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Precise orientation of thermally-sensitive biomolecules using DNA nanostructures: An exploration of non-thermal techniques for controlling DNA nanoassemblies

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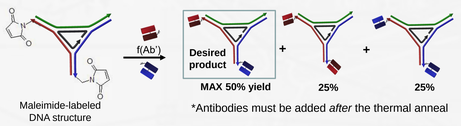
Introduction

The commercialization of synthetic DNA strands has led to exquisite control over sequence design. With the predictability of the A-T, C-G DNA alphabet, many researchers have begun to design DNA nanostructures to precisely position functional groups in 2D and 3D environments. This approach has been successful in positioning small molecules, fluorophores, polymers, etc. However, many opportunities remain in the field of biomolecules, where enzymes, antibodies, and proteins could be arranged to create novel classes of drugs. To date, such biomolecule-DNA nanoassemblies have been limited due to the high heat required to assemble DNA structures. Here, we pursue the use of non-ionizing radiation to control DNA assembly at room temperature.

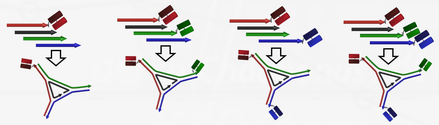
DNA Structures with Proteins

Current Approach: post-assembly labelling*

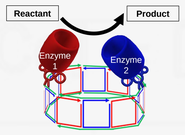


*Antibodies must be added *after* the thermal anneal

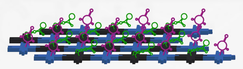
Our Goal: Pre-assembly labelling gives **100% desired product**



Other Possibilities

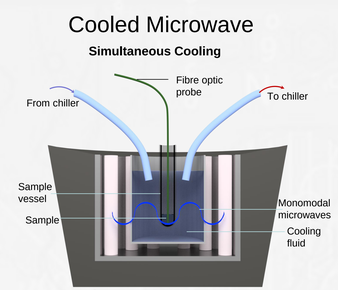


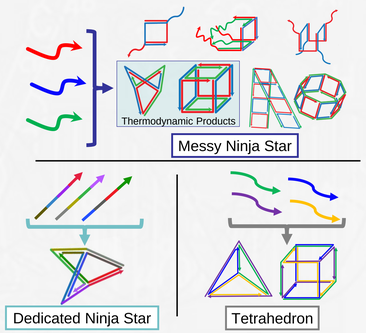
Templated Catalysis

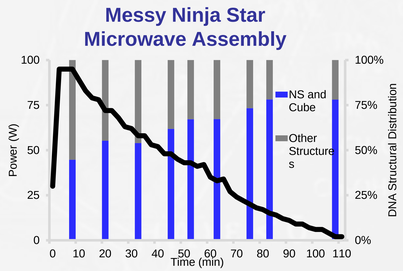


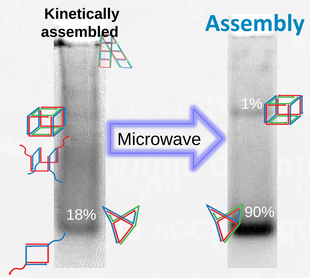
Pre-arranged peptide networks for sensing

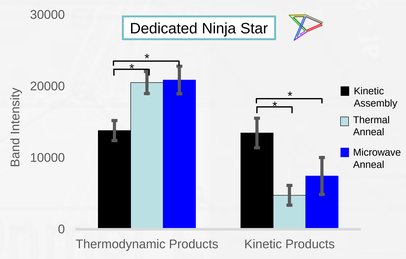
Non-Thermal Assembly



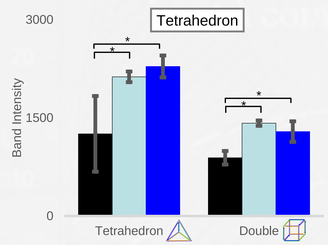








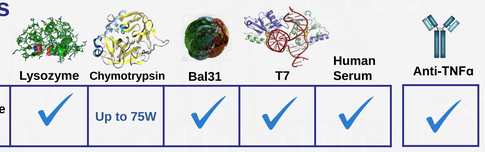
51% increase in thermodynamic products

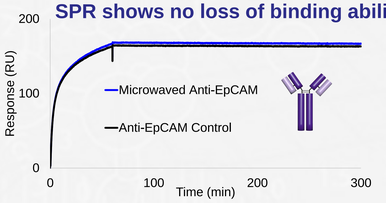


75% increase

Proteins and Microwaves

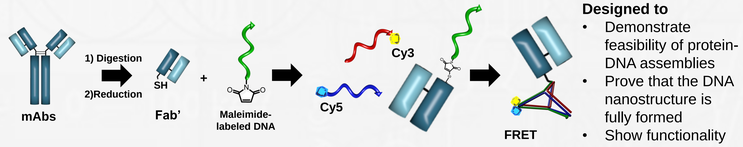
Enzymes



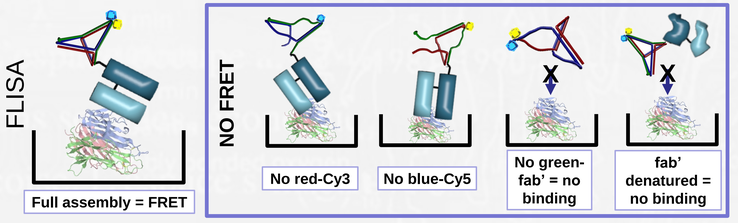


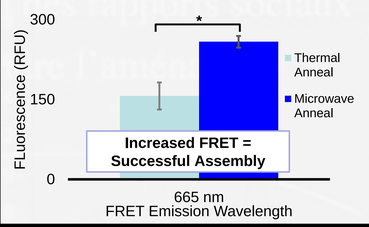
6 of 7 proteins were unaffected by microwaves

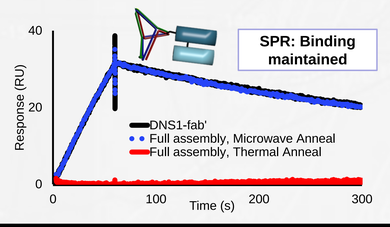
Putting it Together



Designed to
- Demonstrate feasibility of protein-DNA assemblies
- Prove that the DNA nanostructure is fully formed
- Show functionality





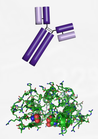


Conclusions

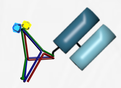
Assembly without heat
- Done at room temp
- Demonstrated on three different structures
- 105 W max power

Proteins
- Retain function after exposure to cooled microwave*

*6 out of 7 proteins



Successful conjugate assemblies
- Antibody fragment conjugated to DNA prior to assembly
- Precisely positioned with FRET pair
- Maintains binding ability



Funding

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NSERC CRSNG
ISBNA International Society of Nucleosides, Nucleotides, & Nucleic Acids
Fonds de la recherche en santé Québec
CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

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