Fall [redacted]

[redacted] **CHEM 6756**
DISCOVERY OF SIGNALING MOLECULES

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Course summary: The diversity of chemical signals between organisms and their structural specificities will be presented along with chemical and biological approaches for identifying signaling molecules.

Learning objectives: In this course, I intend for students to explore the mechanisms and consequences of chemical signaling between organisms, integrating biological and chemical points of view. Using original articles published by experts in this field, students are encouraged to critically analyze recent research. Class meetings will involve a combination of lectures, group discussions, and student presentations to enable students to learn how to express and assess scientific hypotheses, understand research methods, and interpret findings and conclusions based upon experimental data. Students will need to regularly apply their earlier foundation in freshman-to-sophomore level biology and chemistry including organic chemistry; therefore this course is most appropriate for advanced undergraduates (juniors and seniors) and for graduate students in the sciences.

By the end of this course, it is my goal that students are able to:

- Explain how chemical cues mediate ecological interactions, including examples from predator-prey, host-parasite, competitive, mating, and cooperative interactions.
- Describe (in words and drawings) the molecular structures of some important chemical cues and propose which structural features of a molecule contribute to its solubility, volatility, reactivity, or interaction with certain biomolecules.
- Predict the biosynthetic pathways and propose some reaction mechanisms by which signaling molecules are produced by living organisms.
- Understand molecular mechanisms by which chemical cues exert their physiological and behavioral effects.
- Critically analyze the primary scientific literature, summarizing hypotheses and outcomes, identifying strengths and weaknesses, and proposing future directions.

This class meets on Tuesdays & Thursdays from 8:05 to 9:25 in EST L1105. There is no textbook. Required readings will be made available on the course t-square website (tsquare.gatech.edu) and students are encouraged to use library databases and the scientific literature to pursue topics in more detail. Since there is no textbook and many of the sessions involve class discussion rather than formal lecture, attendance and class participation are required.

Evaluation:	**BIOL 4746**	**BIOL/CHEM 6756**
Exam #1	**25%**	**20%**
Exam #2	**25%**	**20%**
Literature assignment	**20%**	**20%**
Grad student-led online activity		**10%**
Student presentation	**20%**	**20%**
Class participation	**10%**	**10%**

Exam #1 will be based on material covered in lectures, class discussions, and readings up to the date of that exam. **Exam #2** will be based on material covered since immediately after Exam #1 until Exam #2, although concepts from before Exam #1 may need to be utilized to succeed in Exam #2. Both exams will require a combination of short (single sentence) answers, longer (paragraph) answers, and drawings including molecular structures and biosynthetic reaction mechanisms.

The **literature assignment** will be a short paper written by each student (maximum 2 pages single spaced, 12 point font), reporting on a recent article from the scientific literature (not a review) that each student chooses by

conducting their own literature search. The chosen article should be one that the student found particularly interesting and important, and can focus on any area of chemical signaling between organisms. In their paper, the student should cite the article that was selected, present a brief overview of the field, report the important findings of the chosen article, argue why this article represents an important contribution, and critically evaluate its strengths and weaknesses. For this assignment and the student presentation described below, it is not acceptable for students to re-structure an assignment from a course they have previously taken, nor should they base their assignments on assigned readings for this or another course.

For the **grad student-led online activity**, each student registered in BIOL/CHEM 6756 will be assigned one of the class readings, and will prepare 3 short questions to help guide students to develop their own understanding of that reading. The student assigned a specific reading will post their 3 questions on piazza.com on our course site at least 72 hours prior to the class dealing with that reading, and will respond to student questions and comments related to that article until the next exam. Full points will be awarded to the grad student leading their assigned reading for insightful design of questions and appropriate guidance to other students by answering clearly, accurately, and in a reasonable time frame. All students, including those in BIOL 4746, need to register at piazza.com and sign up for our course site in order to participate in this activity (and thus earn class participation points).

The **student presentations** will be performed in pairs (with some groups of 3, if class size exceeds 20), with 40 minutes for each group to present and answer questions. Topics, chosen in consultation with the instructor, should be related to recent developments and/or applications of chemical signaling. It is important to present experimental data and critical interpretation of results, and to cite the scientific literature (at least 10 citations are expected per presentation). Topics from past years include: Natural Product-Based Chemical Weapons; Signaling Molecules in Wound Healing; Insect Pheromones to Protect Crops; Settlement Cues for Restoring Coral Reefs; Bioremediation by the Manipulation of Bacterial Quorum Sensing; Production and Engineering of Plant Terpenoids; Applications of Canine Olfaction; Plant Volatiles as SOS Signals.

Class participation will be judged by the degree to which each student participates in class discussions (by asking questions, answering questions, offering ideas, opinions, and critiques of readings), during student presentations (by asking questions during others' presentations, by engaging the audience during their own presentation, by connecting their presentation to previous class discussions), during lectures (by asking questions and offering opinions), and online in response to the grad student-led online activity (by posting questions, comments, and answers). Thus all students, including those in BIOL 4746, need to register at piazza.com and sign up for our course site in order to earn class participation points for the online activity, even though this activity will be led specifically by graduate students.

Please see www.honor.gatech.edu for Georgia Tech's Academic Honor Code, which you are required to uphold.

Class calendar:

Week	Date	Topic	Reading assignment (read BEFORE class)
1	Aug 21	Course objectives and expectations; Introduction to molecules as information in nature (lecture)	
	Aug 23	Overview of classes of natural products and their biological origins (lecture)	Meinwald (2011)
2	Aug 28	Human sex pheromones (part 1): are there or aren't there? (discussion)	Wedekind et al (1995) *<u>Find & bring to class:</u> 1 story on human pheromones from the popular (non-scientific) media*
	Aug 30	Pheromones in mammals (part 1): linking chemical cues to reproductive physiology in mice (discussion led by Drew Sieg)	Novotny et al (1999)
3	Sept 4	Pheromones in mammals (part 2): linking chemical cues to aggressive behavior in mice (discussion)	Chamero et al (2007)
	Sept 6	Human sex pheromones (part 2): how smelling others drives behavior, feelings, and physiology (discussion)	Bensafi et al (2004)
4	Sept 11	Biosynthesis of signaling molecules (part 1): polyketide and fatty acid metabolism in plants, microbes, and animals (lecture)	
	Sept 13	Bacterial quorum sensing in mutualistic interactions that make squid shine light, focusing on confirming the role of a candidate fatty acid-derived signaling molecule (discussion) ***Literature assignment due in class***	Boettcher & Ruby (1995)
5	Sept 18	Bacterial quorum sensing in cholera disease, focusing on identifying a new fatty acid-derived signaling molecule (discussion)	Higgins et al (2007)
	Sept 20	The importance of blends of molecules as chemical cues: Fatty acid-derived pheromones in the nematode worm *C. elegans* (discussion)	Srinivasan et al (2008)
6	Sept 25	Evolution of resistance to *C. elegans* pheromones, via mutations to chemoreceptor genes (discussion)	McGrath et al (2011)
	Sept 27	Study session – practicing reaction mechanisms for polyketide and fatty acid metabolism	
7	Oct 2	***Exam#1***	
	Oct 4	Biosynthesis of signaling molecules (part 2): isoprenoid metabolism in plants, microbes, and animals (lecture)	
8	Oct 9	Chemical defense against predators, competitors, and microbes, focusing on isoprenoid-derived chemical cues in a marine sponge (discussion)	Kubanek et al (2002)
	Oct 11	Chemoreception of chemical defenses: how fish predators recognize noxious prey on coral reefs (discussion)	Cohen et al (2010)
9	Oct 16	*Fall break – no class*	
	Oct 18	Marine algae use isoprenoid-derived chemical weapons to harm corals (discussion)	Rasher et al (2011)
10	Oct 23	Biosynthesis of signaling molecules (part 3): shikimate and peptide metabolism in plants and	

		microbes (lecture)	
	Oct 25	Interactions of natural toxins with receptors: ecological and evolutionary consequences of amino acid-derived saxitoxin binding to animal sodium channels (discussion)	Bricelj et al (2005)
11	Oct 30	Why chili peppers taste hot to mammals but not to birds: chemoreception of shikimate-derived capsaicin (discussion)	Jordt & Julius (2002)
	Nov 1	Ant-associated bacteria produce antibiotic to protect their fungal symbiont from invasion by another (pathogenic) fungus (discussion)	Currie et al (1999)
12	Nov 6	Identification of peptide-derived molecule as ant-associated chemical weapon (discussion)	Oh et al (2009)
	Nov 8	Surface-associated role of marine algal isoprenoid/shikimate-derived defenses against fungi (discussion)	Lane et al (2009)
13	Nov 13	Long sought-after cockroach mating pheromone turns out to be rare isoprenoid/shikimate-derived molecule (discussion)	Nojima et al (2005)
	Nov 15	***Exam #2***	
14	Nov 20	Student presentations Presenting group #1: Presenting group #2:	
	Nov 22	*Thanksgiving break – no class*	
15	Nov 27	Student presentations Presenting group #1: Presenting group #2:	
	Nov 29	Student presentations Presenting group #1: Presenting group #2:	
16	Dec 4	Student presentations Presenting group #1: Presenting group #2:	
	Dec 6	Student presentations Presenting group #1: Presenting group #2:	

Reading list – articles available on T-square

Bensafi M, Brown WM, Khan R, Levenson B, Sobel N (2004) Sniffing human sex-steroid derived compounds modulates mood, memory and autonomic nervous system function in specific behavioral contexts. Behavioural Brain Research 152:11-22

Boettcher KJ, Ruby EG (1995) Detection and quantification of *Vibrio fischeri* autoinducer from symbiotic squid light organs. Journal of Bacteriology 177:1053-1058

Bricelj VM, Connel L, Konoki K, MacQuarrie SP, Scheuer T, Catterall WA, Trainer VL (2005) Sodium channel mutation leading to saxitoxin resistance in clams increases risk of PSP. Nature 434:763-767

Chamero P, Marton TF, Logan DW, Flanagan K, Cruz JR, Saghatelian A, Cravatt BF, Stowers L (2007) Identification of protein pheromones that promote aggressive behavior. Nature 450:899-903

Cohen SP, Vincent KK, Halstead-Nussloch GE, Hatt H, Kubanek J, McCarty NA (2010) RL-TGR, a co-receptor involved in aversive chemical signaling. Proceedings of the National Academy of Sciences 107:12339-12344

Currie CR, Scott JA, Summerbell RC, Malloch D (1999) Fungus-growing ants use antibiotic-producing bacteria to control garden parasites. Nature 398:701-704

Higgins DA, Pomianek ME, Kraml CM, Taylor RK, Semmelhack MF, Bassler BF (2007) The major *Vibrio cholerae* autoinducer and its role in virulence factor production. Nature 450:883-886

Jordt SE, Julius D (2002) Molecular basis for species-specific sensitivity to "hot" chili peppers. Cell 108:421-430

Kubanek J, Whalen KE, Engel S, Kelly SR, Henkel TP, Fenical W, Pawlik JR (2002) Multiple defensive roles for triterpene glycosides from two Caribbean sponges. Oecologia 131:125-136

Lane AL, Nyadong L, Galhena A, Shearer TL, Stout EP, Parry RM, Kwasnik M, Wang MD, Hay ME, Fernandez F, Kubanek J (2009) Desorption electrospray ionization mass spectrometry reveals surface-mediated antifungal chemical defense of a tropical seaweed. Proceedings of the National Academy of Sciences 106:7314-7319

McGrath PT, Xu Y, Ailion M, Garrison JL, Butcher RA, Bargmann CI (2011) Parallel evolution of domesticated *Caenorhabditis* species targets pheromone receptor genes. Nature 477:321-328

Meinwald J (2011) Natural products as molecular messengers. Journal of Natural Products 74:305-309

Nojima S, Schal C, Webster FX, Santangelo RG, Roelofs WL (2005) Identification of the sex pheromone of the German cockroach, *Blattella germanica*. Science 307:1104-1106

Novotny MV, Jemiolo B, Wiesler D, Ma W, Harvey S, Xu F, Xie TM, Carmack M (1999) A unique urinary constituent, 6-hydroxy-6-methyl-3-heptanone, is a pheromone that accelerates puberty in female mice. Chemistry & Biology 6:377-383

Oh DC, Poulson M, Currie CR, Clardy J (2009) Dentigerumycin: a bacterial mediator of an ant-fungus symbiosis. Nature Chemical Biology 5:391-393

Rasher DB, Stout EP, Engel S, Kubanek J, Hay ME (2011) Macroalgal terpenes function as allelopathic agents against reef corals. Proceedings of the National Academy of Sciences 108:17726-17731

Srinivasan J, Kaplan F, Ajredini R, Zachariah C, Alborn HT, Teal PEA, Malik RU, Edison AS, Sternberg PW, Schroeder FC (2008) A blend of small molecules regulates both mating and development in *Caenorhabditis elegans*. Nature 454:1115-1119

Wedekind C, Seebeck T, Bettens F, Paepke AJ (1995) MHC-dependent mate preferences in human. Proceedings of the Royal Society B 260:245-249