

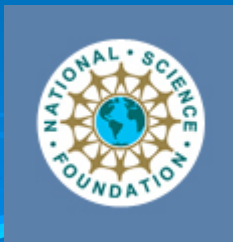
Design of Cancer-Targeting Therapeutic Micelles

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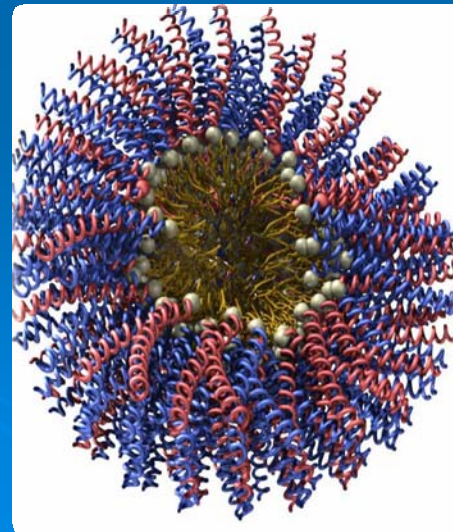
Matt Tirrell's Research Group



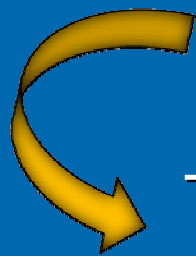
An Alternative Delivery System For Cancer Therapy

- Chemotherapy is highly toxic
- Currently research is developing more effective ways to deliver therapeutics
- **Our Approach**
 - Molecules that are able to target tumor cells
 - Synthesis of peptide-amphiphiles that self-assemble into micelles

Micelles could be multifunctional: tumor cell targeting and therapeutic



Courtesy of
Amanda Trent



Surfactant Number Theory

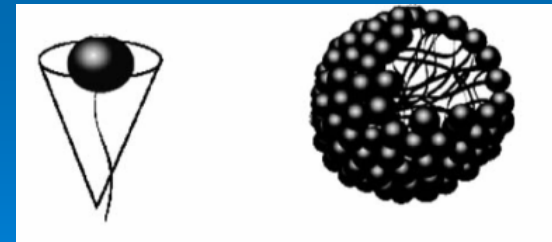
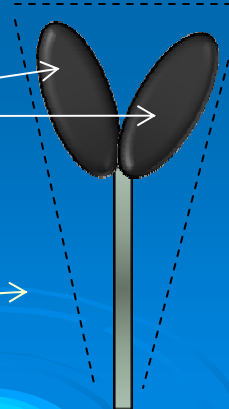
Theoretical approximation to predict micro and nano structures

- Our goal is to conjugate peptides to tails in a way that allows the resulting molecules to self-assemble into spherical micelles.

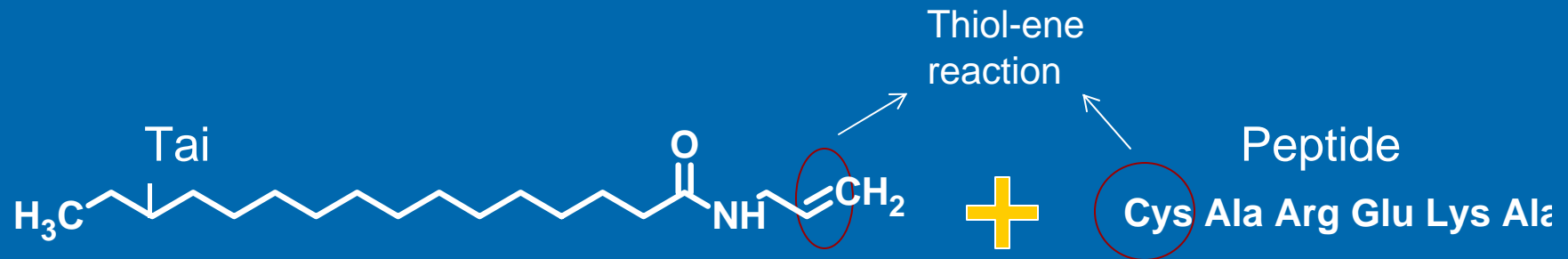


Cancer-targeting peptides
(Hydrophilic head)

Hydrophobic tail

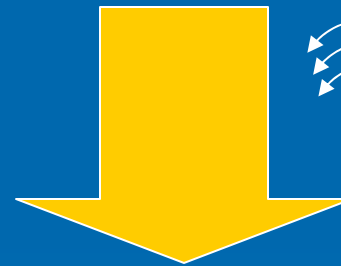


1. Conjugation of a Peptide to a Hydrophobic Tail

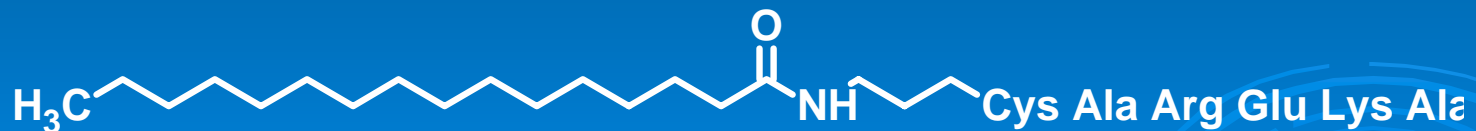


DMPA
(2,2-dimethoxy-2-phenyl
acetophenone)

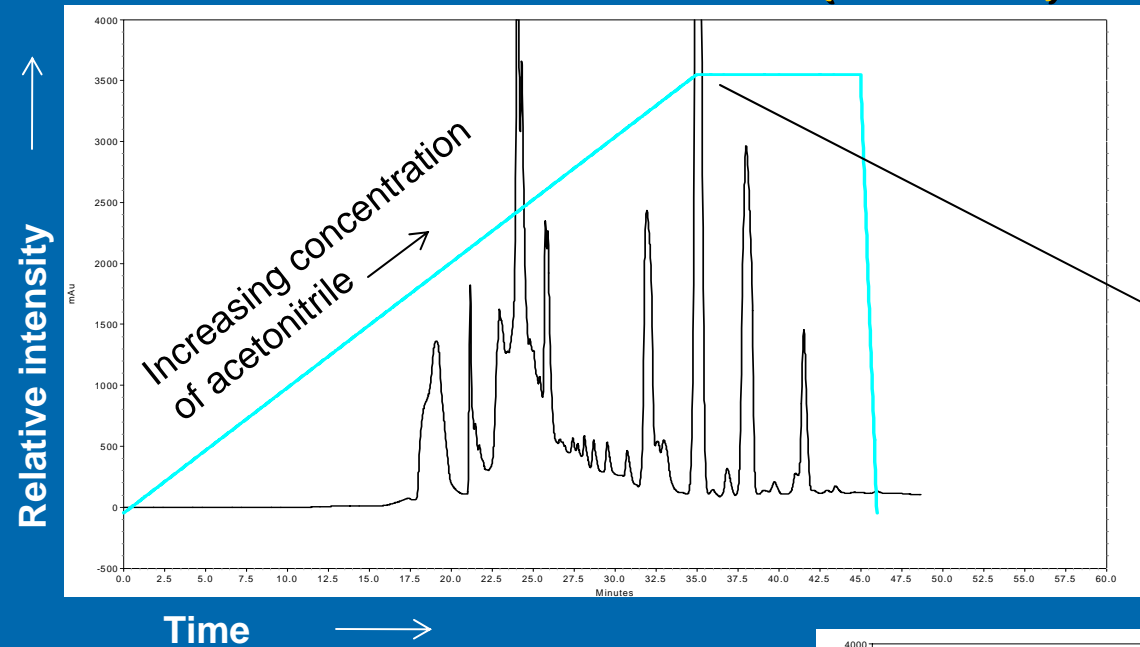
UV light



Tail-head group



2. High Performance Liquid Chromatography (HPLC)

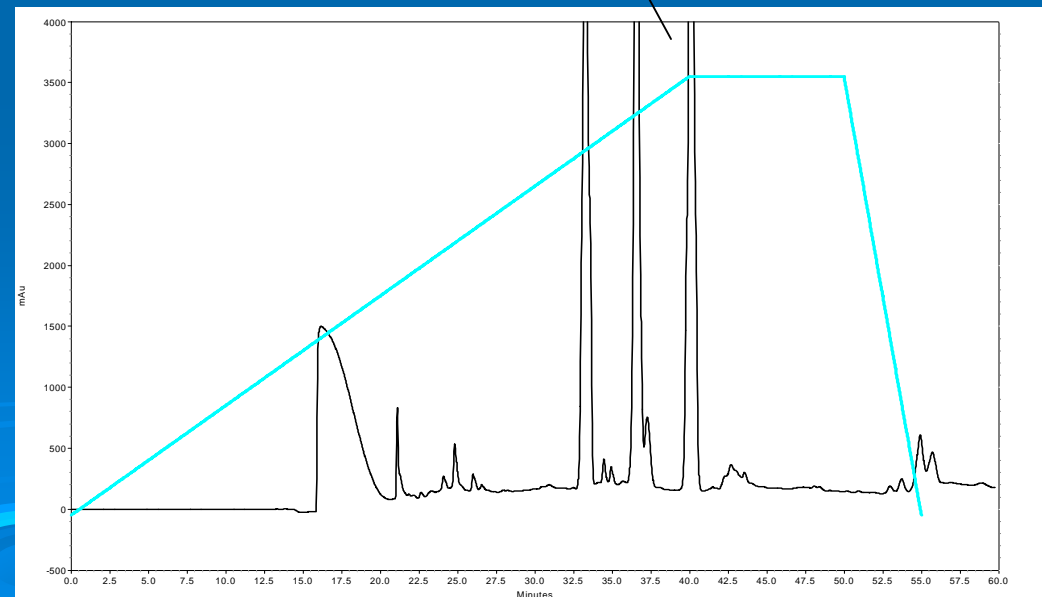


Sparged Reaction

Peaks correspond to the tail-head group

Sealed Reaction

Tail-head group :
Tail-Cys (Gly)₇ Ala Arg Glu Lys Ala



3. Mass Spectrometry

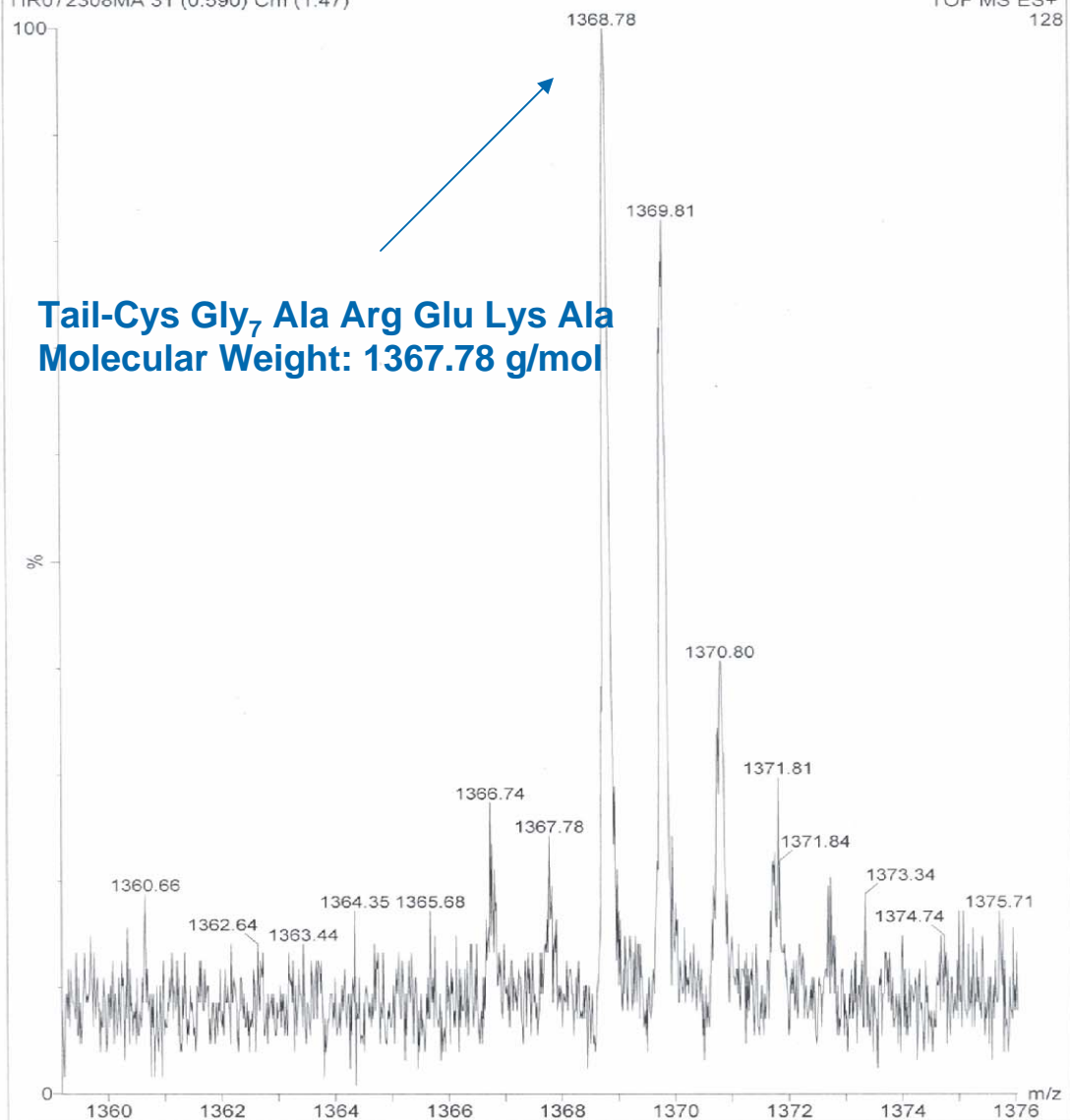
- After separating the different molecules in our solution, through the HPLC, we collect the ones we are interested in to analyze their molecular weight.
- In order to do so, we use a mass spectrometer.



UCSB Chem & Biochem Mass Spec Lab
C16CG7AREKA, +ESI/TOF
TIR072308MA 31 (0.590) Cm (1:47)

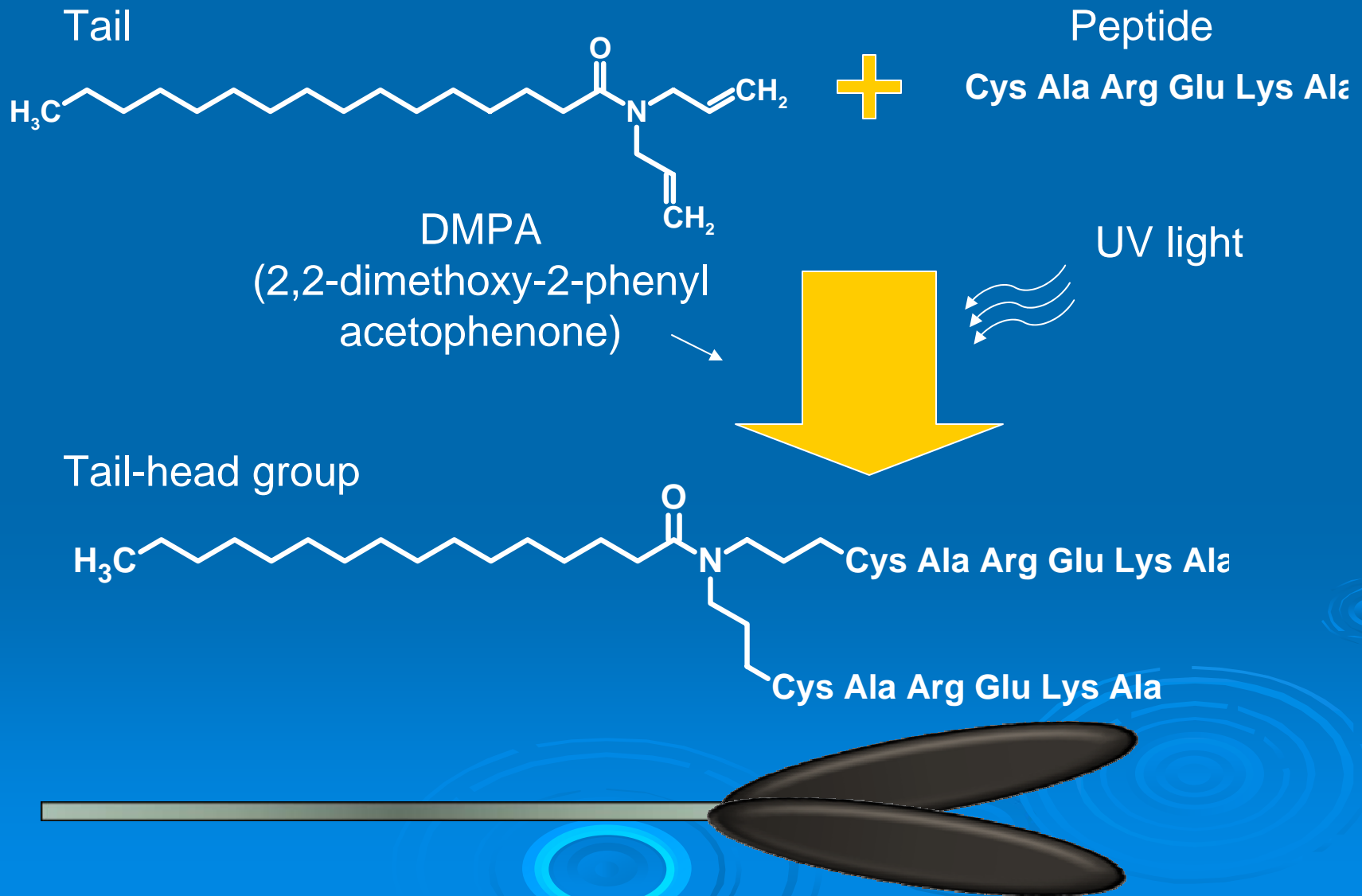
23-Jul-2008 11:41:16

TOF MS ES+
128



Tail-Cys Gly₇ Ala Arg Glu Lys Ala
Molecular Weight: 1367.78 g/mol

Our Next Step: Conjugate Two Peptides to One Tail



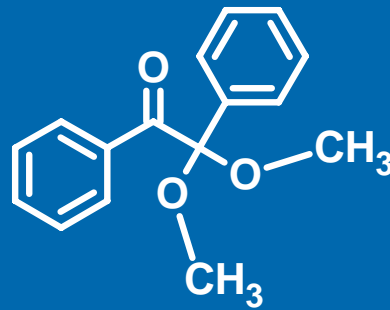
Acknowledgements

- Brian Lin, from Matt Tirrell's Research Group
- Dr. Nick Arnold and Dr. Jens Kuhn, from the INSET Program.
- Evelyn Hu and Liu-Yen Kramer, from CNSI
- Dr. Michael Young and Dr. Alexander Horwitz, from Santa Barbara City College

Thank you!
Any questions?

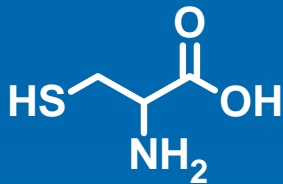


DMPA (2,2-dimethoxy-2-phenyl acetophenone) is used as an initiator:

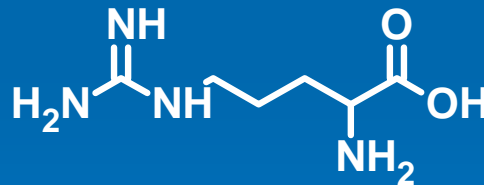


Under presence of UV light, cysteine will react with the tail (thiol-ene reaction):

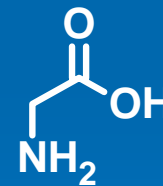
Cysteine (Cys)



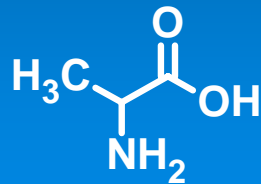
Arginine (Arg)



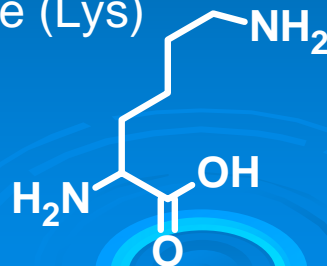
Glycine (Gly)



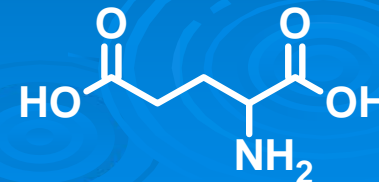
Alanine (Ala)



Lysine (Lys)



Glutamic acid (Glu)


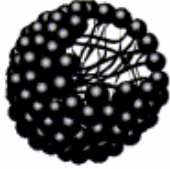



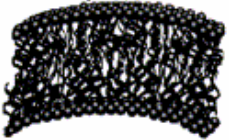

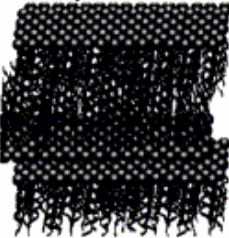



Surfactant Number Theory

Theoretical approximation to predict micro and nanostructures:

$$N_s = \frac{v}{a_0 l}$$

v: volume of the tail group
 a: head group area
 l: fully extended hydrocarbon tail

Critical Packing parameter ($v/a_0 l$)	Critical packing shape	Structure Formed
$<1/3$	Cone 	Spherical micelle 
$1/3 - 1/2$	Truncated cone 	Cylindrical micelle 
$1/2 - 1$	Truncated cone 	Flexible bilayers 
~ 1	Cylinder 	Planar bilayers 
>1	Inverted truncated cone 	Inverted micelles 