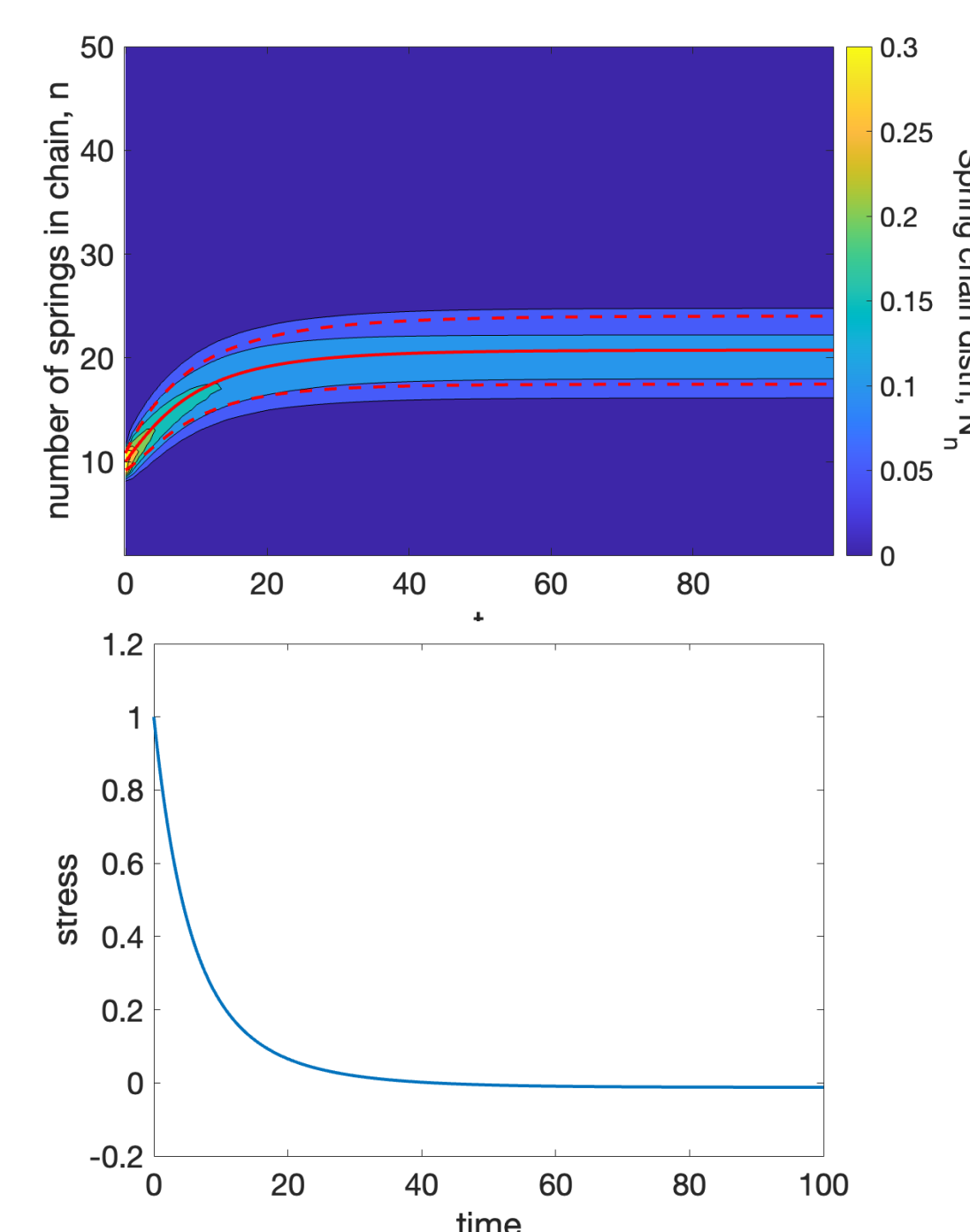
As each chain contains a variable number of identical springs, chains with fewer springs are more stretched than chains with more springs. To calculate the total stress and strain in the system, we first measure the evolution of the number of chains with a given number of springs, N_n , which depends on the turnover parameters p and q , resulting in the evolution equation:

$$\frac{dN_n}{dt} = p_{n-1}N_{n-1} - (p_n + q_n)N_n + q_{n+1}N_{n+1}$$

Solved numerically on MATLAB.

Example results

The results below are obtained from a system which has walls initially separated by chains of 10 springs, that is stretched to a length of 20 springs.



With the chosen turnover parameters, the number of springs in each chain (spring density) adjusts towards a steady state.

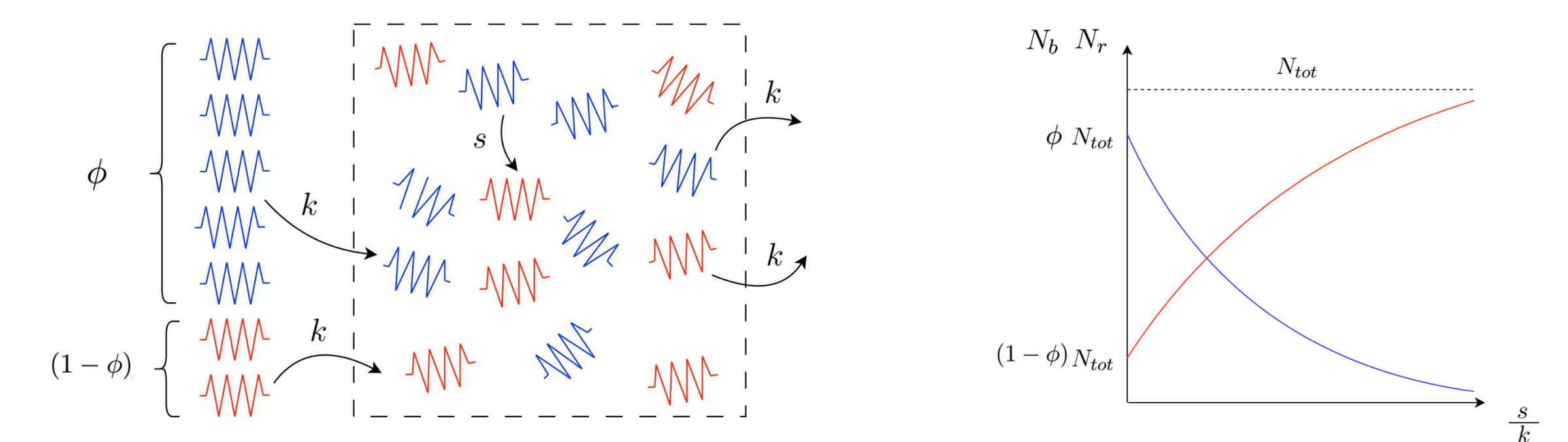
Stress appears to decrease exponentially over time, a phenomenon known as **stress relaxation**, which is typical of **viscoelastic materials**, substances that exhibit both elastic and viscous characteristics.

Fluorescent timers

Our experimental collaborators use **fluorescent-timer** technology to measure the turnover rate of the collagen in the ECM. By genetic modification, their organisms produce fluorescent collagen, which **changes colour** from red to blue over time. We expand our model to include this colour change in our springs.

Mechanics-free colour change

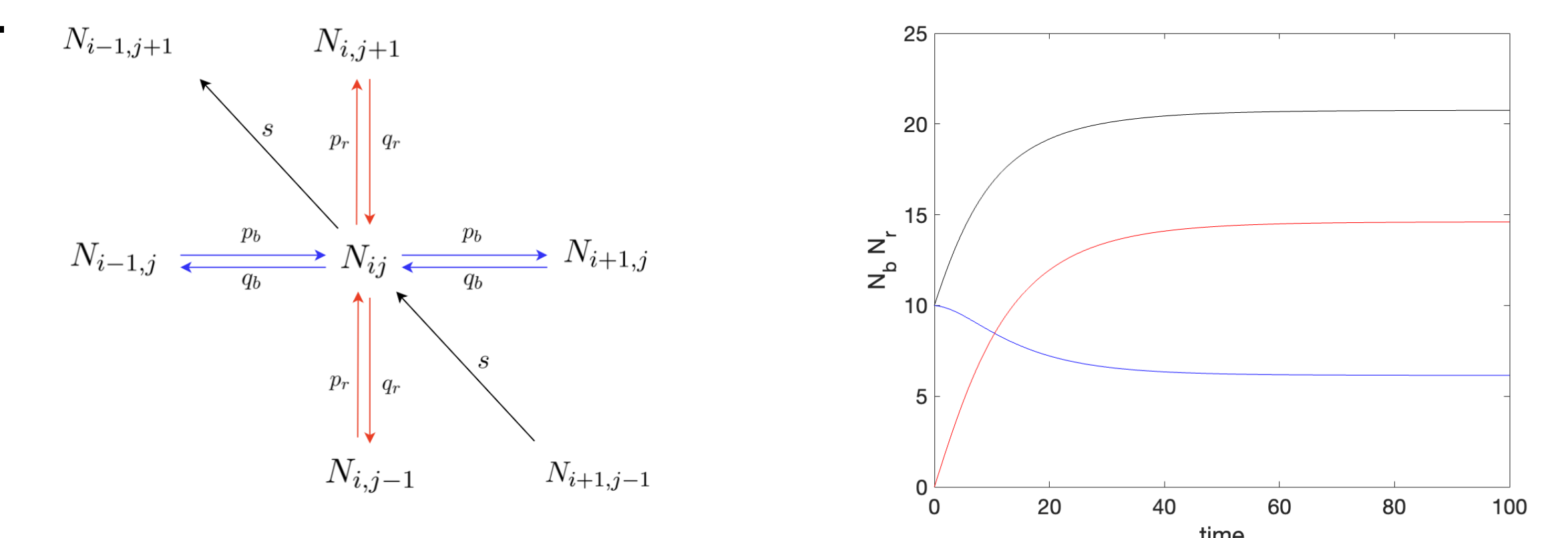
We now consider a system with turnover at rate k and colour change at rate S , but no mechanical elements (see left figure). Knowing the initial proportion of blue springs in the system, ϕ , steady-state solutions can be found (see right figure). This shows that by observing the ratio between red and blue springs, the ratio between the turnover parameter and the colour change parameter can be determined.



Spring turnover model with colour change

We extend our mechanical spring turnover model to include colour change by considering the spring density, $N_{i,j}$, where there are i blue and j red springs in a chain. This model can be summarised by the figure on the left.

Example results, obtained using the same initial conditions as those for the model without colour change, are shown in the figure on the right.



Bibliography

- [1] C. Frantz, K. M. Stewart, and V. M. Weaver. The extracellular matrix at a glance. *Journal of Cell Science*, Dec 2010.
- [2] A. D. Theodoris, S. S. Skandalis, C. I. Giannelis, and N. K. Karamanos. Extracellular matrix structure. *Advanced Drug Delivery Reviews*, Feb 2016.
- [3] N. Khalilgharibi and Y. Mao. To form and function: on the role of basement membrane mechanics in tissue development, homeostasis and disease. *Open biology*, 2021.
- [4] O. Cioflu, C. Moser, P. Østrup Jensen, and N. Høiby. Tolerance and resistance of microbial biofilms. *Nature News*, Feb 2022.