# 21.11.24 Model Setup

## Set-up

We aim to grow cells on a substrate with the following conditions:

- Ensure that the cells adhere well and are aligned (via actin filaments).
- Understand how senescence can influence our system, trying to decrease it if possible
- Focus on the response to **shear stress**.

## Objective

The goal is to observe how cells:

- React to shear stress ($\sigma$) at the substrate level.
- Adjust their cytoskeletal structure, particularly actin and cadherin proteins.
- Can decrease their senescence levels

## Preliminary Modeling

The system is described by the following equations:

$$
\begin{aligned}
\dot{\theta} &= f_1(\theta_t) + g_1(u_t), \quad \text{where } \theta = \text{cell orientation angle} \\
\dot{a}_t &= f_2(a_t) + g_2(u_t), \quad \text{where } a_t = \text{actin concentration} \\
\dot{c}_t &= f_3(c_t) + g_3(u_t), \quad \text{where } c_t = \text{cadherin concentration} \\
\dot{s}_t &= s_t + g_4(u_t), \quad \text{where } s_t = \text{senescence level.}
\end{aligned}
$$

### Variable Definitions

- $u_t$: Shear stress [Pa]
- $\theta_t$: Orientation of cell alignment
- $a_t$: Actin concentration
- $c_t$: Cadherin concentration (or other junctional proteins)
- $s_t$: Senescence (aging factor)

## Proposed Approach

To control cell response to shear stress:

- Influence $u_t$ to regulate actin polymerization.
- Reduce inflammation to minimize senescence.

## Tentative Equations

The functional forms of $f_i$ are hypothesized as follows:

$$
\begin{aligned}
f_1(\theta_t) &= f_1(\theta_t)(1 - a_t)(1 - s_t)(1 - c_t), \\
f_2(a_t) &= f_2(a_t)(1 - \theta_t)(1 - s_t)(1 - c_t), \\
f_3(c_t) &= f_3(c_t, a_t)
\end{aligned}
$$

## Next Steps

- Analyze actin dynamics (*image analysis*).
- Analyze cadherin expression (*image analysis*).
- Investigate cellular mechanical responses (e.g., under shear stress) and external factors such as inflammation.

# Modified Cell Response Model

## Gaussian Function Definition

First, we define our gaussian function for optimal ranges:

$$\text{gaussian}(x, \mu, \sigma) = \exp\left(-\frac{(x-\mu)^2}{2\sigma^2}\right) \tag{1}$$

## Modified System Equations

The complete system with time delays and optimal ranges:

$$\dot{\theta}(t) = f_1(\theta_t) \prod_{i \in \{a,s,c\}} \text{gaussian}(x_{i,t-\tau_i}, \mu_i, \sigma_i) + g_1(u_{t-\tau_u}) \tag{2}$$

$$\dot{a}(t) = f_2(a_t) \prod_{i \in \{\theta,s,c\}} \text{gaussian}(x_{i,t-\tau_i}, \mu_i, \sigma_i) + g_2(u_{t-\tau_u}) \tag{3}$$

$$\dot{c}(t) = f_3(c_t, a_{t-\tau_a}) + g_3(u_{t-\tau_u}) \tag{4}$$

$$\dot{s}(t) = f_4(s_t)\left(1 + h(u_{t-\tau_u}, \text{inflammatory\_factors}_{t-\tau_i})\right) \tag{5}$$

Where:

- $x_{i,t}$ represents the state variable (actin, senescence, or cadherin) at time $t$
- $\tau_i$ represents the time delay for each respective variable
- $\mu_i$ represents the optimal value for each variable
- $\sigma_i$ represents the tolerance around the optimal value
- $u_t$ represents the shear stress input at time $t$

## Expanded First Equation

For clarity, the first equation fully expanded:

$$\begin{aligned}\dot{\theta}(t) = f_1(\theta_t) &\cdot \exp\left(-\frac{(a_{t-\tau_a} - \mu_a)^2}{2\sigma_a^2}\right) \\ &\cdot \exp\left(-\frac{(s_{t-\tau_s} - \mu_s)^2}{2\sigma_s^2}\right) \\ &\cdot \exp\left(-\frac{(c_{t-\tau_c} - \mu_c)^2}{2\sigma_c^2}\right) \\ &+ g_1(u_{t-\tau_u})\end{aligned} \tag{6}$$