Design of artificial stimuli-responsive polypeptides (SRPs)

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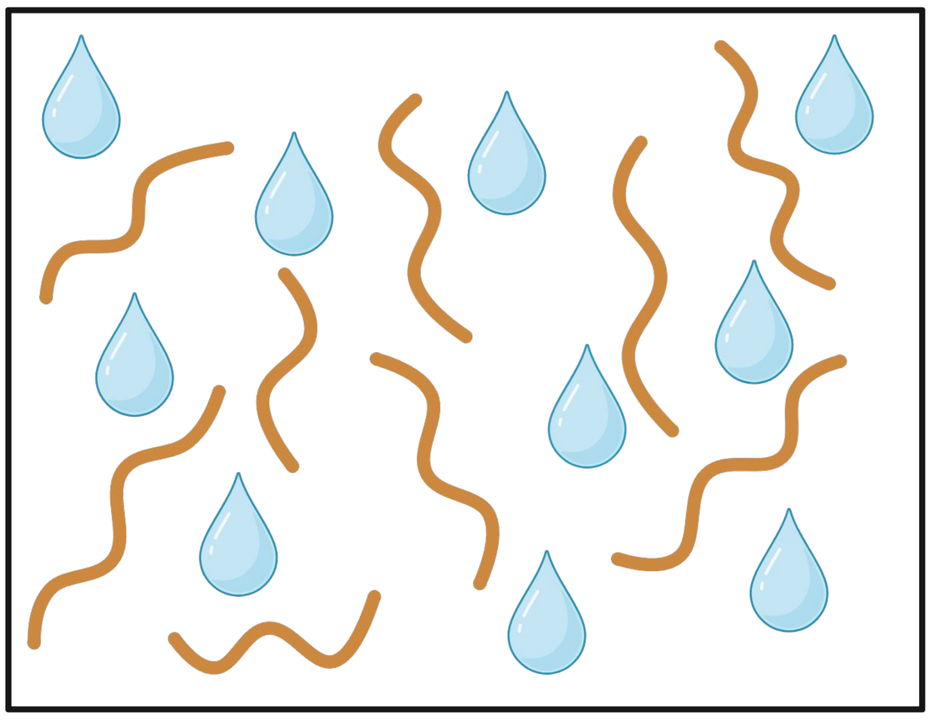
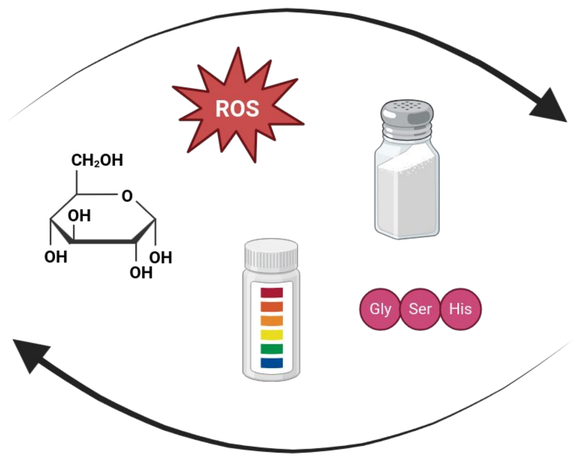
Background

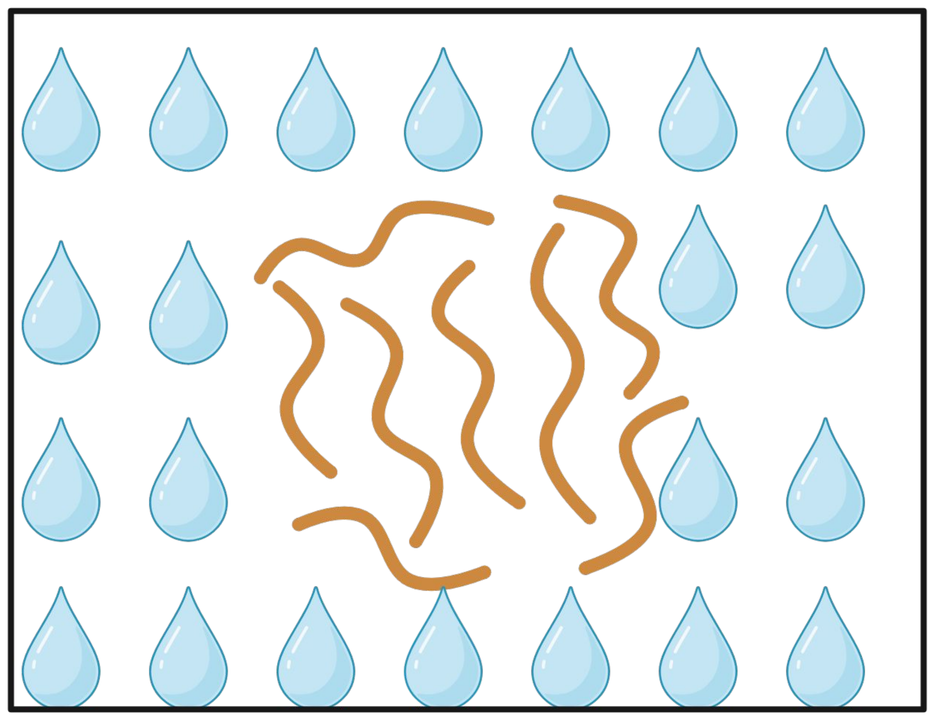
Stimuli-responsive polypeptides (SRPs) are synthetic proteins that react to chemical conditions, such as pH, oxido-reductive stress, salt or glucose concentration, by undergoing phase separation and forming liquid-like condensates. Their response to stimuli is highly sensitive to their amino acid sequence, meaning that even small changes can dramatically alter when and how they condense.

Uncondensed





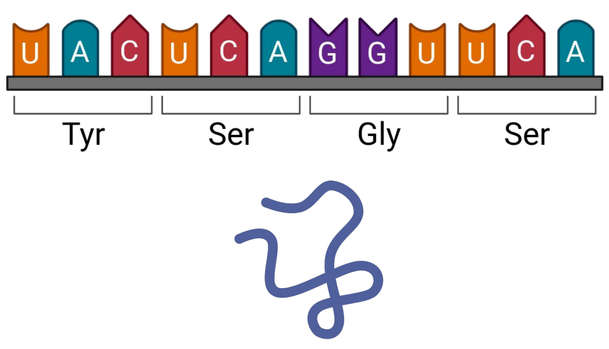
Condensed

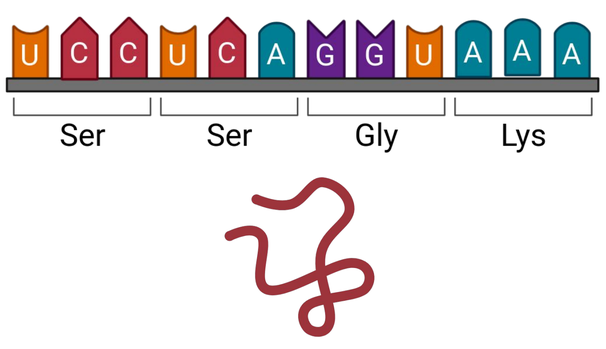


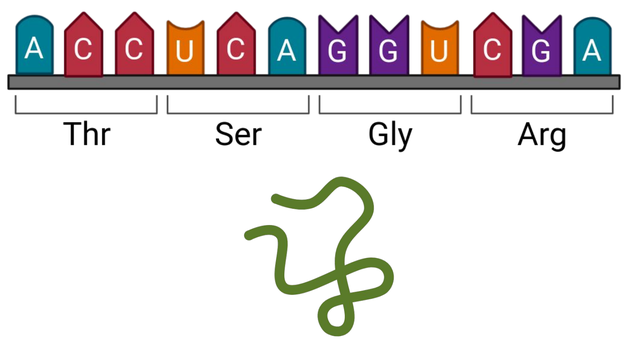
Biotechnological Application

Tumors microenvironments often present particular chemical characteristics, such as lower pH or higher oxidative stress.
SRPs could be designed to specifically recognize these features and change their physical state only when present within the tumor.
SRPs could therefore be used as smart drug carriers…

HOWEVER, small changes in the sequence of SRPs can lead to big changes in their behaviour.
This makes them currently difficult/impossible to design.
What is required is: 1) additional experimental data and 2) proper mathematical models.



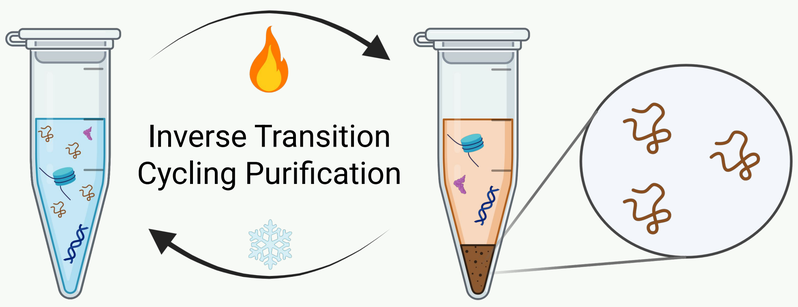




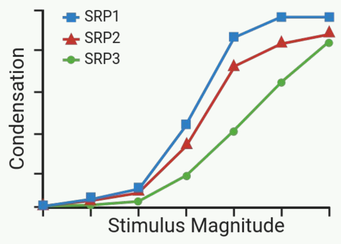
EXPERIMENTAL PART

Objective: generate new data

Cloning and Purification



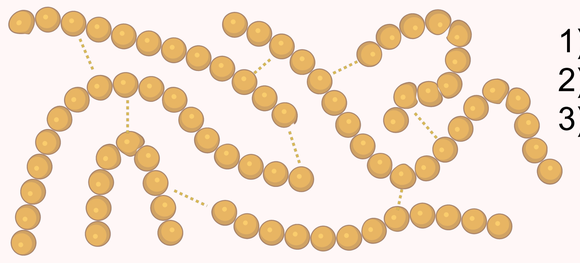
Testing



1) Explore new SRPs
2) Do they behave similarly?
3) Do they tolerate mutations well?
4) What do they taste like?

COMPUTATIONAL PART

Objective: identify limitations of the computational models



1) Do simulations work on SRPs?
2) What are their strengths?
3) What are their weaknesses?

1) What is the status of machine learning?
2) Can we better it?