ABSTRACT

THESIS: Application of fluorogenic RNA aptamers to construct Boolean Logic nanodevices

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RNA aptamers that bind non-fluorescent dyes and activate fluorescence are highly sensitive, nonperturbing, and convenient probes in the field of synthetic biology. These artificial aptamers operate as molecular nano-switches, which alter folding and function in response to ligand binding. We demonstrate a computational approach for designing smart RNA nano-devices based on the malachite green (MG) binding RNA aptamer, which binds to triphenylmethane dye and activates fluorescence. Fluorescence output is controlled by the binding of short DNA oligonucleotides inputs. Four types of such RNA switches, possessing AND, OR, NAND, NOR Boolean logic functions, were created in modular form. These switches allowed the MG dye binding affinity to be changed by altering 3D conformation of the RNA aptamer. Furthermore, we have developed a higher-level logic circuit half adder by "in parallel" integration of the two logic gates XOR and AND within a single RNA nanoparticle. The design utilizes fluorescence emissions from two different RNA aptamers: MG RNA aptamers that bind triphenylmethane dye (AND gate) and Broccoli RNA aptamers which bind DFHBI dye (XOR gate). All computationally designed RNA devices were synthesized and experimentally tested *in vitro*. The ability to design smart nanodevices based on RNA binding aptamers offers a new route to engineer "label-free" ligand-sensing regulatory circuits, nucleic acid detection systems, and gene control elements.