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## Peptide Functionalized Surfactant MSNs

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# Peptide Functionalized Surfactant MSNs

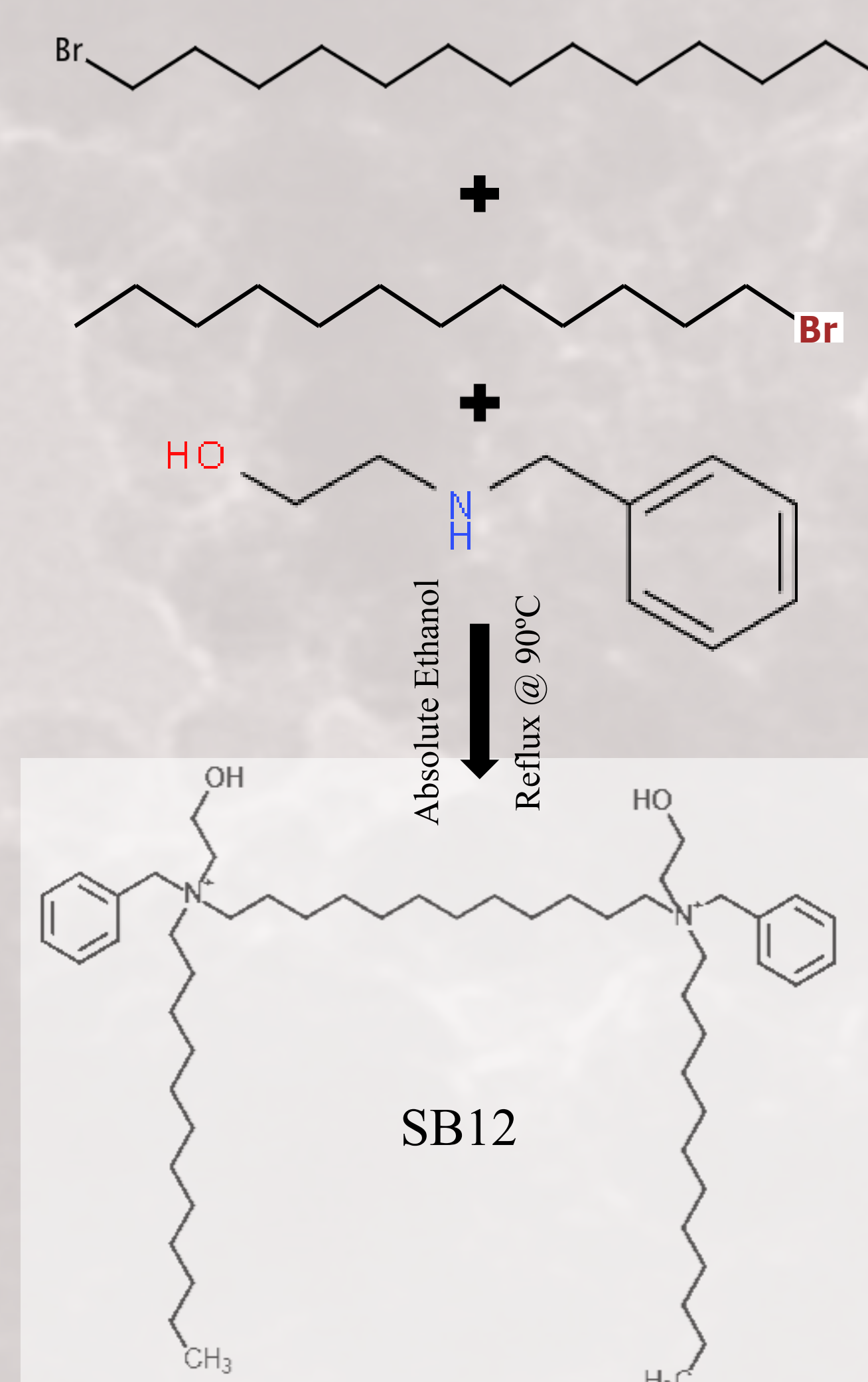
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## Abstract

Antibiotic resistance in bacteria has become a rising problem since the first antibiotic was created, further aggravated by the improper overuse to treat common infections. Because of this pharmaceutical companies must keep making new and stronger antibiotics. Surfactants are plentiful and effective killers of many surface bacteria and are also varied in their structure. All have a hydrophilic head and long hydrophobic carbon chain. These long hydrophobic carbon chains can pierce through the lipid bilayers that make up bacteria cell membranes and cause cytoplasmic leakage and lysis of the cell wall, leading to cell death. One proposed surfactant is synthesized by taking N-benzylamino ethanol dissolved in absolute ethanol and adding 1-bromododecane in excess then left to reflux. Mesoporous silica nanoparticles, or MSNs, are versatile drug delivery vessels that can uptake a variety of drugs in simple one pot synthesis. The desired drug is dissolved in a typically basic solvent at critical micelle concentration, then Tetraethyl orthosilicate (TEOS) is added and the reaction is allowed to reflux until a precipitate is formed. The MSN can then be further functionalized with a gatekeeper to help target bacteria and force the loaded drug inside the MSN to be released when desired. In this case a peptide chain with Vancomycin attached to the end will be used to functionalize the MSNs. Both the synthesized surfactants and the loaded MSNs are tested against the model pathogen *Micrococcus luteus* to test for their effectiveness in killing bacteria. In future work MSNs loaded with various surfactants will be synthesized and possible use of different bulky gatekeepers to functionalize the outside of MSNs will be considered.

## Surfactant Synthesis



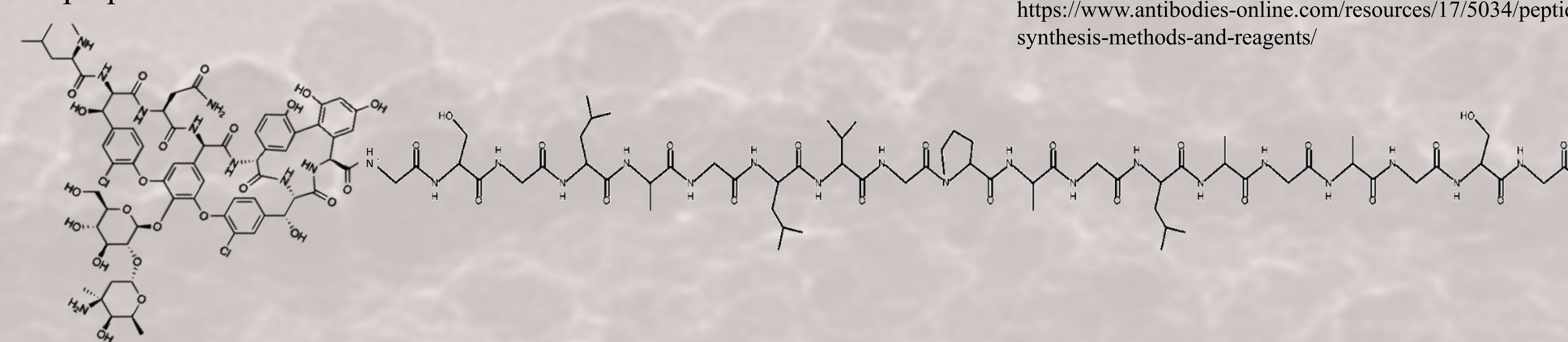
1-Bromododecane, 1,12-Dibromododecane, and N-Benzylethanolamine in 2:1:2 ratio dissolved in absolute ethanol and left to reflux at 90° C for 48 hours

## Peptide Synthesis

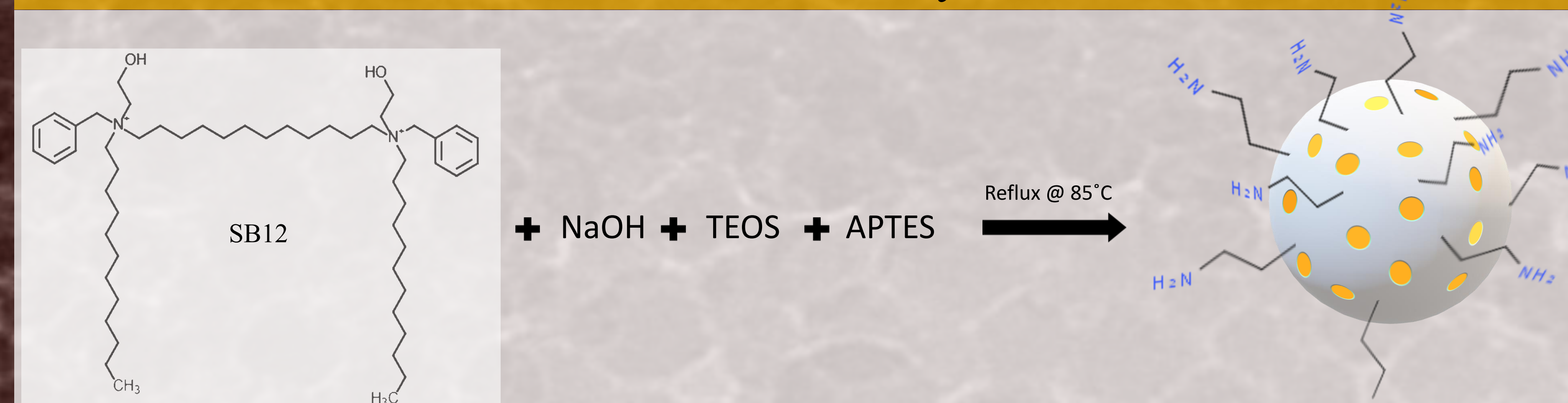
Using solid phase synthesis the following peptide was made:  
Vancomycin-GSGLAG-LVGPAG-LAGAGSG  
Vancomycin was attached just like any other amino acid or florescent dye to the N-terminus end.

- It was mixed with HBTU in a 1:2.9 ratio by molecular weight.
- Dissolved in a solvent mixture of DIEA and DMF in a 1:29 ratio by volume.
- Left to spin with Peptide chain for a full 24 hours.

The completed peptide chain then has its protective resin group cleaved off to prepare for attachment to surfactant loaded MSN.

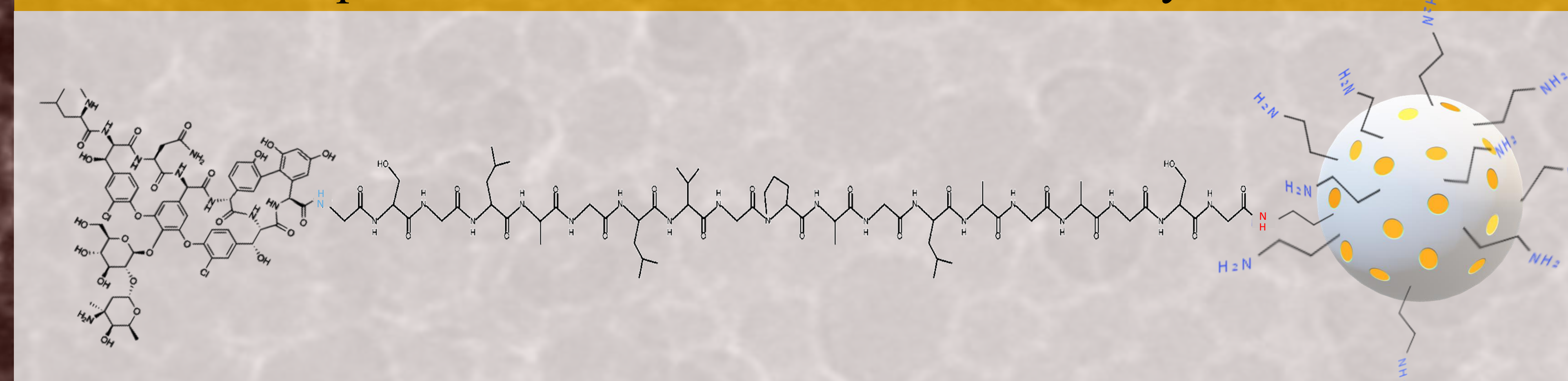


## Surfactant MSN Synthesis



- Surfactant SB12 at critical micelle concentration and 350μL 2M NaOH dissolved in water.
- 700μL TEOS and +100mg APTES mixed and added to solution slowly dropwise to avoid aggregation.
- Stirred and refluxed at 85°C overnight.

## Peptide Functionalized Surfactant MSN Synthesis



The surfactant MSN is treated like an amino acid in solid phase peptide synthesis, attaching one of the various amine groups of the MSN to the C-terminus tail of the peptide chain.

- The surfactant MSN is mixed with HBTU in a 1:2.9 ratio by molecular weight.
- This mixture is dissolved in a solution of DIEA and DMF in a 1:29 ratio by volume.
- The dissolved MSN and HBTU is then swirled with the peptide for 24 hours.

The end product theoretically results in a MSN with a peptide chains attached to each amine groups on the surface of the MSN.

## Conclusion

- Surfactant SB12 is a deadly antibiotic that kills by disrupting the cellular membrane lipid bilayer causing cytoplasmic leakage.
- The MSNs made in our lab are made using a simple one pot synthesis.
- The drug loaded into the MSN can be almost anything theoretically.
- The MSN is functionalized with a peptide chain connected to a large, bulky antibiotic.
  - Peptide chain acts as a targeting system. Cleaving itself around certain enzymes found around infection sites and releasing the gatekeeper and therefore releasing the surfactant loaded into the MSN.
- Vancomycin acts as a gatekeeper, sterically blocking SB12 from being released, to control drug emission rate of SB12 loaded in the MSN.

## Future Work

- Characterization of SB12 loaded MSN using DLS and TGA
- Cell studies with model pathogen *Micrococcus luteus*
  - Studies with unaltered peptide functionalized surfactant MSN to show that gatekeeper works and isn't allowing SB12 to be released
  - Studies with enzymes to show that peptide will cleave properly to allow the release of SB12
- Functionalize MSN with different peptide sequences
- Load MSN with different surfactant

## Acknowledgments

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## References

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- (2) Wendel, S. O.; Menon, S.; Alshetaiwi, H.; Shrestha, T. B.; Chlebanowski, L.; Hsu, W.-W.; Bossmann, S. H.; Narayanan, S.; Troyer, D. L., Cell based drug delivery: *Micrococcus luteus* loaded neutrophils as chlorhexidine delivery vehicles in a mouse model of liver abscesses in cattle. *PLoS One* 2015, 10(5), e0128144/1-e0128144/13.