Nanosorter: A high-throughput nanoshell sorting device

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Motivation

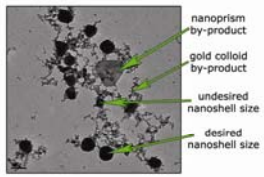
Nanoshells offer promising oncology treatment solutions

- Non-invasive destruction of cancer tissue
- Low collateral damage to surrounding healthy tissue
- Superior biocompatibility and side effect profile
- Treatment individualized to patients

Problem:

- Nanoshell production methods yield unwanted by-products
- Current purification methods cause a manufacturing bottleneck
- Current by-product removal techniques are low yield and time-consuming
  - Size exclusion chromatography recovers less than 1% of input nanoshells
  - Repeated centrifugation recovers approximately 30% of input nanoshells

Crude Nanoshell Solution



Solution:

- Nanosorter implements a high-throughput, scalable nanoshell purification process
- Generalizable to other types of nanoparticles

Design Objectives

- High-throughput, scalable process
  - Repeatable nanoshell purification
  - Greater than 40% recovery of desired nanoshells input (> 40% yield)
  - Per device production cost < $2000
  - Device footprint < 4 ft^2

Acknowledgements

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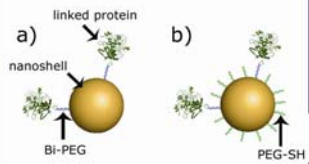
Protein-to-nanoshell Conjugation

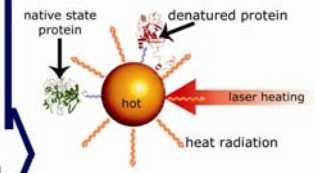


a) Bifunctional poly-ethylene glycol (Bi-PEG) links proteins to nanoshell surface

b) Remaining nanoshell surface area coated with PEG-thiol (PEG-SH)

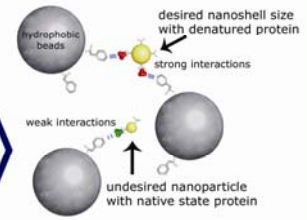
- Reduces nanoshell aggregation
- Promotes longevity of nanoshells

Size-Selective Nanoshell Heating



- Nanoshell light absorption wavelength is governed by nanoshell size and shell thickness
- Applying high intensity laser to a sample causes some nanoshells to heat up
- Nanoshell heat radiation denatures (unfolds) conjugated protein
- Only nanoshells of resonance corresponding to the applied laser wavelength become hot

Hydrophobic Interaction Chromotography



- Desired nanoparticles have denatured (unfolded) protein attached
  - Denatured proteins have many exposed hydrophobic regions
  - Hydrophobic regions have strong attraction to hydrophobic beads
- Undesired particles have native (folded) protein attached
  - Very few exposed hydrophobic regions
  - Weak attraction to hydrophobic beads

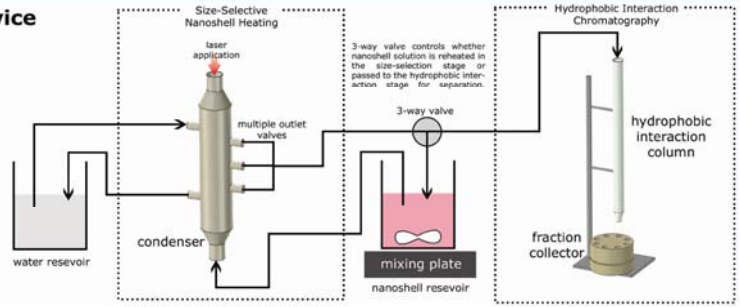
The Nanosorter Device

Input:
Crude nanoshell solution where both nanoshells and by-products are protein conjugated

Purification:
Input nanoshell solution circulated though heating stage multiple times

Heat-treated nanoshell solution sent through hydrophobic interaction column

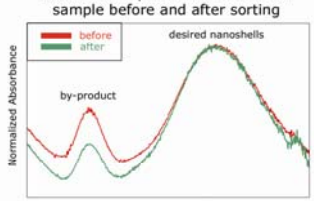
Output:
Multiple solutions of fractionated nanoshell product



Result: removal of unwanted by-product

- Spectral analysis of crude nanoshell sample before nanosorting shows large amount of undesired by-product.
- After passing crude sample through nanosorter, a relative decrease in by-product population is shown.
- Nanosorter does not produce 100% yield of desired nanoshells, but ability to purify crude samples is demonstrated.
- Successful proof of concept

Normalized spectra of a nanoshell sample before and after sorting



Conclusions

The size-selective purification method presented has shown to be a viable alternative to current nanoshell separation techniques.

Future Work

Examine the effect of adjusting experimental parameters to optimally enhance hydrophobic interactions during chromotography stage

Optimize size-selective nanoshell heating running time to maximally denature protein conjugated to desired nanoshells while minimizing non-specific heating