“The worst thing that can happen during the 1980's is not energy depletion, economic collapse, limited nuclear war, or conquest by a totalitarian government. As terrible as these catastrophes would be for us, they can be repaired within a few generations. The one process in the 1980's that will take millions of years to correct is the loss of genetic and species diversity by the destruction of natural habitats. This is the folly that our descendants are least likely to forgive us.”

Biology 5865 – Conservation Biology

• Introduction
• What is Conservation Biology?
Biology 5865 – Conservation Biology - Overview

- Review syllabus
- Grading
- Attendance?
- Prerequisite – General Ecology
- Special needs
- Keep up with reading!
- Lectures not strictly from Primack (2010)
- Two guest lectures
- Current events
- Ambassadors of conservation biology
Words from a previous student

• “My words of wisdom for the next class is to read the book and attend lecture. (And if it's 8 a.m. again, bring a cup of coffee).”
What is Conservation Biology?

• “The science of scarcity and diversity.” M. Soule (1986)
• “The applied science of maintaining the Earth’s biological diversity” or more simply “biology as applied to conservation issues.” M. Hunter (1996, 2002)
• “Conservation biology is the new, multidisciplinary science that has developed to deal with the crisis confronting biological diversity.” R. Primack (2006)
• “Conservation biology should be considered a crisis discipline.” R. Primack (2006)
Conservation is not new

- "People have been doing conservation for decades even centuries…” (Meffe and Carroll 1994)
- What is new?
  - Every natural ecosystem on the planet has been altered by humans
  - Vast numbers of species on the planet have become prematurely extinct
  - Natural hydrological and chemical cycles have been disrupted
  - Billions of tons of topsoil have been lost
  - Genetic diversity has been eroded
  - Earth’s climate has been altered
Goals of Conservation Biology from Primack (2010, p. 7)

• To document the full range of biological diversity on Earth – “taxonomy, natural history, ecology”

• To investigate human impact on species, genetic variation, and ecosystems – “ecology, genetics, biogeography, etc.”

• To develop practical approaches to prevent the extinction of species, maintain genetic diversity within species, and protect and restore biological communities and their associated ecosystem function – “conservation biology, communication, natural and social sciences, economics, politics, management, etc.”
Figure 1.2 Conservation biology

**Basic Sciences**
- Anthropology
- Biogeography
- Climatology
- Ecology:
  - Community ecology
  - Ecosystem ecology
  - Landscape ecology
- Environmental studies:
  - Ecological economics
  - Environmental ethics
  - Environmental law
- Ethnobotany
- Evolutionary biology
- Genetics
- Population biology
- Sociology
- Taxonomy
- Other biological, physical, and social sciences

**Resource Management**
- Agriculture
- Community education and development
- Fisheries management
- Forestry
- Land-use planning and regulation
- Management of captive populations:
  - Zoos
  - Aquariums
  - Botanical gardens
  - Seed banks
- Management of protected areas
- Sustainable development
- Wildlife management
- Other resource conservation and management activities

FIELD EXPERIENCE AND RESEARCH NEEDS

NEW IDEAS AND APPROACHES
The interdisciplinary nature of conservation biology merges many traditional fields of natural and social sciences, and the humanities. This list of relevant subdisciplines and interactions is not exhaustive. Many connections have been made, and more could productively be created in the future.

From Grooom et al. (2006)
Historical context of conservation biology

- Humans ‘may’ have been responsible for the extinction of most of the large mammal fauna of North America shortly after human colonization from Asia about 11,000 years ago.
- Aristotle (382 – 334 B.C.) commented on the widespread destruction of forests in the Baltic Region.
- Barren landscapes of Turkey, Syria, Iraq, and Iran are unnatural deserts that resulted from massive exploitation of fragile woodlands.
Historical Context continued - 2

• India, Bangladesh, and Pakistan - it is hard to imagine the changes that have occurred in those areas over the past 2000+ years
• Deforestation of most of Europe by the early 18\textsuperscript{th} Century, forest areas maintained as private game management and royal preserves
• In Great Britain, many of the native forests were gone by the 12\textsuperscript{th} Century
• Southeastern Minnesota and southern Wisconsin were largely deforested during the past 150 years
Deforestation of Cadiz Township – southern Wisconsin

1831

1882

1902

1950
Ethical Principles of Conservation Biology (Primack 2010, p. 10-11)

• The diversity of species and biological communities should be preserved
• The ultimate extinction of populations and species should be prevented
• Ecological complexity should be maintained
• Evolution should continue (The Red Queen Hypothesis)
• Biological diversity has intrinsic value
Guiding Principles of Conservation Biology
(from Meffe and Carroll 1994)

• Principle 1: Evolution is the basic axiom that unites all of biology (The evolutionary play)

• Principle 2: The ecological world is dynamic and largely non-equilibrial (The ecological theater)

• Principle 3: The human presence must be included in conservation planning (Humans are part of the play)
Figure 1.1 The human population in 2010 stands at around 6.8 billion
Figure 1.4  Tanah Lot Temple is a Hindu temple on the island of Bali in Indonesia—illustration of the connection of the human spirit with the natural world.
Three Major Philosophical Conservation Movements in the USA

1. Romantic-Transcendental Conservation Ethic

- Movement traced to Ralph Waldo Emerson and Henry David Thoreau in the Eastern US and John Muir in the West (legacy of the Sierra Club today) – mid 1800’s

- Spoke of nature in a quasi-religious sense, a temple in which to commune with and appreciate the works of God; nature has other uses than for human economic gain; preserve nature; nature was seen as a place to cleanse and refresh the soul

- Referred to by Primack (2006) as including the ‘preservation’ ethic
2. Resource Conservation Ethic

- Popularized by the forester Gifford Pinchot (founder of the USDA Forest Service) and an ally of Teddy Roosevelt at the turn of the century that arose out of the writing on the utilitarian philosophy of John Stuart Mill, etc.

- Primarily spoke of nature as natural resources and “the greatest good of the greatest number for the longest time;” the approach stressed equity – a fair distribution of resources among consumers both present and future – led to the concept of “multiple use”
3. Evolutionary-Ecological Land Ethic

- Developed by Aldo Leopold and his classic essays published in ‘A Sand County Almanac’ (1949) – note Leopold had earlier been educated in the Pinchot tradition

- Leopold began to see the Pinchot perspective as inadequate and scientifically inaccurate; the emerging development of ecology and evolution as scholarly disciplines began to demonstrate that nature was not a simple collection of independent parts but rather a complicated and integrated system of interdependent processes and components
Rachel Carson – An American Hero
European Origins

- Primack (2006, p. 12) emphasizes that the European perspective has been guided by the bible
- Genesis, the first book of the bible, states “be fruitful and multiply and fill the Earth and subdue it; have dominion over every living thing that moves upon the Earth”
- Western philosophy – nature should be converted into wealth as rapidly as possible and used for the benefit of humans – “anthropocentric approach”
- But in many European colonies – it has been long recognized that conservation is important – e.g.,
  - French Island of Mauritius – in 1769 – ordinance that 25% of land holdings must remain forested
  - In 1852 – English scientists recognized that forest reserves must be established
- Moreover – both linked deforestation to decreased water supplies, erosion, and local climate impacts!
Conservation Biology Today – a summary

- Modern conservation biology is a mixture of these perspectives
- Leopold and the Evolutionary-Ecological view of the world as a dynamic, non-equilibrium system has the most well-founded perspective regarding the science of conservation biology; yet the economic, spiritual, and social needs of people must also be met
- These philosophical underpinnings have led and still lead to many confrontations among “special interest” groups
- Can we ‘fix’ these systems? -- M. Hunter states that the dynamic interface between people and nature is the crux of conservation and conservation biology
Society for Conservation Biology

- Scientifically – the First International Conference on Conservation Biology held in San Diego, California in 1978 – attributed to the “origin” of the field of Conservation Biology
- Ultimately led to the establishment of the scientific organization – **Society for Conservation Biology**
- Journal *Conservation Biology* was first published in 1987
- SCB now has over **10,000 members** and is similar in size to the Ecological Society of America which was established over 90 years ago
- And comprised of relatively young individuals
Spiroindolones, a Potent Compound Class for the Treatment of Malaria

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Recent reports of increased tolerance to artemisinin derivatives—the most recently adopted class of antimalarials—have prompted a need for new treatments. The spirotrypetalid-β-carbolines, or spiroindolones, are potent drugs that kill the blood stages of Plasmodium falciparum and Plasmodium vivax clinical isolates at low nanomolar concentrations. Spiroindolones rapidly inhibit protein synthesis in P. falciparum, an effect that is ablated in parasites bearing nonsynonymous mutations in the gene encoding the P-type cation-transporter ATPase4 (PfATP4). The optimized spiroindolone NITD609 shows pharmacokinetic properties compatible with once-daily oral dosing and has single-dose efficacy in a rodent malaria model.

Almost half the world's population is exposed to malaria, which causes over 500,000 deaths each year and kills more under 5-year-olds than any other infectious agent.1 Fifty years ago, malaria had been eliminated from many areas of the world through a combination of drug treatments and vector control interventions.2 However, the global spread of drug resistance together with a collapse of vector control programs resulted, by the 1980s, in a resurgence in disease incidence and mortality. Today, epidemiological data suggest that the introduction of new drugs (notably the artemisinin-based combination therapies on ACTs) may have reversed that trend.3 Recent reports suggest that resistance to the endoperoxide artemisins is now emerging (4–6). These observations have triggered a concerted search for new drugs that could be deployed if artemisinin resistance were to spread.

Many of the therapies currently in development use known antimalarial pharmacophores (e.g., artemisinins and/or peroxidones) chemically modified to overcome the liabilities of their predecessors (7). Although these compounds may become important in the treatment of malaria, it would be preferable to discover chemotypes with novel mechanisms of actions (8). However, despite important advances in our understanding of the Plasmodium and Plasmodium gene expression, the identification and validation of new drug targets have been challenging (9).

To identify novel antimalarial leads, we and others have screened diverse chemical libraries using Plasmodium whole-cell proliferation assays with cultured intracellular parasites (10–12). From a library of about 12,000 pure natural products and synthetic compounds with structural features found in natural products, we screen identified 275 primary hits with submicromolar activity against Plasmodium falciparum. We discarded these hits whose activity was not reproducible against multidrug-resistant parasites and/or that displayed some cytotoxicity against mammalian cells (more than 50% viability inhibition at 10 μM). Plasmodiokinin and physical properties were then determined for the remaining 17 compounds. From this, a synthetic compound related to the spiropyrroloindolone class, having a favorable pharmacological profile, stood out as a starting point for a medicinal chemistry lead optimisation effort. Synthesis and evaluation of about 200 derivatives yielded the optimized spiroindolone-β-carbolone (spiroindolone) compound NITD609 (Fig. 1A). This compound in synthetic routes, including clear separation of the active enantiomer, and is amenable to large-scale manufacturing. NITD609 has good drug-like properties (see below) and displays pharmacokinetic properties compatible with conventional tablet formulations.

There is general agreement that a new antimalarial should ideally meet the following criteria: (i) kills parasite blood stages; (ii) is active against drug-resistant parasites; (iii) is safe (i.e., no cytotoxicity, genotoxicity, and/or cardiotoxicity); and (iv) has pharmacokinetic properties compatible with once-daily oral dosing. NITD609 meets all these criteria. We also gained insight into a mechanism of drug resistance involving the P-type cation-transporter ATPase4 (PfATP4). Activity against drug-resistant Plasmodium. Antimalarial blood-stage activity was evaluated in vitro against a panel of culture-adapted P. falciparum strains. NITD609 displayed single-digit nanomolar average 50% inhibitory concentration values [IC50 range, 0.5 to 1.4 μM; table S1], with no evidence of diminished potency against drug-resistant strains (table S1). This compound was also tested in ex vivo assays with fresh isolates of P. falciparum and P. vivax (14), collected from malaria patients on the Thai-Burmaese border where chloroquine resistance has been widely reported (15, 16). NITD609 was found to be as effective as artemunate, with potency in the low nanomolar range (IC50 values consistently <10 nM) against all P. vivax (Fig. 1B) and P. falciparum (Fig. 1C) isolates. NITD609 was also similar to artemisate in its ability to kill both mature trophozoite and immature P. vivax ring stages, in contrast to the trophozoite-stage-specific activity observed with chloroquine (17). Regardless of their initial developmental stages, NITD609-treated parasites displayed morphological hallmarks of dying parasites, including pycnotic nuclei and abnormal digestive vacuoles and nuclear segmentation. Collectively, in vitro and ex vivo data showed that spiroindolones were potent against the intraerythrocytic stages of the major human malaria pathogens P. falciparum and P. vivax, including a range of drug-resistant strains.

The rapid activity of artemisine derivatives against all Plasmodium asexual erythrocytic stages is a key feature of their therapeutic efficacy (6). To precisely determine which blood stages are most sensitive to the spiroindolones, and to evaluate the time required for these drugs to act, we conducted in vitro drug sensitivity assays with synchronized parasites treated at ring, trophozoite, and schizont stages for various durations (1, 2, 6, 12, and 24 hours) before removal of drug and continuation of culture for 24 hours in the presence of 100 nM hypoxanthine. At a high concentration of NITD609 (≥10 μM), all stages (rings, trophozoites, and schizonts) were similarly sensitive (fig. S1). However, at low concentrations (<1 or 10 ± IC50 value), schizonts were the most susceptible. We speculate that the target is present in all assexual blood stages but might be particularly vulnerable in schizonts. Although clearly faster-acting than the former first-line antimalarial pyrethroid artemisine, NITD609 did not inhibit parasite growth as quickly as the artemisinin derivative artemether (fig. S1). Strong growth inhibition (~90%) was achieved with artemether treatment at 8 nM for only 6 hours, whereas similar activity was achieved with NITD609 at 1.6 nM for 24 hours. Although at least 12 hours of continuous drug exposure was required to reduce by 90% the in...
Artemisinin from *Artemisia annua* or “wormwood”

- **From Wikipedia - Artemisinin** (pronounced /ɑrtiˈmɪsɨnɨn/), also known as qinghaosu, and its derivatives are a group of drugs that possess the most rapid action of all current drugs against *falciparum malaria*[^1]. Treatments containing an artemisinin derivative (artemisinin-combination therapies, ACTs) are now standard treatment worldwide for falciparum malaria. The starting compound, artemisinin (a sesquiterpene lactone), is isolated from the plant *Artemisia annua*, a herb described in Chinese traditional medicine, though it is usually chemically modified and combined with other medications.
Current Events

Australia’s crocodile – a protected species – now number more than 100,000
“Many of us feel discouraged by the avalanche of species extinctions and the wholesale habitat destruction occurring in the world today. But it is possible – and indeed necessary -- to feel challenged in order to find ways to stop the destruction (Orr 2007). Actions taken – or bypassed– during the next few decades will determine how many of the world’s species and natural areas will survive.”

from Primack (2010, p. 5-6)