Syllabus SIO 264 – Spring 2022

Biosynthesis of Marine Natural Products
9:00 – 10:50 AM Tues/Thurs
Vaughn 100
(4 Units)

Instructor: Bradley Moore (bsmoore@ucsd.edu)

Marine organisms, from microbes and algae to animals, make and use specialized small molecules to support their varied lifestyles. In this course we will examine how and why marine organisms biosynthesize specialized metabolites, from toxins and defense agents to hormones and signaling molecules. We will explore the structures, functions, biosyntheses, and genomics associated with iconic marine compounds and their producing organisms. Students will gain deeper insights into the major classes of marine specialized metabolites, the biosynthetic processes used in their creation, and the bioinformatic tools employed in connecting genes with chemistry. In-class & homework problem-based assignments, assigned readings, and student-led lectures will provide students opportunities to develop their skills in deducing origins of natural products, the process for their assembly, and deduction of structures from genetic sequence information.

Date	Topic	Student Presentation
March 29	Syllabus development and introduction	-----
March 31	Biosynthesis – general principles / pathways	-----
April 5	redox, P450s, heme	-----
April 7	halogenation/dehalogenation	Malia
April 12	degradation of natural products	Lucas
April 14	lipids/DOM	Bo
April 19	terpenes	Hannah
April 21	terpenoids (Vikram Shende – guest lecture)	-----
April 26	bacterial PKS	Hans
April 28	bacterial NRPSs	Neil
May 3	bacterial PKS-NRPSs	Ethan
May 5	Bioinformatics (Alex Chase – guest lecture)	Natalie
May 10	Metabolomics	Nicole
May 12	genome mining	Mariah
May 17	RIPPs	-----
May 19	toxins	Steffaney
May 24	biomineralization	Angus
May 26	metamorposis associated biomolecules	Heidi
May 31	alkaloids	Natalia
June 2	phenylpropanoids (Joe Noel – guest lecture)	-----

Course Objectives

1. To expose students to some of the more impactful and interesting marine natural products, including their discovery, structure determination, chemical ecology, and pharmacological properties
2. To develop an appreciation of the typical biosynthetic units comprising marine natural products in different biosynthetic classes
3. To develop an understanding of the mechanistic chemistry that assmbles the biosynthetic units that comprise marine natural products
4. To develop knowledge of the biosynthetic enzymes that create diverse marine natural products, as well as the corresponding gene clusters and their architecture
5. To learn and practice bioinformatic tools used in genome mining of specialized metabolites.

Text

Primary literature to be assigned in class

Grading

Reading Reflections – 5 x 10 pts = 50 points total
Homeworks – 5 @ 10pts = 50 points total
In-class Presentation – 50 points

Course goal

Understand, appreciate and predict how nature assembles organic molecules from basic primary metabolic building blocks.

Big picture ideas

1. **Retrobiosynthesis** – problem-solving technique for transforming the structure of a natural product to a sequence of progressively simpler structures along a pathway which ultimately leads to primary or common metabolic precursors. This “reflective” reasoning parallels EJ Corey’s retrosynthetic analysis (ACIE, 455-612, 1991).
2. **Genome mining** – outcome-based method to convert genetic information to chemical prediction. This “constructive” thinking approach applies biosynthetic logic to discovery chemistry.
3. **Bioengineering and synthetic biology** – biosynthetic application to reprogram natural metabolic pathways to designer bio-based molecules. Also “forward” thinking.

Essential questions

- How do marine organisms synthesize natural products (NPs)?
- How are primary and secondary/specialized metabolism similar and different?
- How can genomic data be used to solve small molecule structure/function problems?
- How can you engineer / design unnatural NPs or manipulate metabolism?

Learning goals

Students will know how to apply biosynthetic principles / knowledge to MNPs (discovery, structure elucidation, enzymology, genetics, synthesis, etc.)

Teaching goals

Inverted classroom approach will be followed. Five main teaching goals to be achieved:

1. Develop ability to apply principles and generalizations already learned to a new problem and situation.
2. Develop problem-solving skills.
3. Develop ability to synthesize and integrate information and ideas.
4. Develop ability to think holistically to see the whole as well as the parts.
5. Develop ability to think creatively.