Nanoparticle System to Entrap and Deactivate Vesicants

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Overview

- Problem Statement
- Background Information
- Design
- Synthesis of Nanoparticles
- Characterization
- Entrapment Efficiency
- Reaction Testing
- Budget
- Questions

Problem Statement

- To provide a safe, yet more efficient method of protection from vesicants that improves the operational effectiveness of first-responders and soldiers
- Design a nanoparticle system that will absorb, entrap, and deactivate target vesicants

Background Information

History of Use

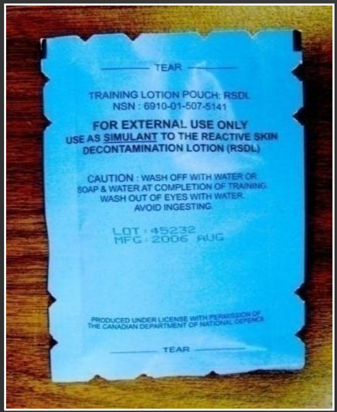
- Mustard agent use in war
  - Easy to make, cheap
- Potential Users
  - First responders
  - Firefighters, Police
  - Military

[1]

Need for a NP System

- Prior products
  - Application issues
  - Not prophylactic
  - Problems with military equipment compatibility

[2]



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Design Overview

Selection of nanoparticle system materials

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Nanoparticle synthesis method and testing plan formation

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Synthesize nanoparticle system

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Characterize nanoparticle system

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Determine entrapment efficiency

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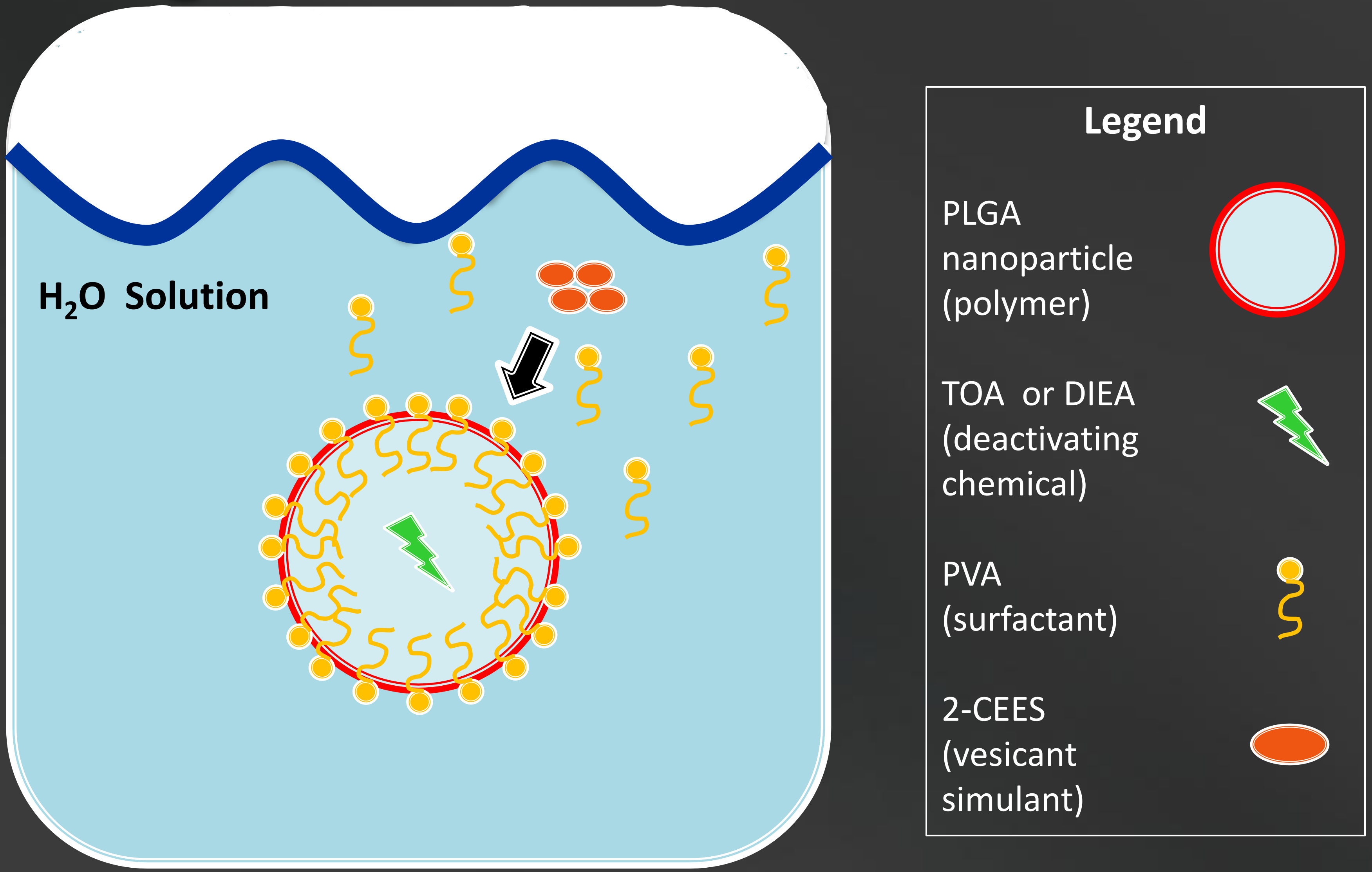
Verify entrapment/deactivation of 2-CEES

Design Schematic

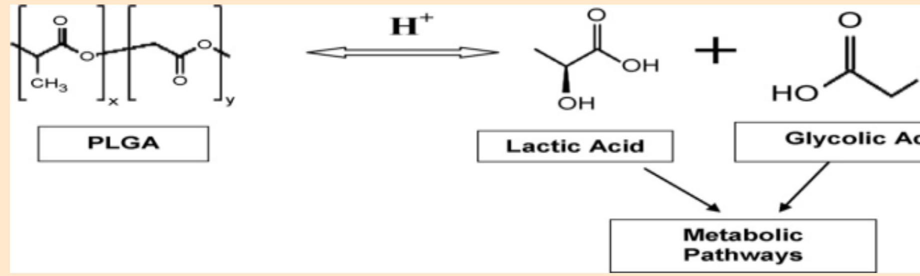


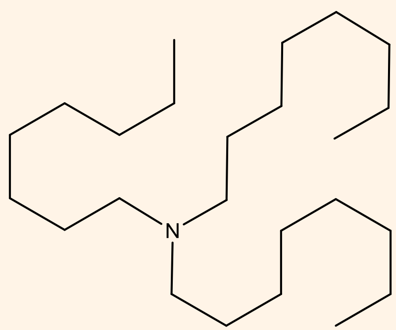
Measurable Objectives

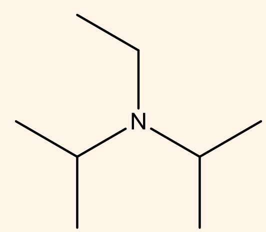
Characterization	Entrapment Efficiency	Reaction Testing

• Size
  ◦ >200 nm to prevent endocytosis
• Polydispersity Index (PDI)
  ◦ Monodisperse <0.1
• Zeta Potential
  ◦ ±30 mV for moderate stability
	• >70% deactivating chemical entrapped within nanoparticle	• NPs instantaneously respond to presence of vesicant
		• Entrapment and deactivation of vesicant
		• Loaded NP deactivation occurs faster than free chemical reaction with vesicant

Design Justification

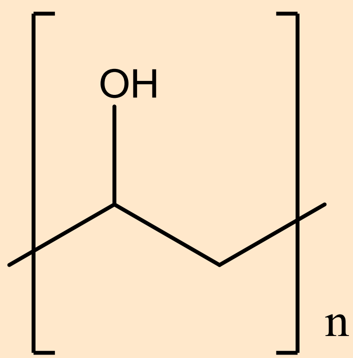
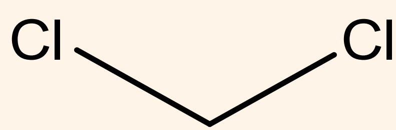
<table>
<tr><th>Component</th><th>Justification</th></tr>
<tr><td>Polymer: poly D, L-lactide-co-glycolide (PLGA)</td><td>FDA approved for human therapy
Well-characterized polymer
Biocompatibility
Biodegradability
Degradation
sub products are
non-toxic


[4]</td></tr>
<tr><td>Deactivating Chemical:
-Trioctylamine (TOA)
-Diisopropyl ethyl amine (DIEA)</td><td>Hydrophobic
Reactive for our purposes (Non-nucleophilic base)
Will not bond with the PLGA to our detriment


TOA


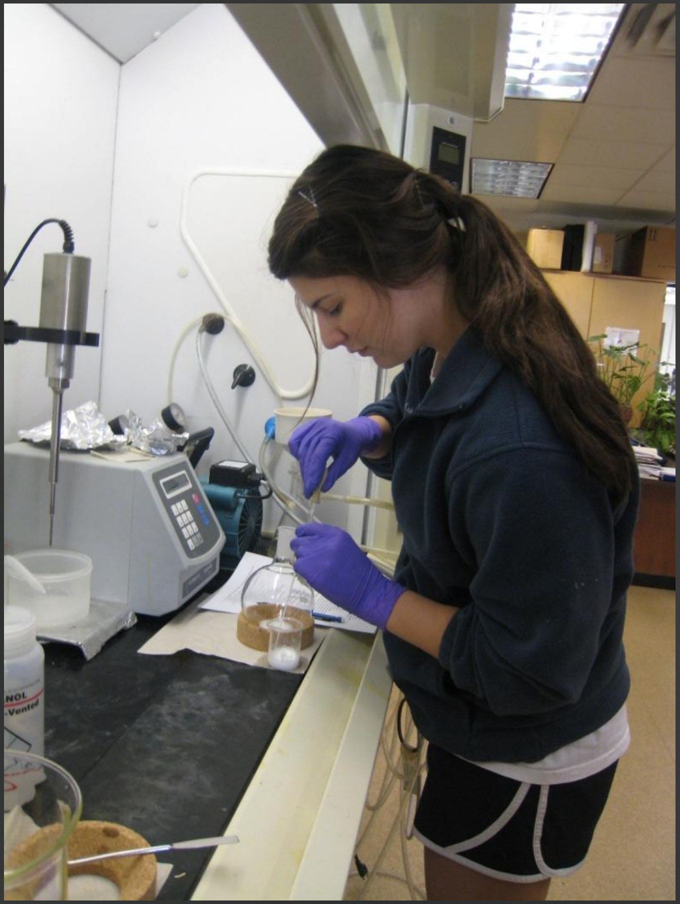
DIEA</td></tr>
</table>

Design Justification

Component	Justification
Surfactant: Polyvinyl alcohol (PVA)	Water soluble Excellent emulsifying properties Reduces surface tension Aids in the solubility of 2-CEES; drives reaction between 2-CEES & TOA 
Solvent: Dichloromethane (DCM)	Ability to dissolve all other NP synthesis components Not reactive with TOA Evaporates easily due to its relatively low boiling point (39.6°C) 

Synthesis of PLGA Nanoparticles

- Emulsion-Solvent Evaporation Technique
  - Top-down technique
  - Biodegradable nanoparticles with entrapped hydrophobic compounds
- Preparation of stock solutions
  - Time efficient
  - More consistent
- Synthesis of blank NPs
  - Provides a control
- Synthesis of loaded NPs
  - Loaded with deactivating agent
    - TOA or DIEA



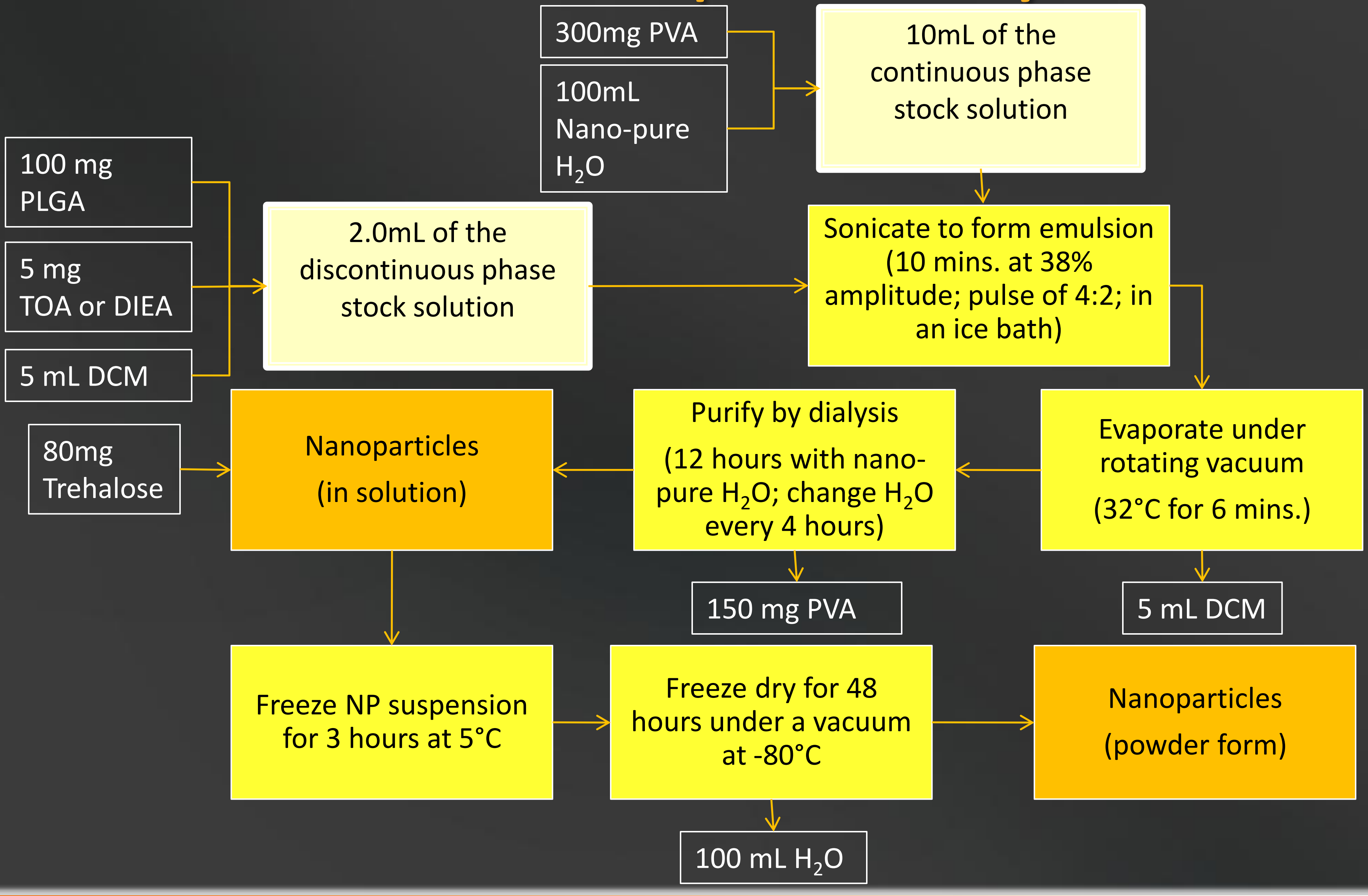
Synthesis of PLGA Nanoparticles

Mixing of continuous and discontinuous phase during sonication

Organic solvent removal

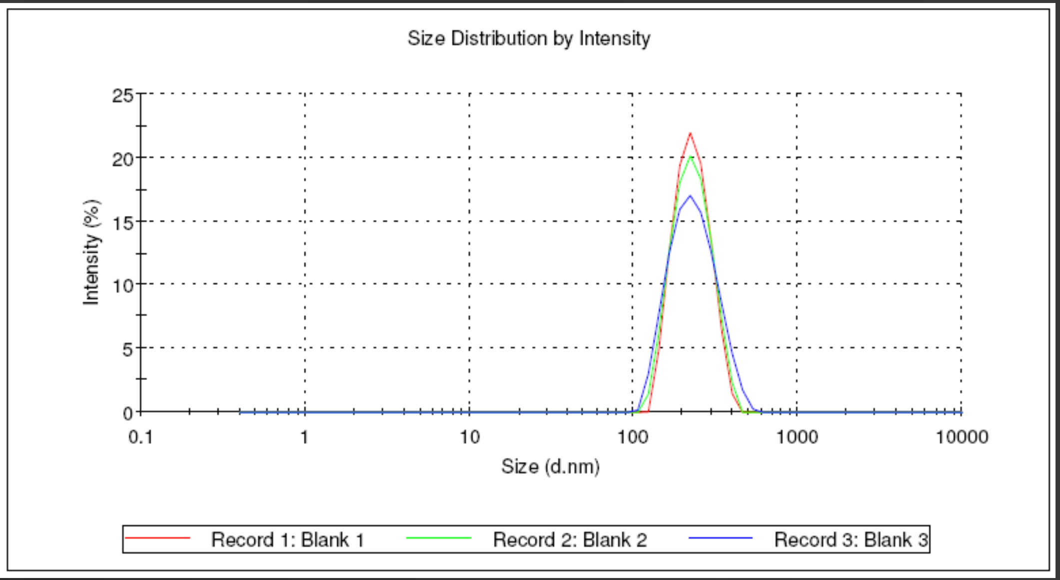
Nanoparticles in solution and powder form

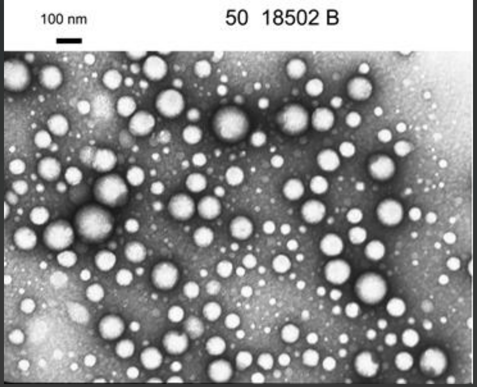
Loaded PLGA Nanoparticle Synthesis

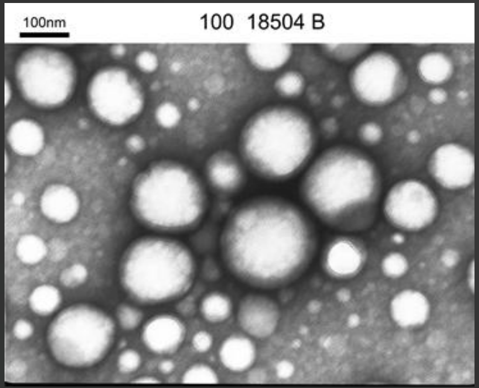


Characterization – Blank NPs

- Average size
  - 216.3 nm
- PDI
  - 0.098
- Zeta potential
  - -21.7 mV

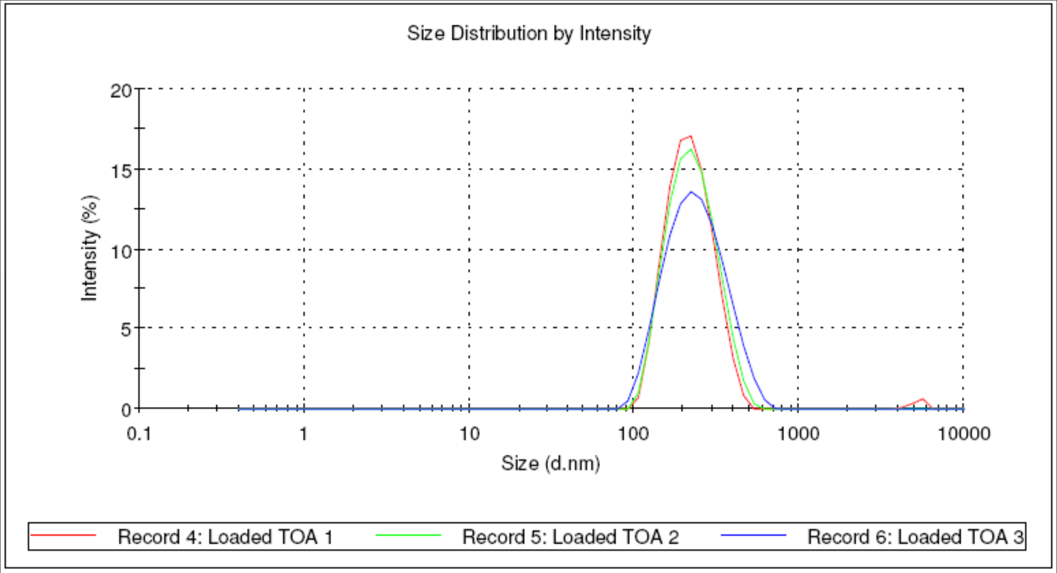


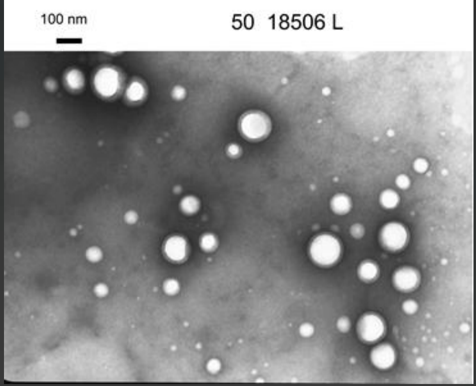


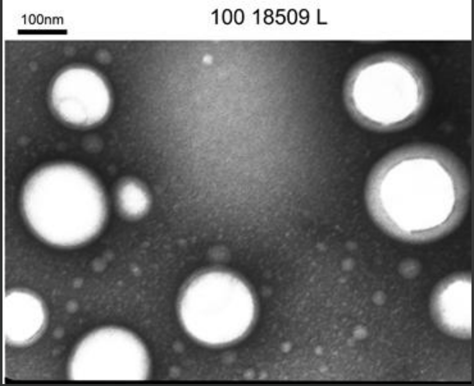


Characterization – Loaded NPs

- Average size
  - 213.1 nm
- PDI
  - 0.142
- Zeta potential
  - -8.4 mV

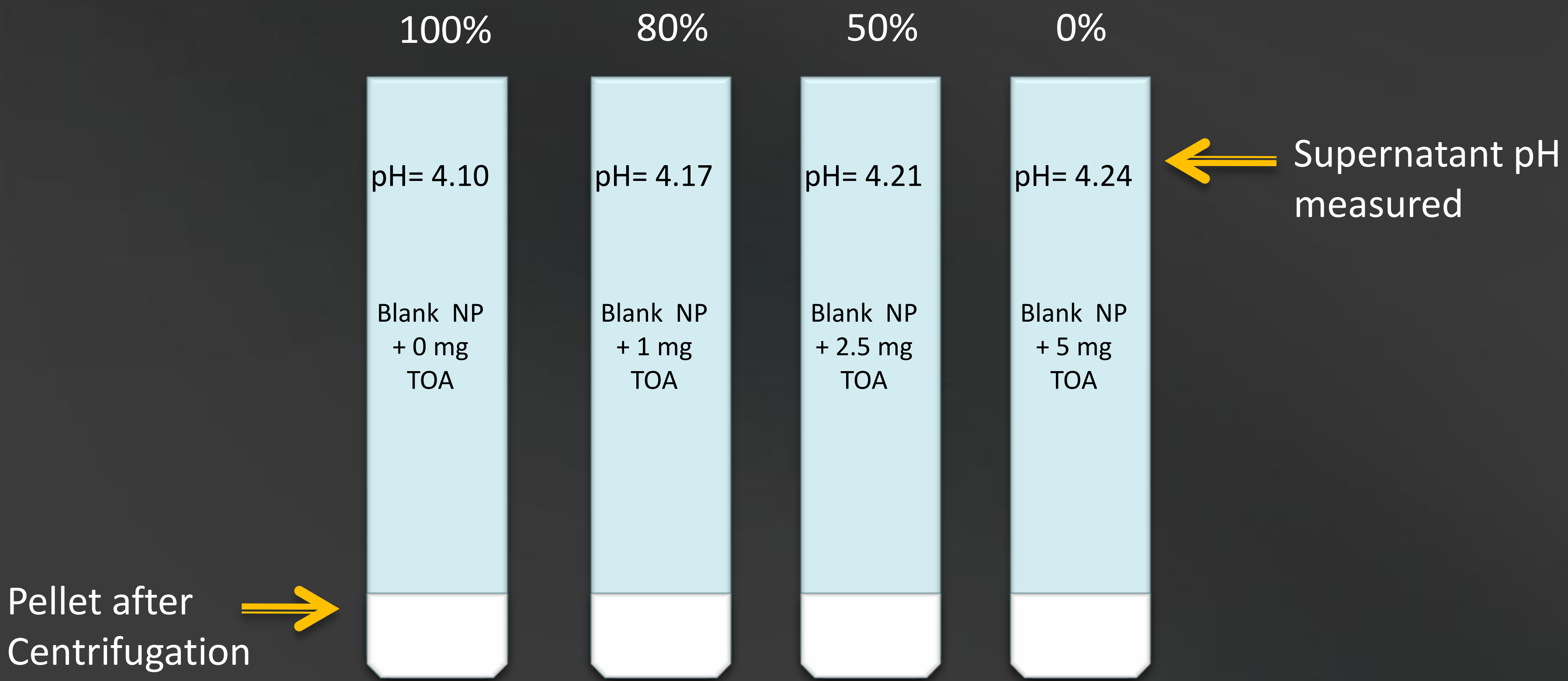






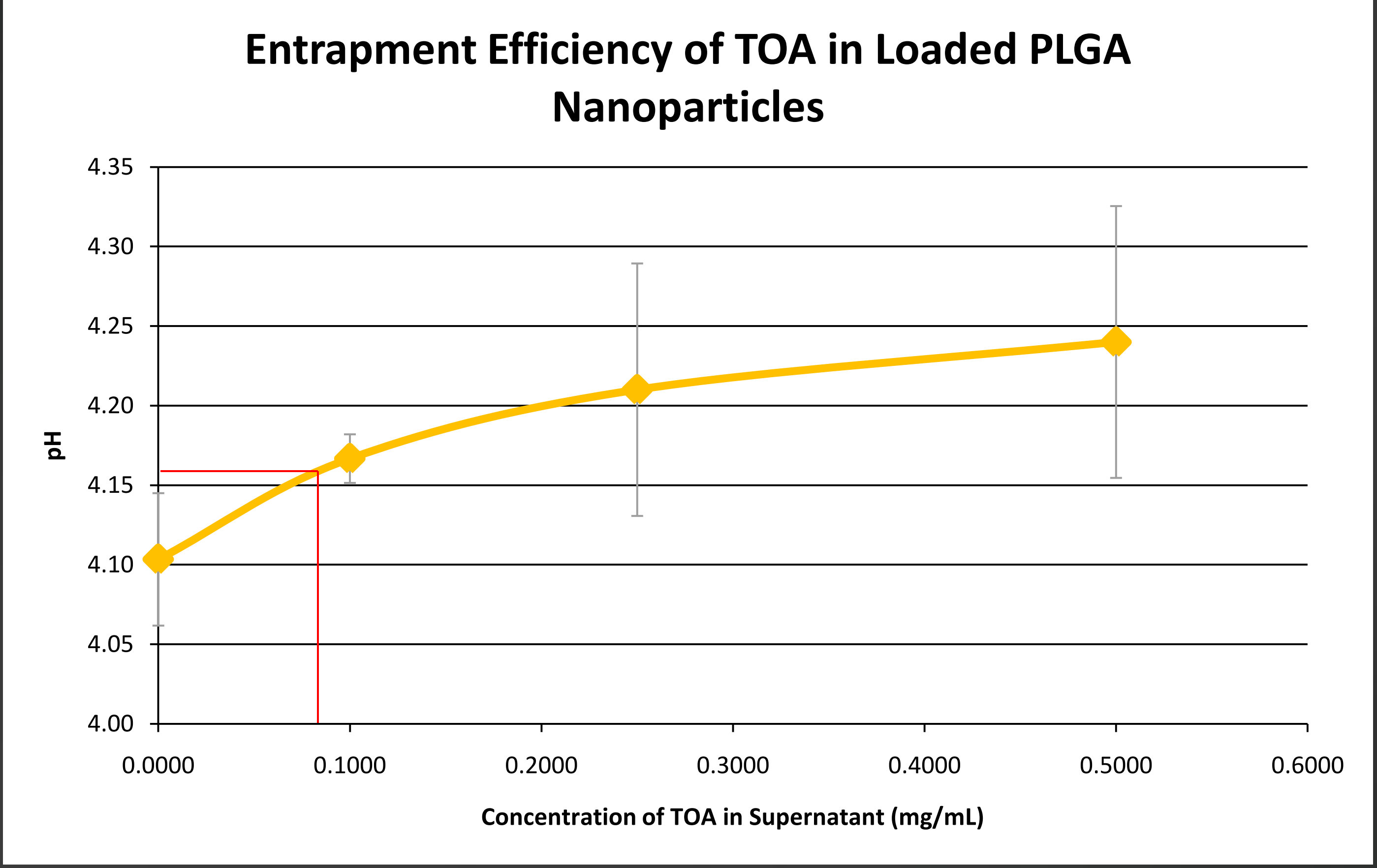
Entrapment Efficiency

- Standard curve of TOA concentration in supernatant vs. pH
- Procedure

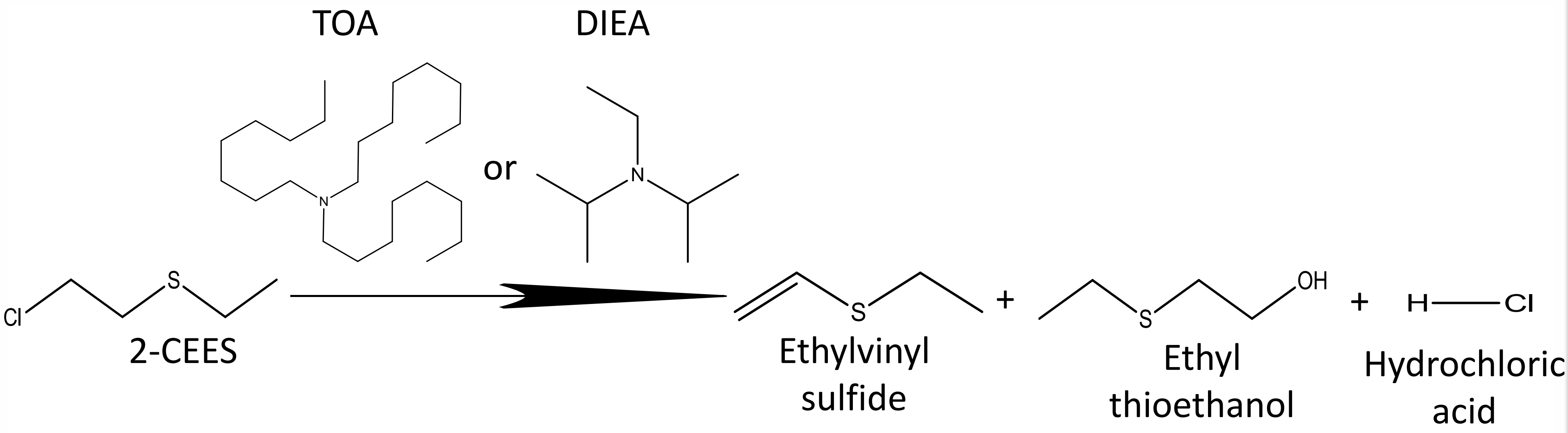


Entrapment Efficiency

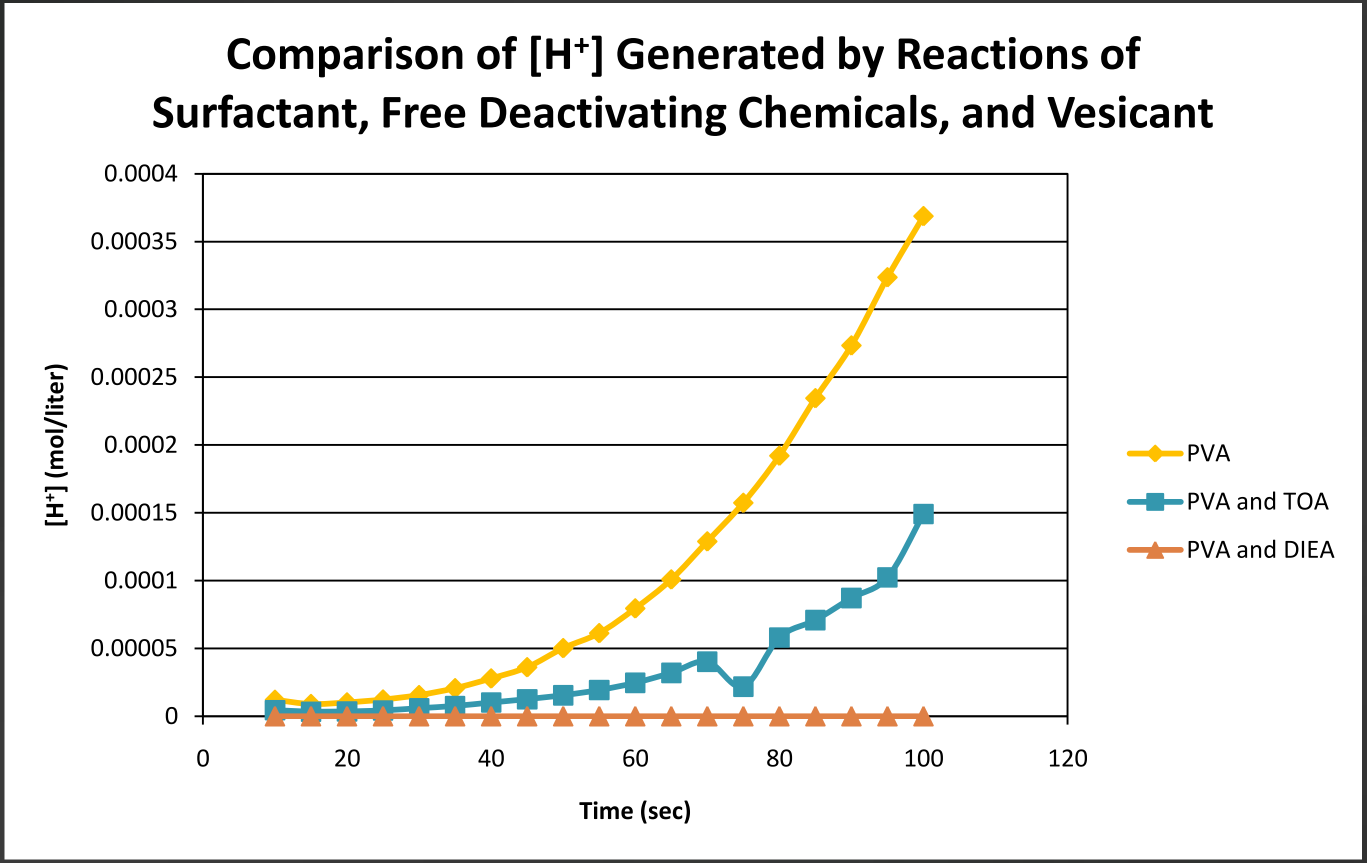
- Entrapment Efficiency (EE): 83%



Deactivation Reaction

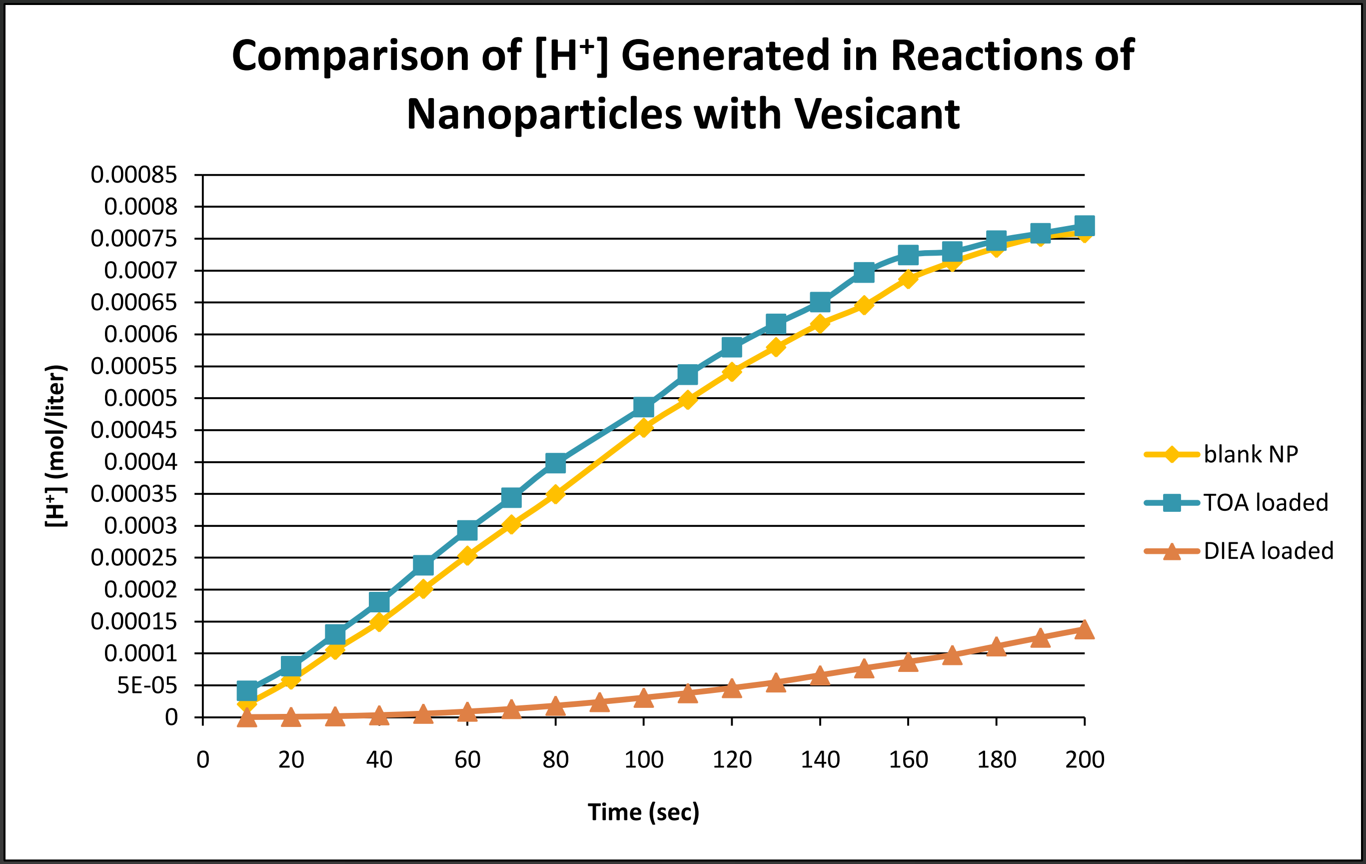


Reaction Testing - Free Chemicals



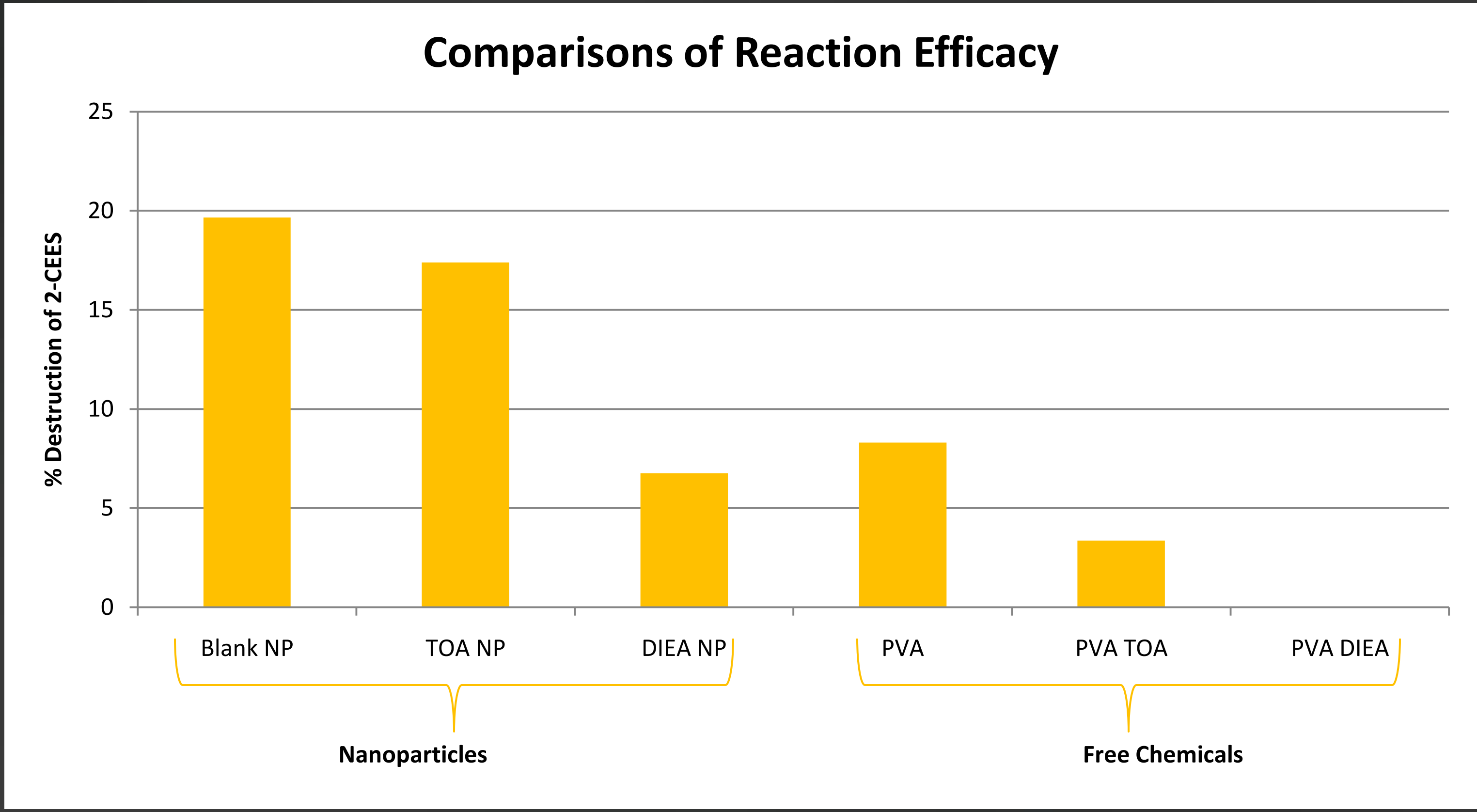
Profile of $[H^+]$ generated after introduction of vesicant to solutions of surfactant and deactivating chemicals.

Reaction Testing - Nanoparticles



Profile of $[H^+]$ generated after introduction of vesicant to solutions of nanoparticles loaded with deactivating chemicals.

Reaction Testing



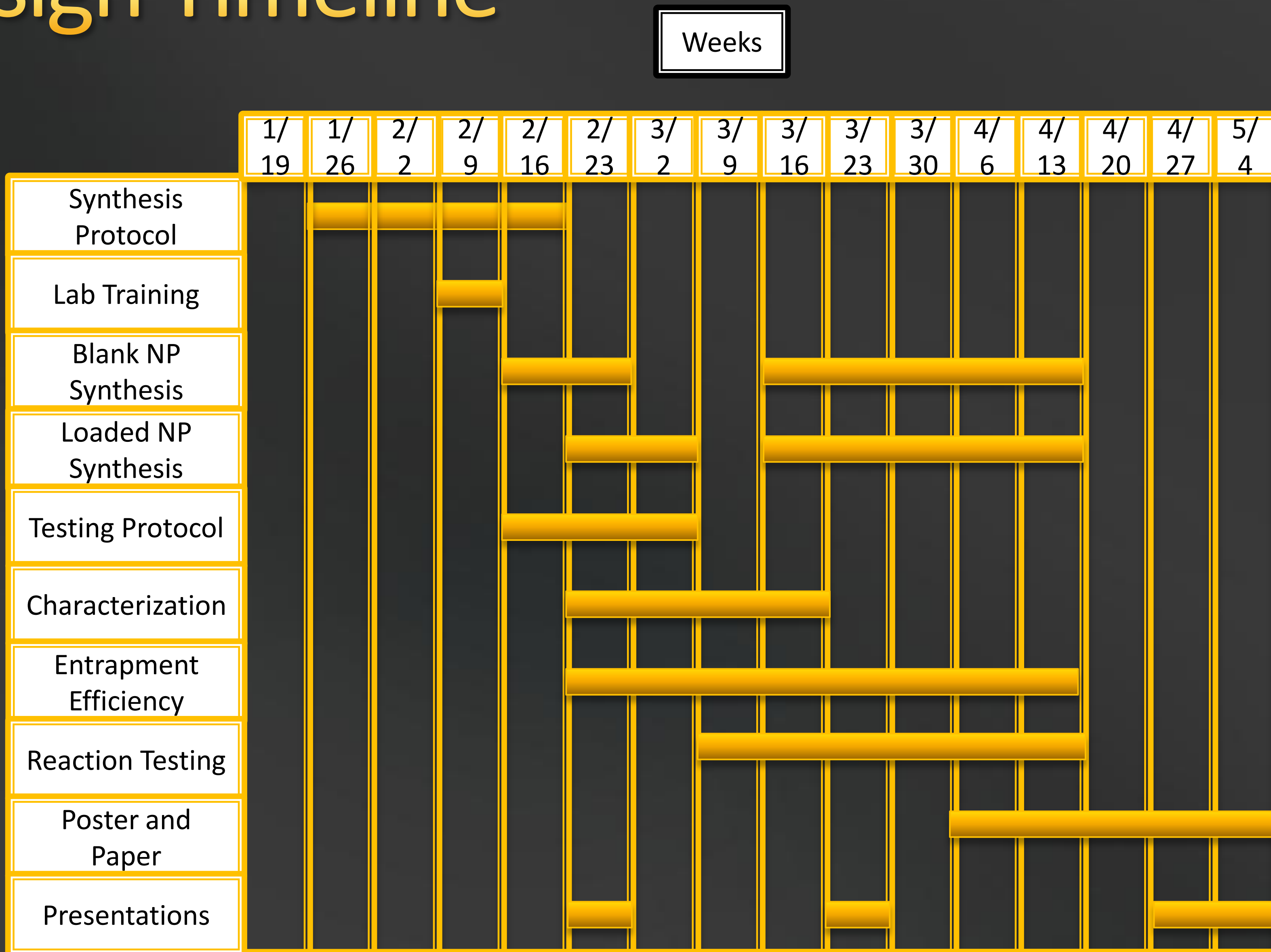
Comparison of percent destruction of vesicant after introduction to various chemical and nanoparticle solutions.

Budget

- Initial budget: $700
- Chemicals ordered from Fisher Scientific and Sigma Aldrich
  - NP synthesis
  - Testing
- Characterization of NPs
  - TEM
  - DLS

Item	Cost
Fisher Scientific	$198.54
Sigma Aldrich	$528.14
Characterization	$130.00
Total spent	**$856.68**

Design Timeline



Conclusion

- NP characterization showed successful synthesis results
  - Consistent with measurable objectives for size, polydispersity index, and zeta potential
- Entrapment efficiency of deactivating chemical was successfully determined
  - Consistent with measurable objectives
- Although no significant change was observed between the loaded and blank nanoparticles, reaction testing showed nanoparticles reacted faster than free deactivating chemical
  - Consistent with measurable objectives

Acknowledgements

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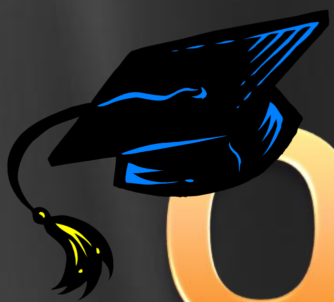
- Nipur Patel
- Balasubramanian Sundar

References:

1. http://imgs.sfgate.com/c/pictures/2006/02/05/rv_war_1.jpg
2. http://www.thesage.com/images/prod/5021605.jpg
3. http://www.chembiokits.com/shop/graphics/00000001/RSDL_Training.jpg
4. http://www.sciencedirect.com.libezp.lib.lsu.edu/science?_ob=ArticleURL&_udi=B6TFS-4X60T8J-2&_user=3787556&_coverDate=01%2F01%2F2010&_alid=1559145087&_rdoc=1&_fmt=high&_orig=search&_origin=search&_zone=rslt_list_item&_cdi=5234&_sort=r&_st=13&_docanchor=&view=c&_ct=3940&_acct=C000061383&_version=1&_urlVersion=0&_userid=3787556&md5=f083aa908da477c47a2bc050091c5238&searchtype=a



Questions?