Signal-processing Biomaterials

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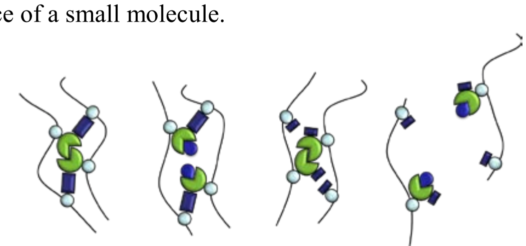
Statement of Purpose: A characteristic of smart materials is the ability to react to a specific external stimulus. These stimuli so far usually have been restricted to e.g. changes in pH, temperature, ions or light. However, biological systems can react to external stimuli in a manifold of processes. The transformation of multiple stimuli into a specific output thereby can be described by Boolean functions. In biological systems these processes are fostered by biological modules which can be used to implement smart biomaterials[1]. The great advantage of biological modules is their modular composition. In order to take advantage of this property we implemented biomaterials with the benefits of synthetic biology. Synthetic biology aims at modularly intertwining biological components of known processivity to develop new signal processing circuits. In our approach we applied this strategy to implement smart biomaterials that are capable of sensing multiple stimuli. Furthermore, by logically combining protein modules, we were able to implement logic operations processing biomaterials as well as interconnected biomaterial signaling.

Methods: The modularly designed recombinant proteins based on F_M protein[2]were produced in *E.coli* and purified via affinity chromatography. For the formation of hydrogels the proteins cross-link linear polyacrylamide thus conferring stimulus-responsiveness to the matrix. The purified proteins were coupled via polyhistidine tags to a linear co-polymer of acrylamide and Ni^{2+}-loaded 2,2'-(5-acrylamido-1-carboxypentylazanediyl)diacetic acid. The dissolution of the gels was monitored by the measurement of a fluorescent protein (mCherry) that was incorporated into the hydrogel matrix.

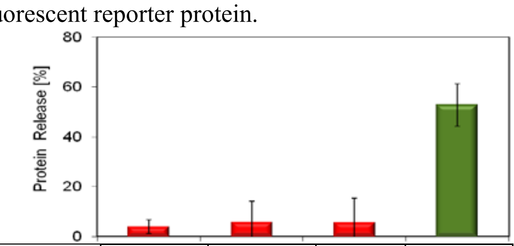
Results: Two different modules have been chosen to be used in the recombinant proteins. One is a protease-sensitive sequence and the other module senses the presence of a small molecule.



Stimulus A	0	0	1	1
Stimulus B	0	1	0	1

Figure 1. A AND B operating hydrogel design.

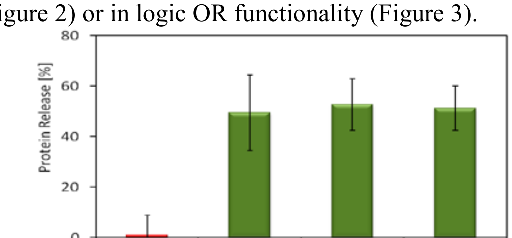
Upon administration of the appropriate stimulus composition the hydrogel dissolves and releases the fluorescent reporter protein.



Stimulus A	0	0	1	1
Stimulus B	0	1	0	1

Figure 2. A AND B operation.

Combinatorial alteration of proteins for cross-linking the hydrogel results in either logic AND functionality (Figure 2) or in logic OR functionality (Figure 3).



Stimulus A	0	0	1	1
Stimulus B	0	1	0	1

Figure 3. A OR B operation.

Conclusions: Our results show that modular design of proteins for the generation of biomaterials provides great opportunity to implement multiple stimuli sensing materials. Furthermore simple combinatorial alterations of protein modules result in the formation of materials with desired responsiveness, representing AND or OR operations. Further logic combinatorial design of biological modules probably will result in various additional logic circuits.

References:

1. Jakobus et al., Chem. Soc. Rev., 2012, 41, 1000–1018
2. Kämpf et al., Adv. Funct. Mater, 2010, 15, 2534-2538

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