Iron-TAML activators: highly successful mimics of peroxidase enzymes for green chemical applications

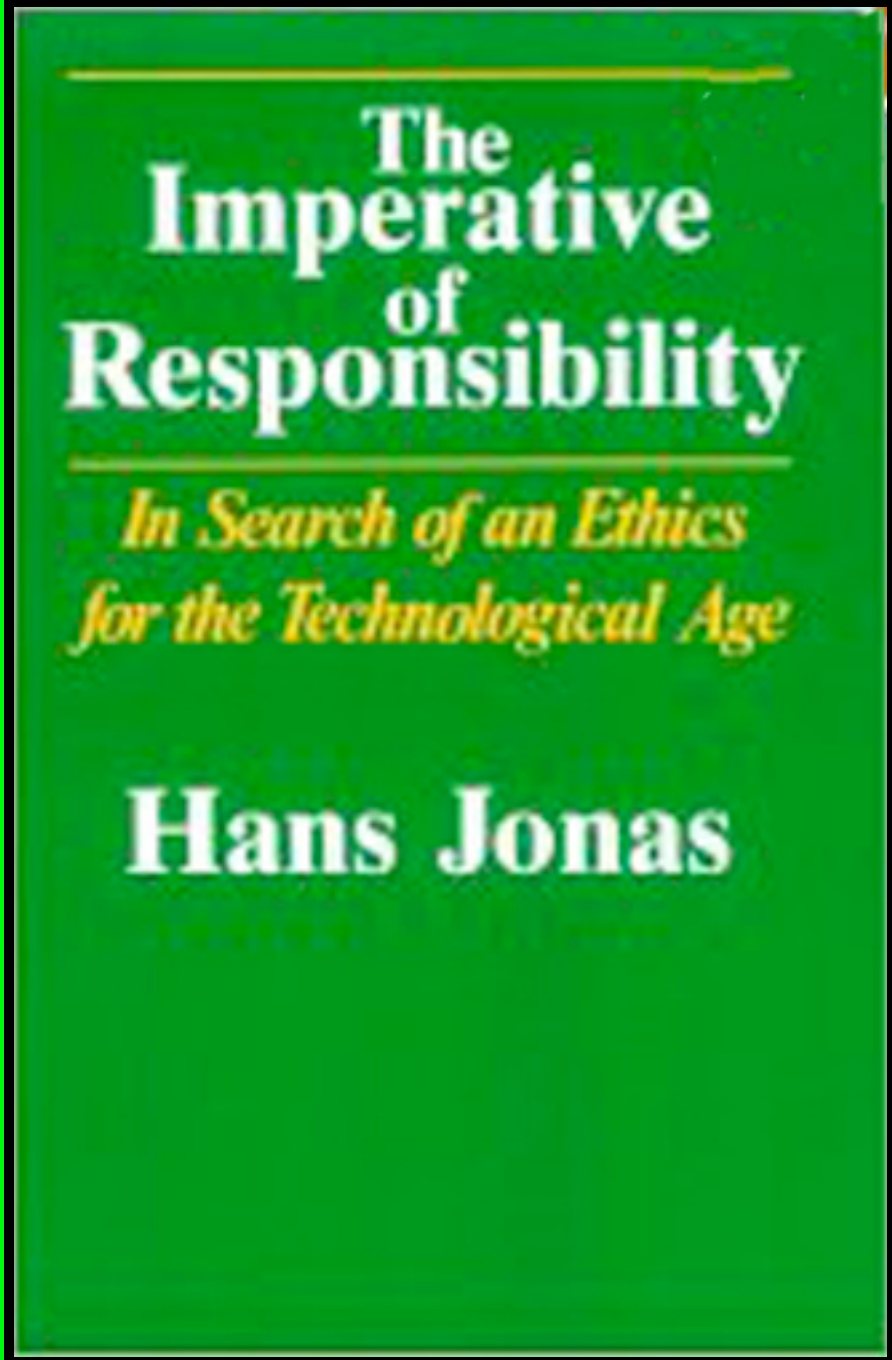
Terry Collins

Blueprints for Sustainable Infrastructure, University of Auckland, December 10, 2008

Great nations write their autobiographies in three manuscripts —the book of their deeds, the book of their words, and the book of their art. Not one of these books can be understood unless we read the two others; but of the three the only quite trustworthy one is the last.

John Ruskin, *St. Mark's Rest: The History of Venice,* Preface, 1887

In 2008, we can recognize that there is another manuscript; ***the book of their technologies.***



"... with certain development of our powers the nature of human action has changed, and … [given rise to] …***a whole new dimension of ethical relevance for which there is no precedent in the standards and canons of traditional ethics.***"

Safe Energy

New chemistry for solar-to-electrical or solar-to-chemical energy conversions

Renewable Feedstocks

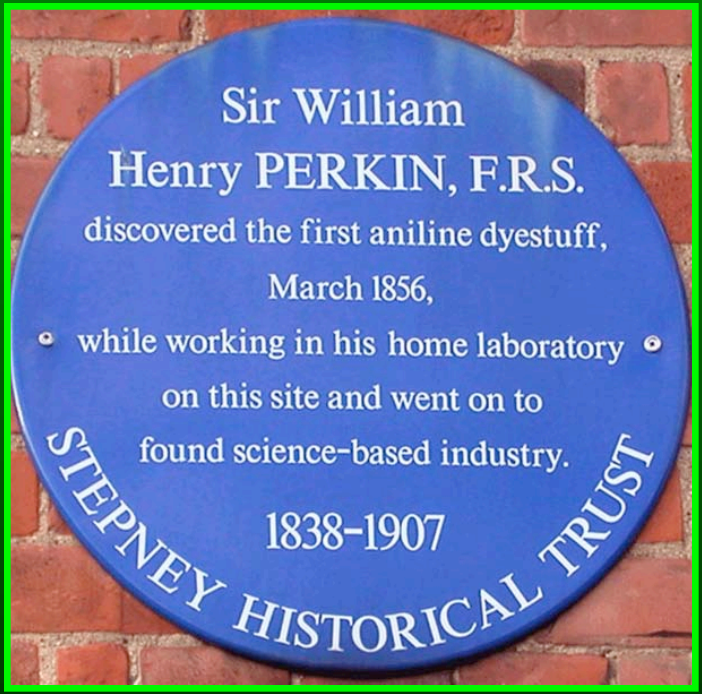
Economical feedstocks for chemical and polymer industries from plants

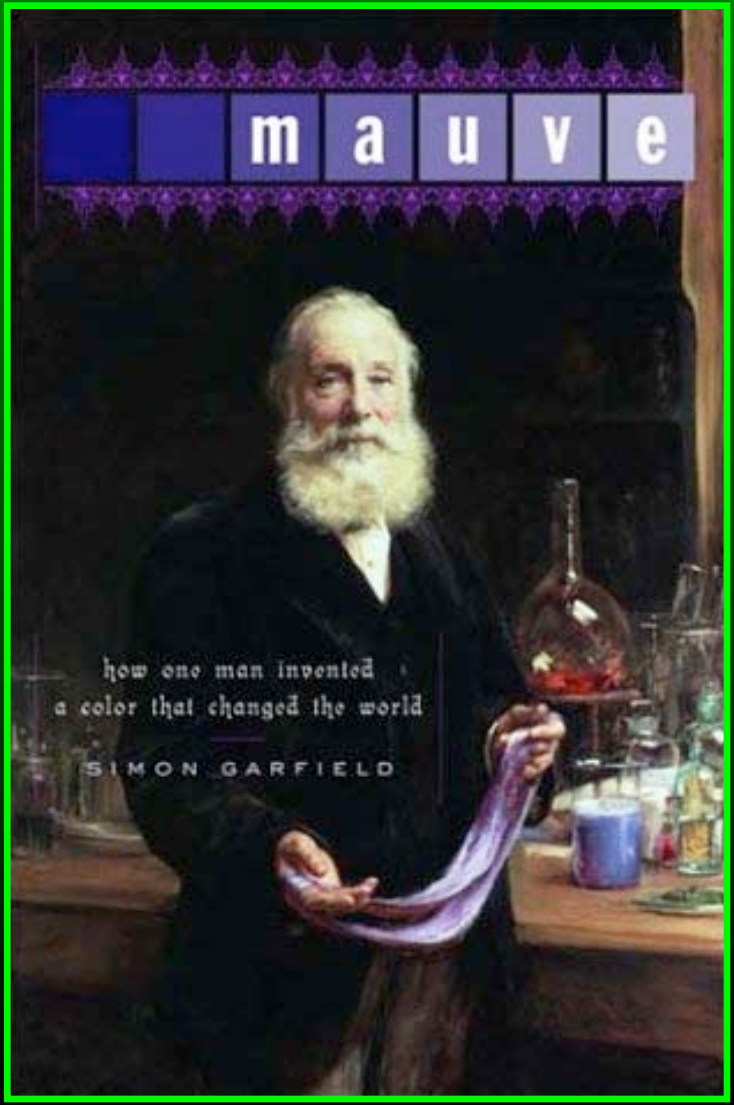
Chemical Focus Areas for Sustainable Technologies

Hazardous Substances

Move the elemental composition of technology closer to biochemistry; eliminate persistent environmentally mobile chemicals; reduce/eliminate developmental disruptors

Where, When and How Did the Chemical Enterprise Begin?



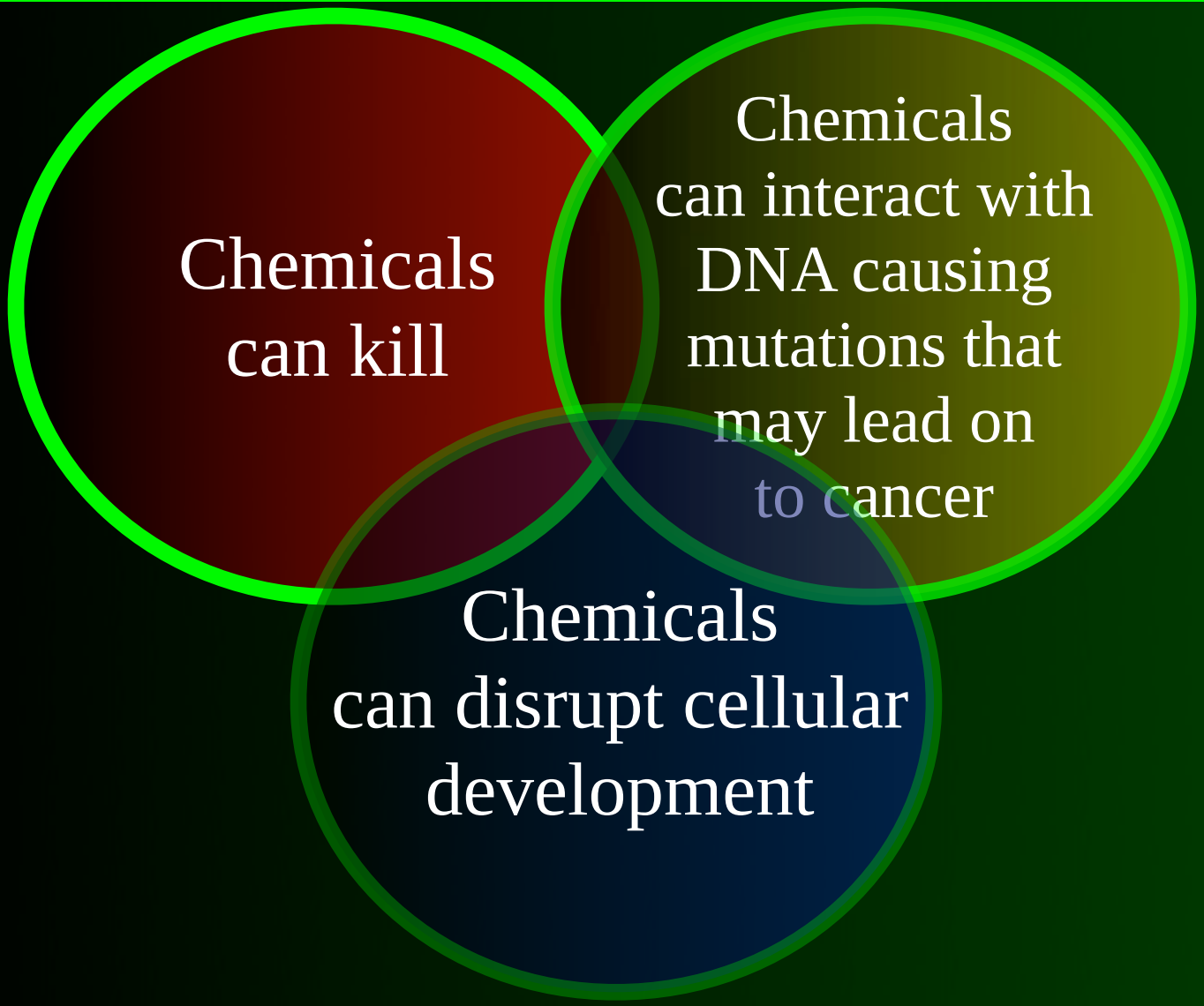


ca. 80,000 chemicals in commerce since, but only ca. 8,300 in wide use that are environmentally mobile

The underlying premise on which the chemical enterprise has been built assumes that any useful chemical, commercialized for anything other than drug purposes, will not have a profound impact on health (or the environment)

This premise is profoundly wrong!

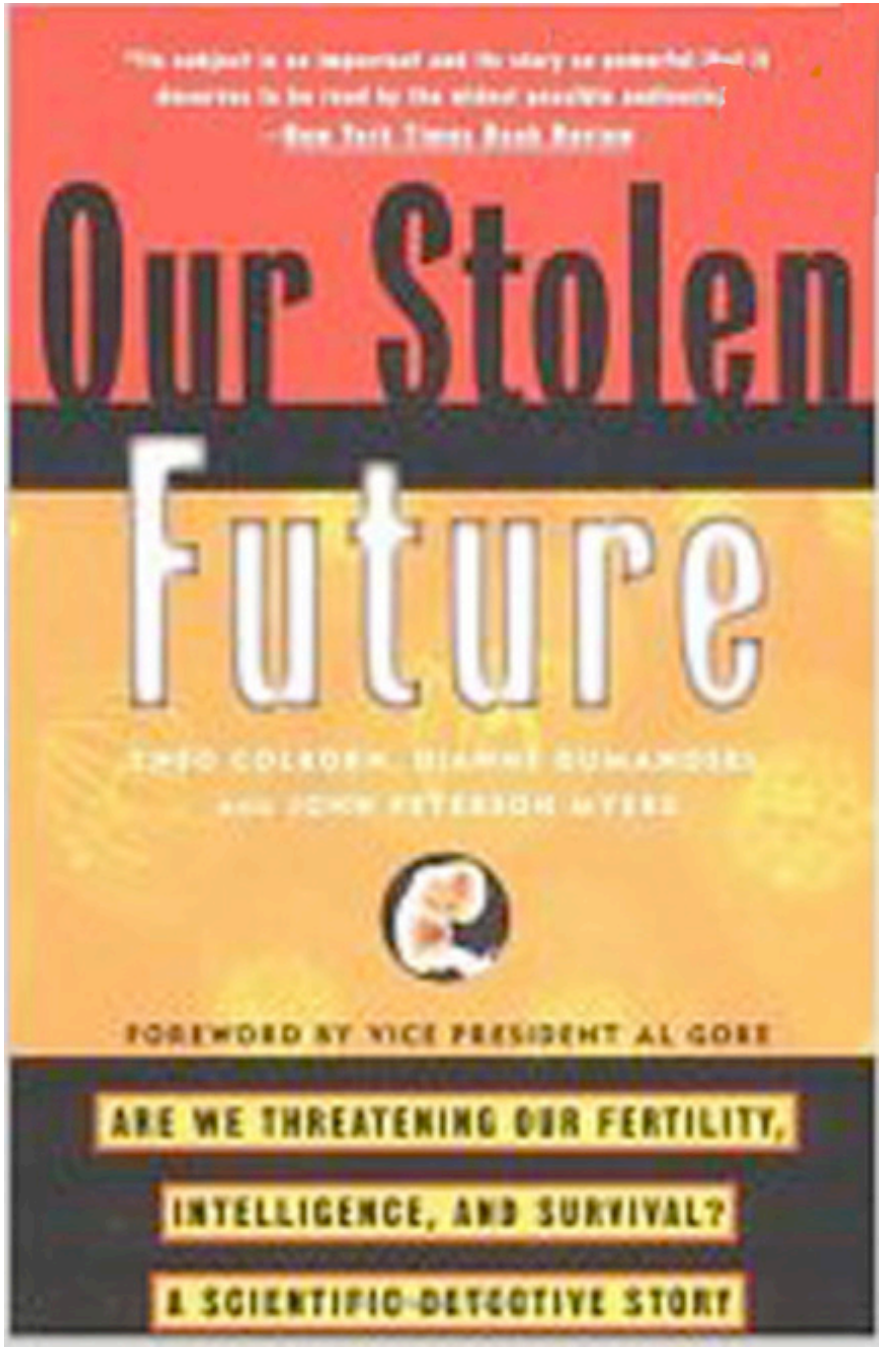
Catastrophic Toxicological Endpoints



Theo Colborn

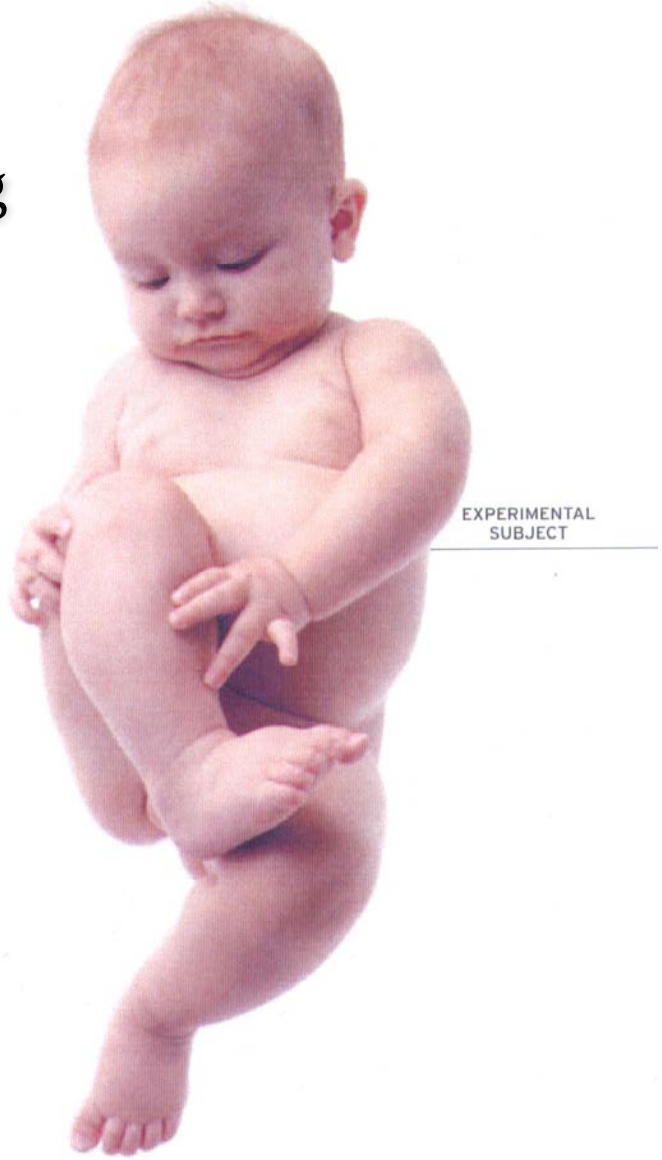
Diane Dumanoski

Pete Myers



The stakes of failing to address the so-called developmentally disrupting chemicals, especially endocrine disrupting chemical (EDCs) are incredibly high!

The vast majority of human beings —those yet to be born— need knowledgeable voices NOW for their rights from within the chemical enterprise



Pete Myers: www.ourstolen future.com

- **Decrease in anogenital distance among male infants with prenatal phthalate exposure,** Shanna Swan et al., *Environmental Health Perspectives* 2005, *113*, 1056—1061

- **Use of di(2-diethylhexyl)phthalate-containing medical products and urinary levels of mono(2-diethylhexyl)phthalate in neonatal intensive care units**, Howard Hu et al., *EHP*, ***2005***, 113, *1222*–1225

- **A population-level decline in serum testosterone levels in American men**, Travison, T.G., et al., *Journal of Clinical Endocrinology and Metabolism*, **2007**, *92*, 196–202.

- **DDT and Breast Cancer in Young Women: new data on the significance of age of exposure**, Barbara A. Cohn, et al., *EHP*, **2007**, *115*, 1406–1414; doi:10.1289-EHP.10260

- **Epigenetic Transgenerational Actions of Endocrine Disruptors and Male Fertility**, Mathew D. Anway et al., *Science* **2005**, *308*, 1466–1469

Pete Myers: www.ourstolen future.com

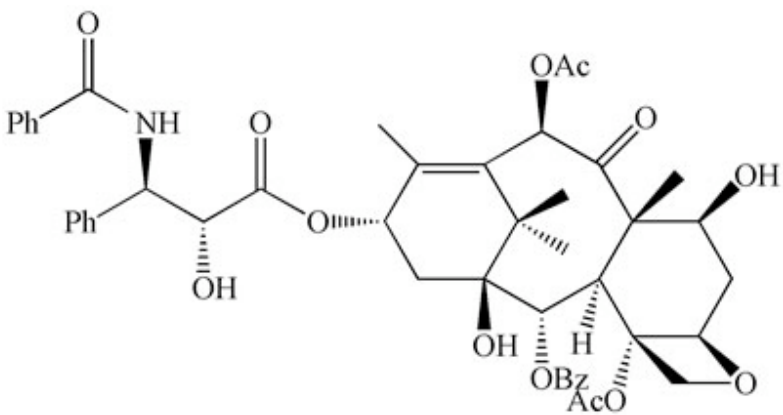
"Green Chemistry is the ***design*** of chemical products and processes that reduce or eliminate the use and generation of ***hazardous*** substances."

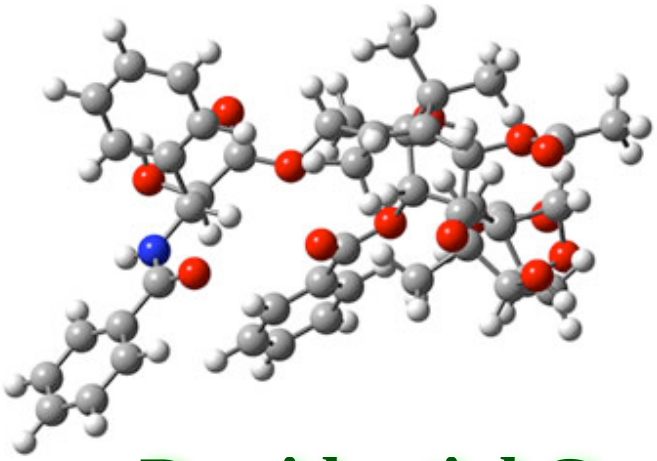
Paul Anastas

Sustainability Science and Green Chemistry Research and Education Challenges

Taxol (paclitaxel)

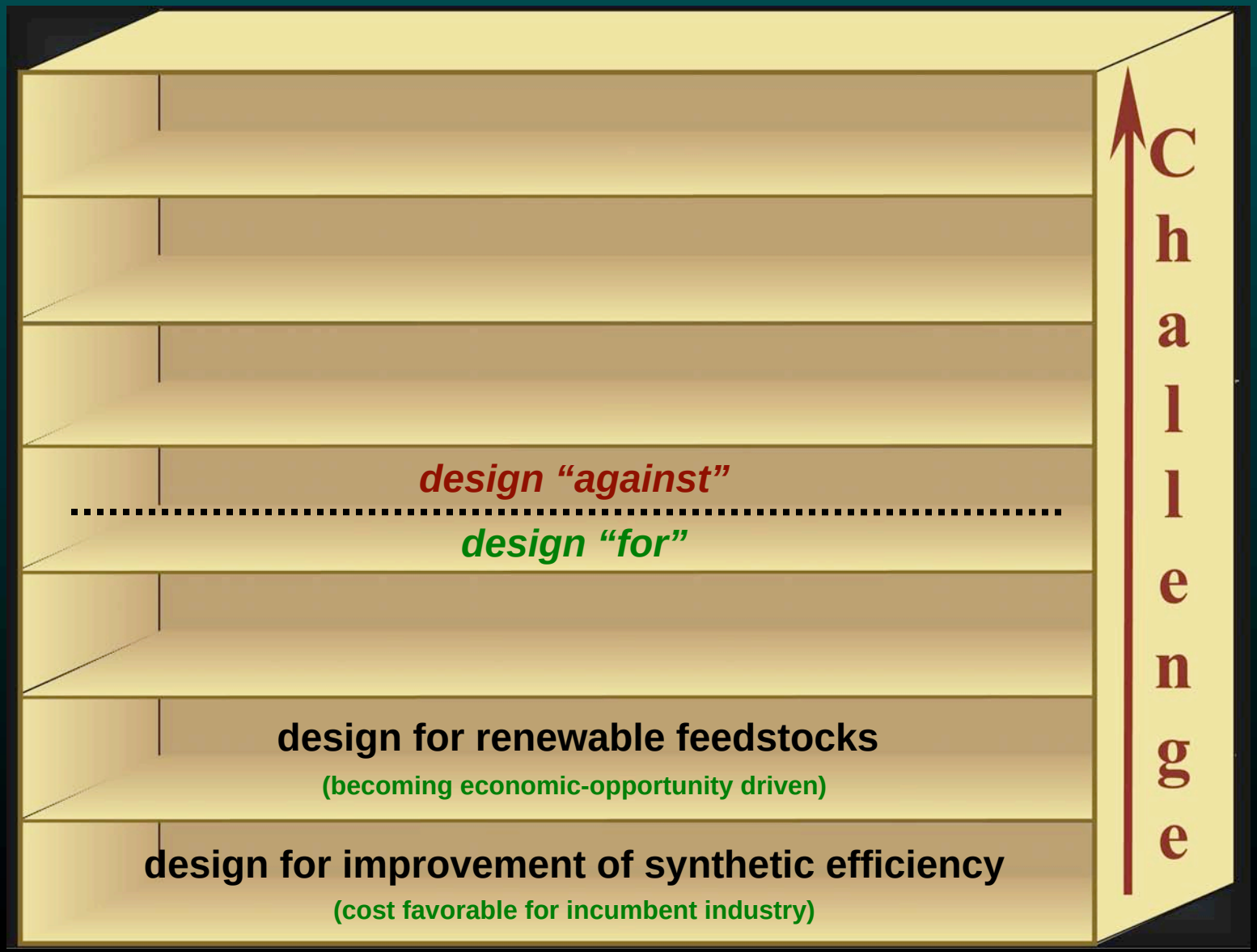
- potent against breast and ovarian cancer
- reported (1971) from the bark of Pacific yew tree, Taxus brevifolia, only ~0.0004% paclitaxel: ~$1 B/yr drug
- early preparations required stripping bark–killing trees (200 yrs to mature)
- published syntheses involve ca. 40 steps with an overall yields of ca. 2%
- Bristol-Myers Squibb developed sustainable process using PCF (Plant Cell Fermentation) based on twigs and leaves
- PCF has no chemical transformations: eliminates 6 intermediates. During first 5 yrs, PCF to eliminate 71K lbs hazardous chemicals and other materials, 10 solvents, and 6 drying steps, saving much energy





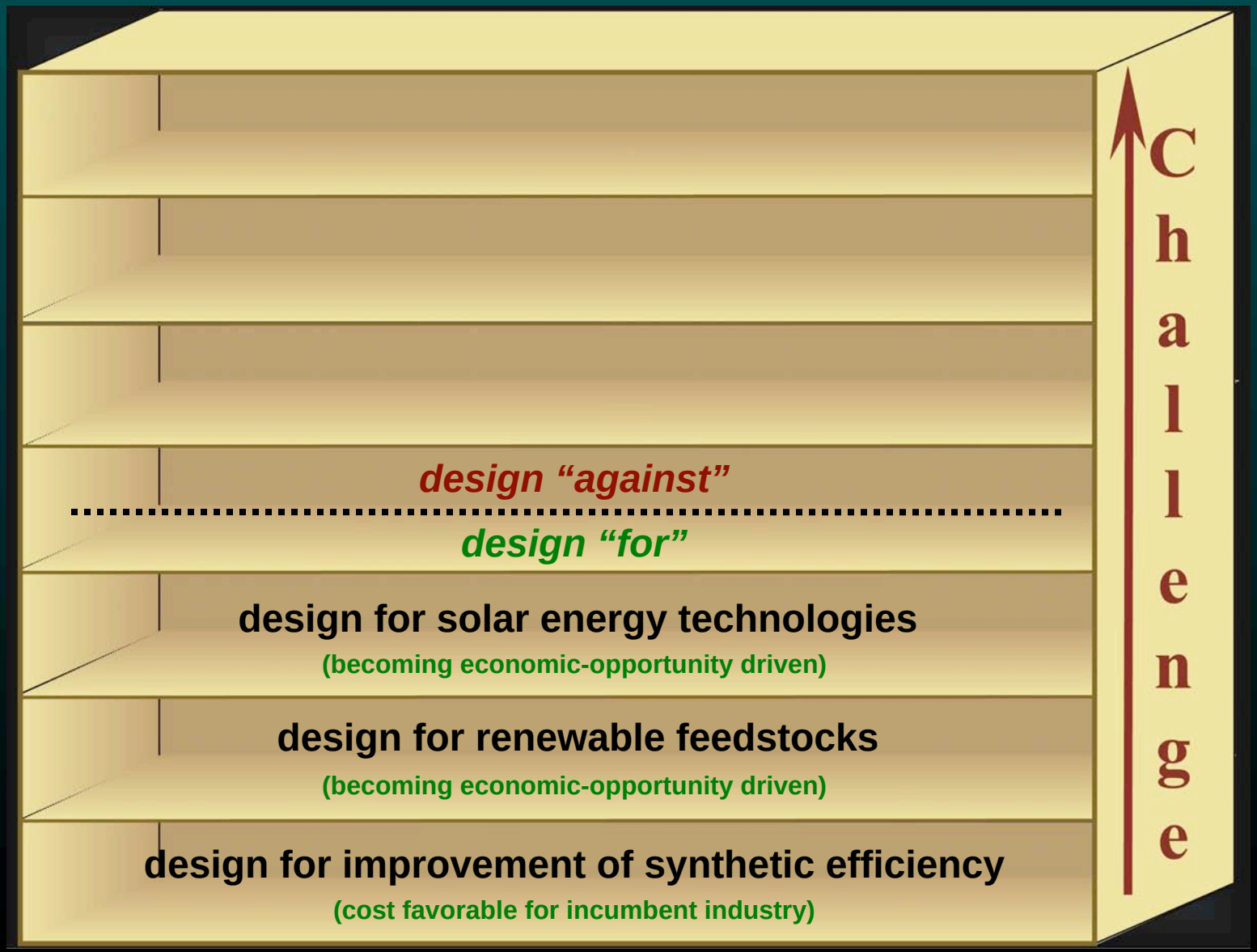
Presidential Green Chemistry Challenge Award

Sustainability Science and Green Chemistry Research and Education Challenges



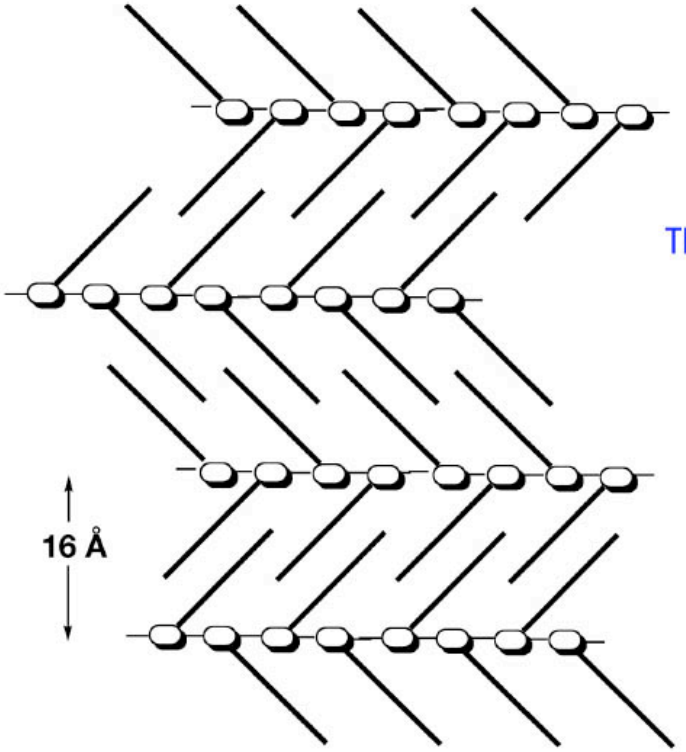

The Natureworks Polylactic Acid Plant in Blair, Nebraska
Presidential Green Chemistry Challenge Award

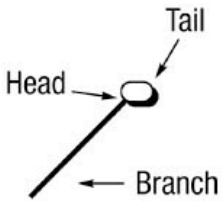
Sustainability Science and Green Chemistry Research and Education Challenges



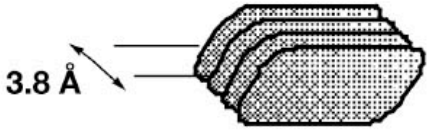
Plextronics, Inc. (CMU, spin-off company) has produced regioregular polythiophene that now holds the record for polymer-based photovoltaic efficiency (>5.9%)

Self-Assembled Conducting Polymers from Regioregular Polythiophenes





Thiophene ring with chemical branch



stacked polythiophenes

McCullough JACS 1993, 115, 4910

Sustainability Science and Green Chemistry Research and Education Challenges

design against endocrine disruptors

(anything beyond a tentative success for green chemistry requires major victories here)

design against persistent and pseudo-persistent environmentally mobile compounds

(pesticides, polymers, their components and their degradation products, ...)

design against toxic elements

(batteries, fluorescent lights, soft metal chalcogenides, agricultural As, ...)

design "against"

.....

design "for"

design for solar energy technologies

(becoming economic-opportunity driven)

design for renewable feedstocks

(becoming economic-opportunity driven)

design for improvement of synthetic efficiency

(cost favorable for incumbent industry)

Challenge

The *Institute for Green Science* at CMU is a research, education and development center working to build sustainability studies and the green economy.

Research Training

Contribute to training the next generation of green science leaders

Education

Create free web-based green chemistry curricula for use throughout the world

Research Leadership

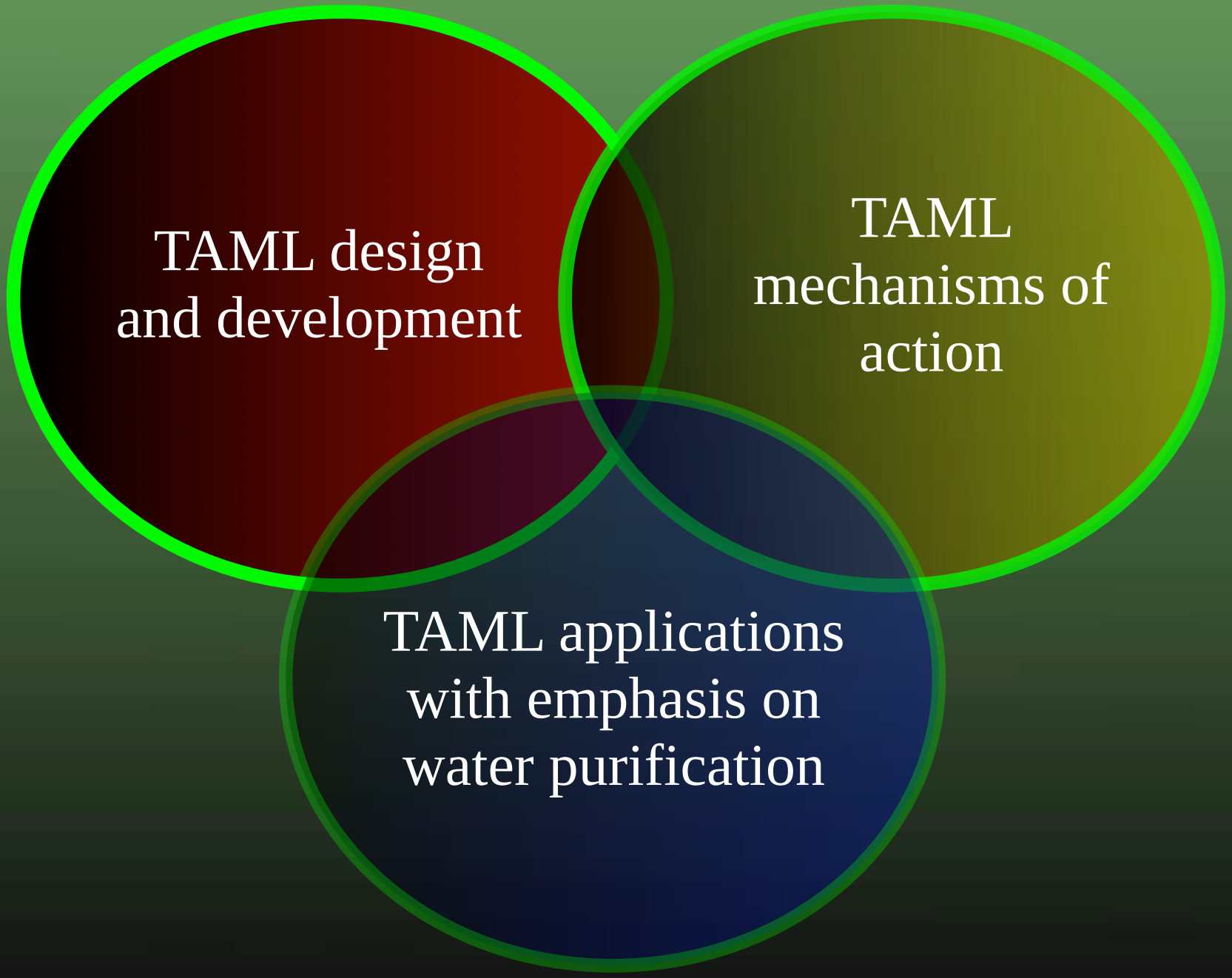
Solve real-world problems through GC research and development

Thank you Heinz Endowments and Johnson Family Foundation!

Conceptualized Website

- Graphic Design
- Navigational Design
- Content

- Interactive Video
- Audio
- PowerPoints
- Notebook
- Learning Tools
- Course Management Tools
- Results Based (real learning)
- Real world applications

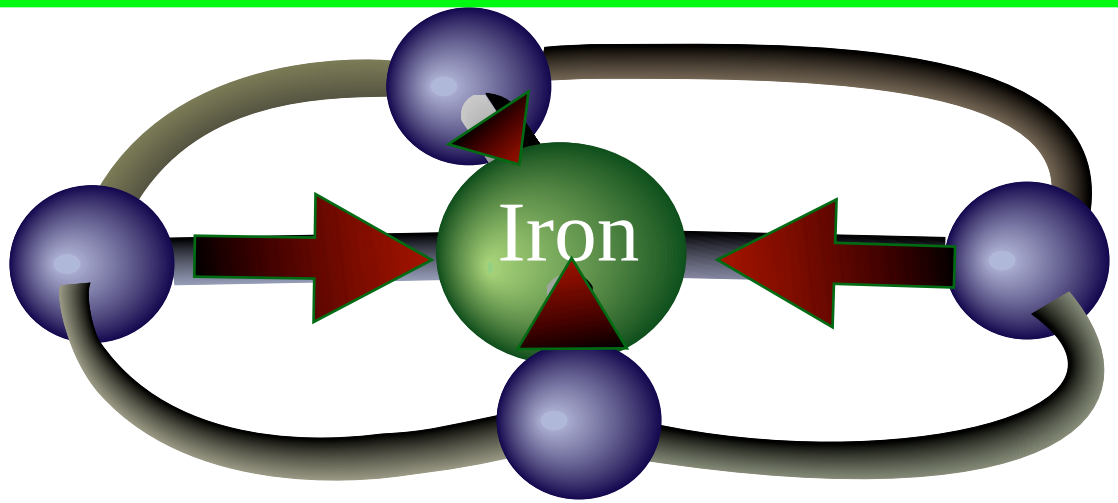

TAML design and development
TAML mechanisms of action
TAML applications with emphasis on water purification

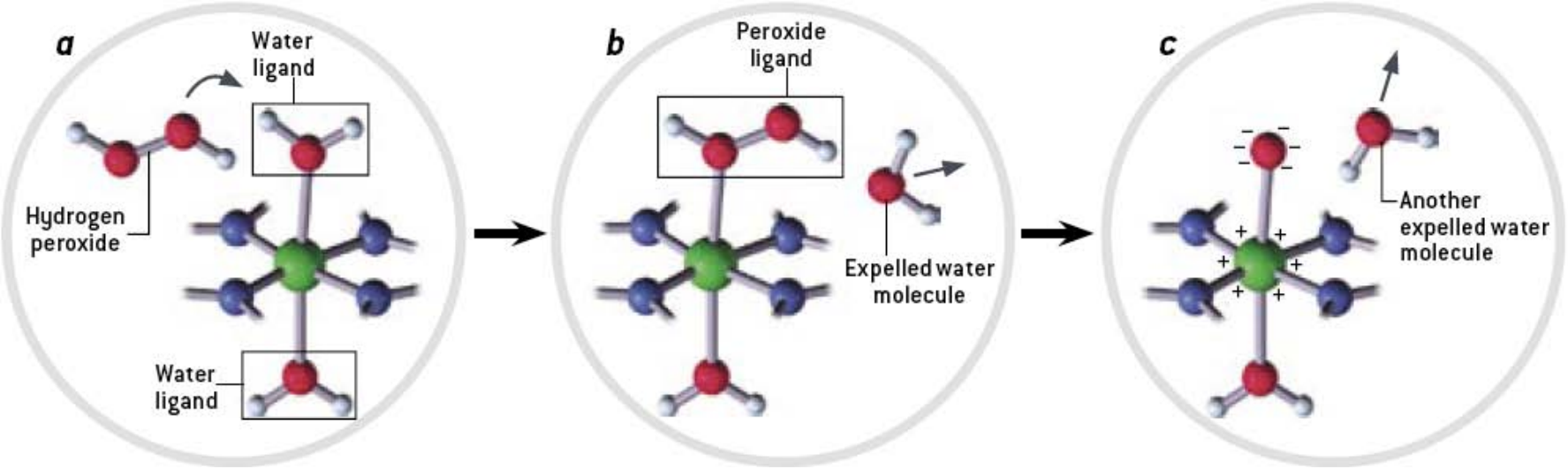
Designing ligands for oxidizing complexes

Collins, T. *Accounts Chem. Res.*, 1994, *27*, 279–285

Little green molecules

Collins, T.; Walter, C.
Scientific American, March 2006, 82–90





Designing ligands for oxidizing complexes

Collins, T. *Accounts Chem. Res.*, 1994, *27*, 279–285

Little green molecules

Collins, T.; Walter, C.
Scientific American, March 2006, 82–90

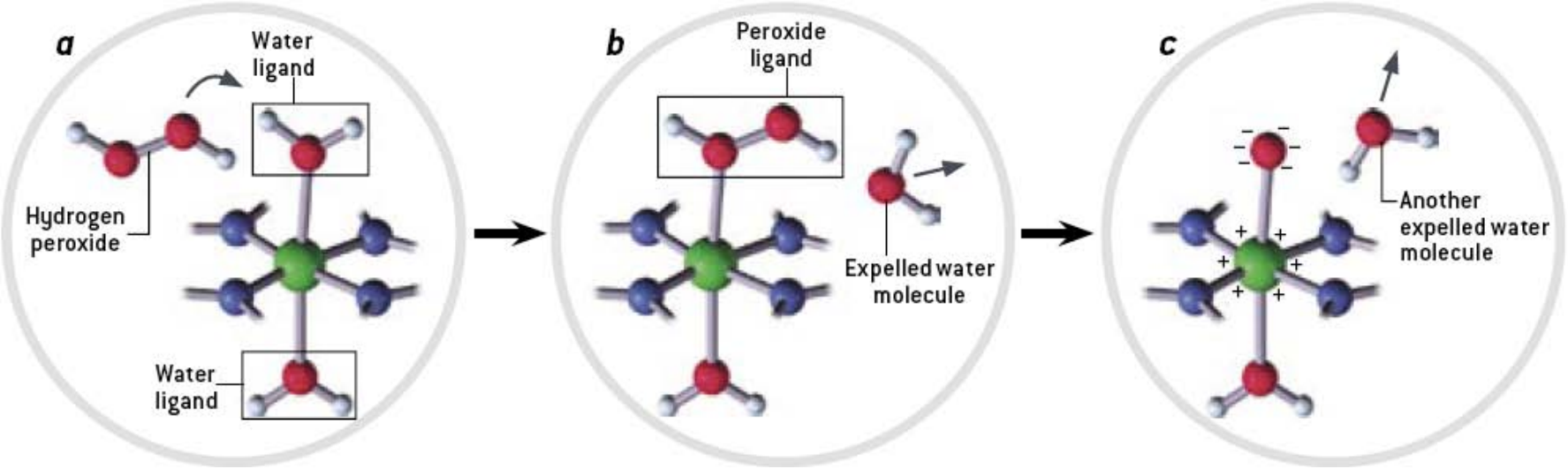
Catalyst Design Protocol

1. Design ligand system thought to have correct electronic and stability properties and make complex

2. Oxidatively and hydrolytically stress complex until system decays

3. Analyze ligand degradation products which we found reveals the most oxidatively vulnerable site

4. Use chemical intuition to make vulnerable site stronger



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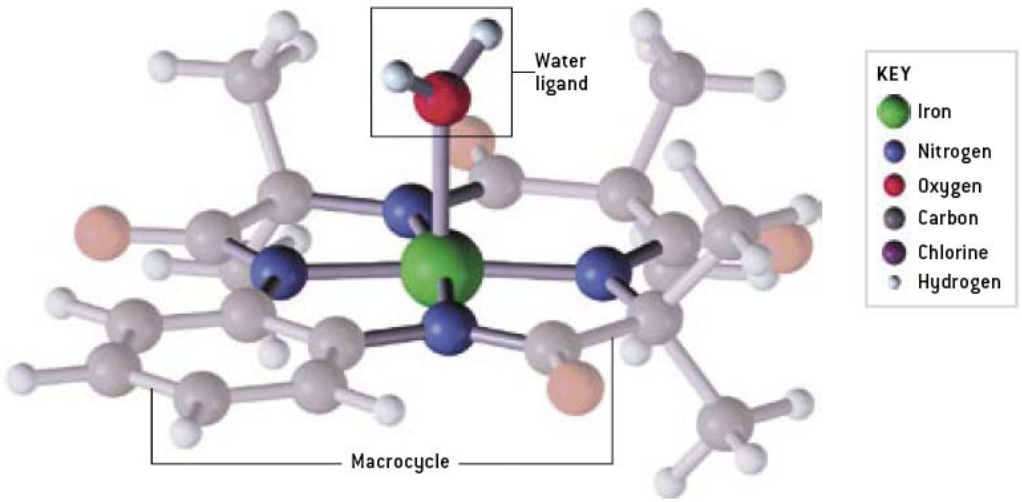
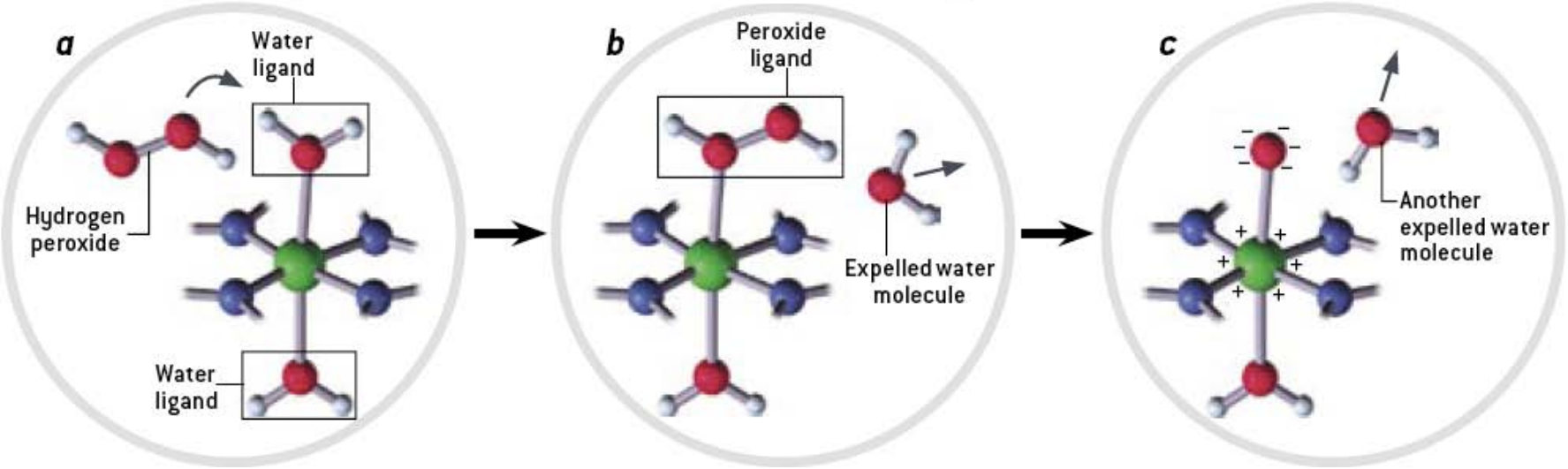
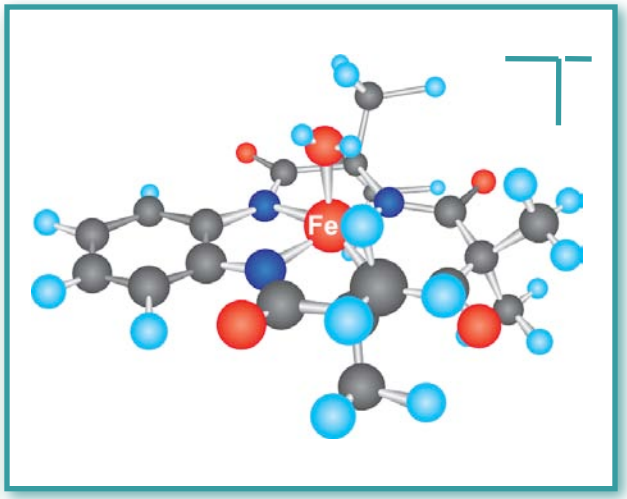




TAML® activators allow hydrogen peroxide to replace chlorine and heavy metals in oxidation technologies



Water Cleaning
EDCs, dye effluents, chlorinated pollutants, phenols, BPA, …

Biological Warfare
Rapid destruction of anthrax-like spores

Chemical Warfare
rapid CWAs/toxic residuals destruction

Agricultural Pollution
removal of estrogens from water

Pharmaceuticals Decontamination
trace pharmaceuticals removed from water

Pesticides Decontamination
thiophosphate & organochlorine pesticides destroyed

Aromatic Hydrocarbons
benzene, toluene, ethylbenzene, xylenes

Laundry
dye transfer inhibition, stain removal

Explosives Site Cleaning
all the problem compounds of the TNT explosives

Pulp and Paper
smells, organochlorine & color abatement, pulp bleaching

Hospital Disinfection
rapid killing of Clostridia (e.g., *C. perfringens as C. difficile surrogate)*

Drinking Water Disinfection
safer drinking water free of chlorinated disinfection byproducts

Petroleum Refining
removal of sulfur from diesel & gasoline

Iron-TAML/
peroxide
gives us
“fire-in-water”

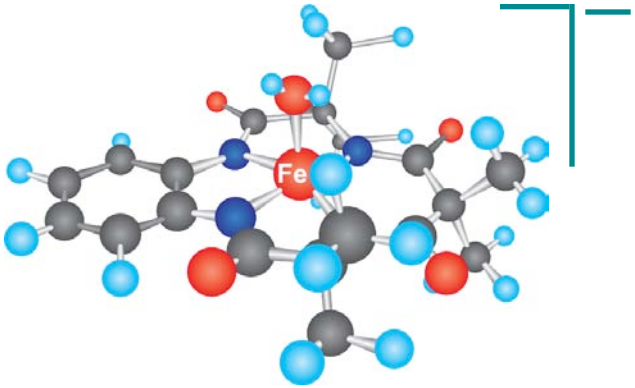
GreenOx Catalysts, Inc.

Carnegie Mellon University spin-off company commercializing TAML® activators in the water, waste-stream and environmental cleanup areas

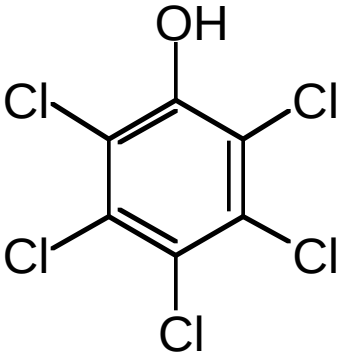
Rapid total destruction of chlorophenol pollutants by activated hydrogen peroxide

Science, 2002, *296*, 326–328

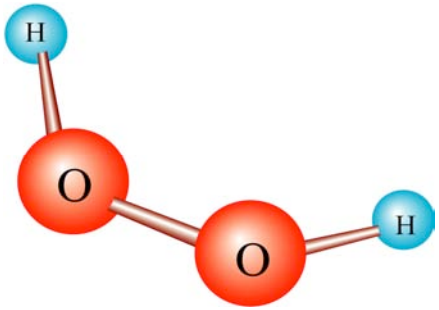
Gupta, S. S., M. Stadler,
C. A. Noser, A. Ghosh,
Brad Steinhoff,
D. Lenoir, C. P. Horwitz,
K.-W. Schramm, T. J. Collins,



1 equivalent
(7 μM)



715 equivalents
(5 mM)



100,000 equivalents
(0.5 M)

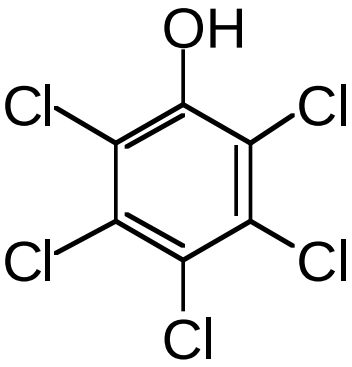
Reaction Conditions

- pH 10, carbonate buffer—base dissolves PCP & achieves highest rate
- 25 °C, 9 minutes reaction time—quench with acid
- 9 equivalents of H_2O_2 stoichiometric for complete mineralization

Fate of the pentachlorophenol

No dioxins within limits of experimental detection

Fe-TAML activators low toxicity

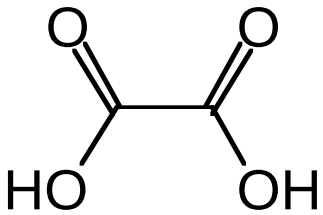


Cl^-

87±4% Cl

CO_2 + CO

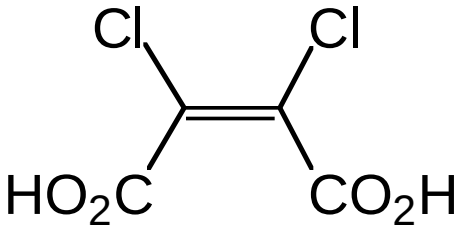
45±3% C



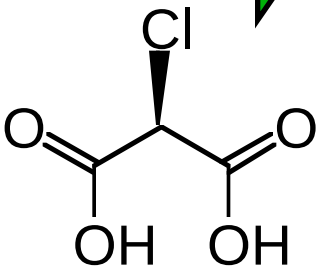
23±1% C

FOUND

- 91±5% C
- 99±4% Cl



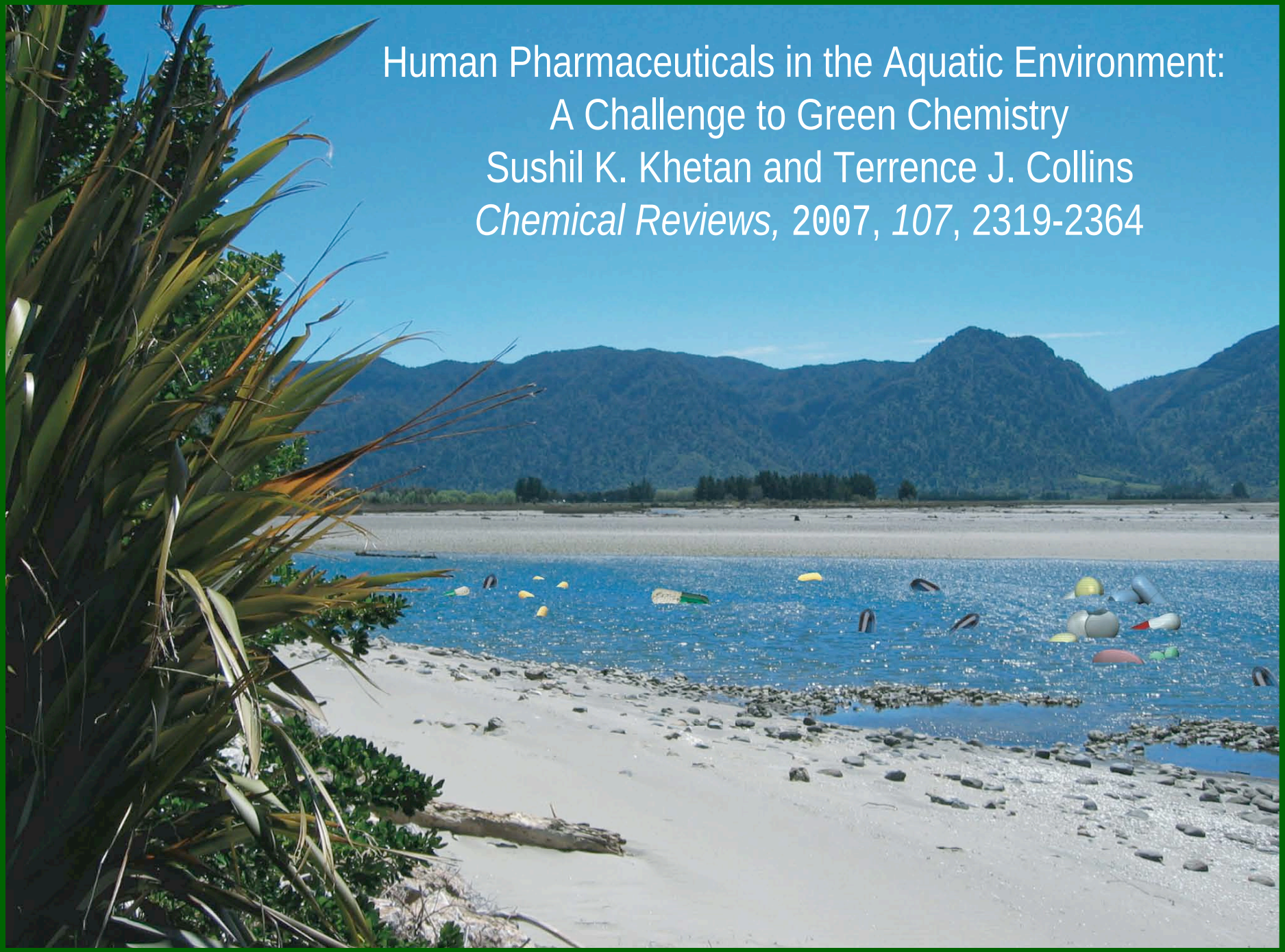
17±1% C



6% C

Single rapid ambient treatment

pH 7 removes RX



Human Pharmaceuticals in the Aquatic Environment: A Challenge to Green Chemistry

Sushil K. Khetan and Terrence J. Collins

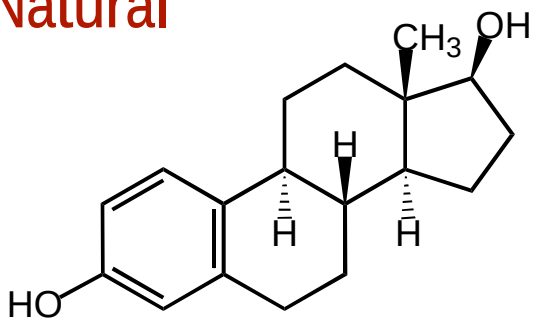
Chemical Reviews, 2007, *107*, 2319-2364

Destruction of estrogens using Fe^{III}-TAML/peroxide catalysis

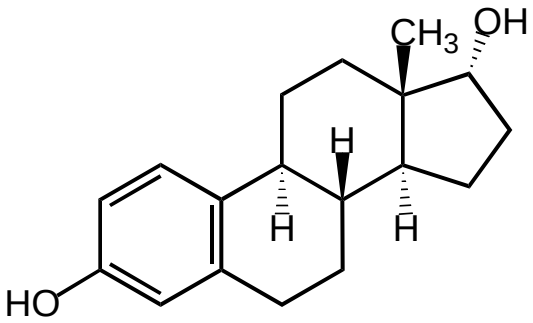
ES&T, 2008, *42* (4), 1296–1300
A "most accessed" EST paper—1st quarter 2008

Shappell, N. W., M. Vrabel, P. Madsen, Jr., G. Harrington, L. O. Billey, H. Hakk, G. Larsen, C. P. Horwitz, E. Beach, K. Ro, P. G. Hunt, T. J. Collins

Natural

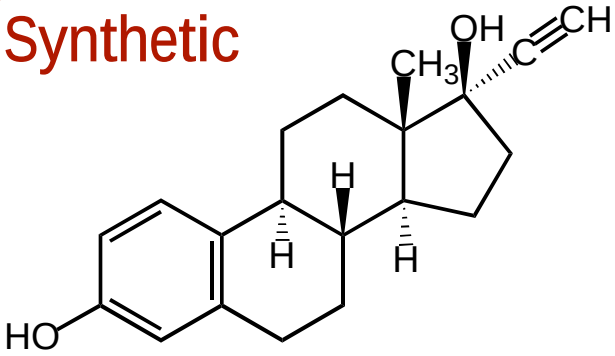


17**β**-estradiol (E_2)
Most potent natural estrogen: 1X



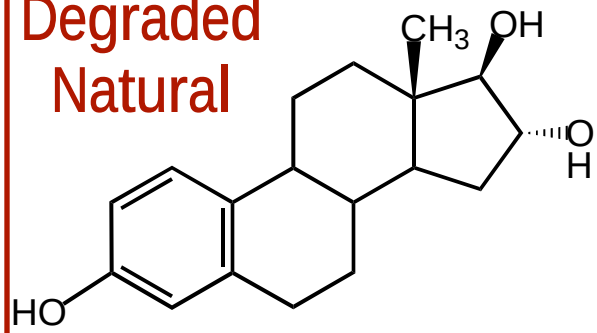
17**α**-estradiol (E_2)
0.1X

Synthetic

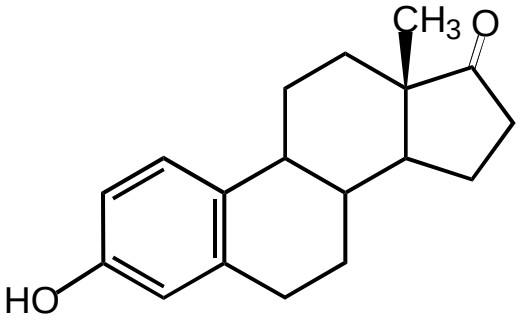


ethinylestradiol (EE_2)
1X

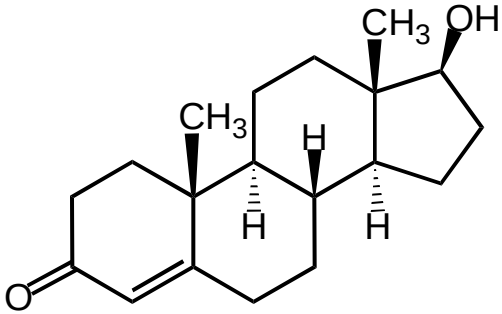
Degraded Natural



estriol (E_3)
0.1X



estrone (E_1)
0.01X



testosterone

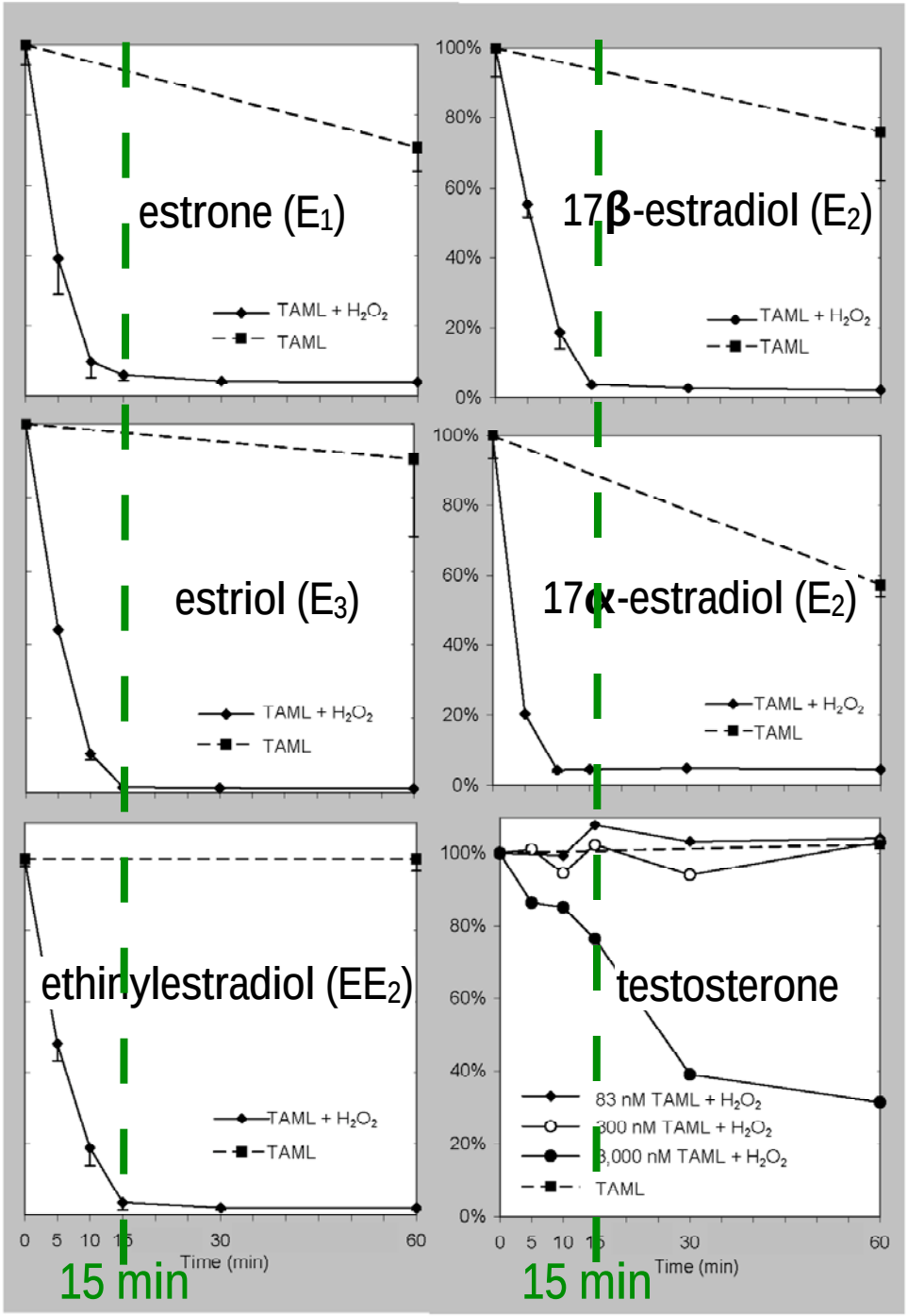
Conditions

- Steroid = 80 μM
- FeB* = 83 nM
- H_2O_2 = 4 mM

  ca. mineralization requirement, e.g., EE_2 requires 38 H_2O_2s or 3 mM

- pH = 8, 10
- Catalase termination

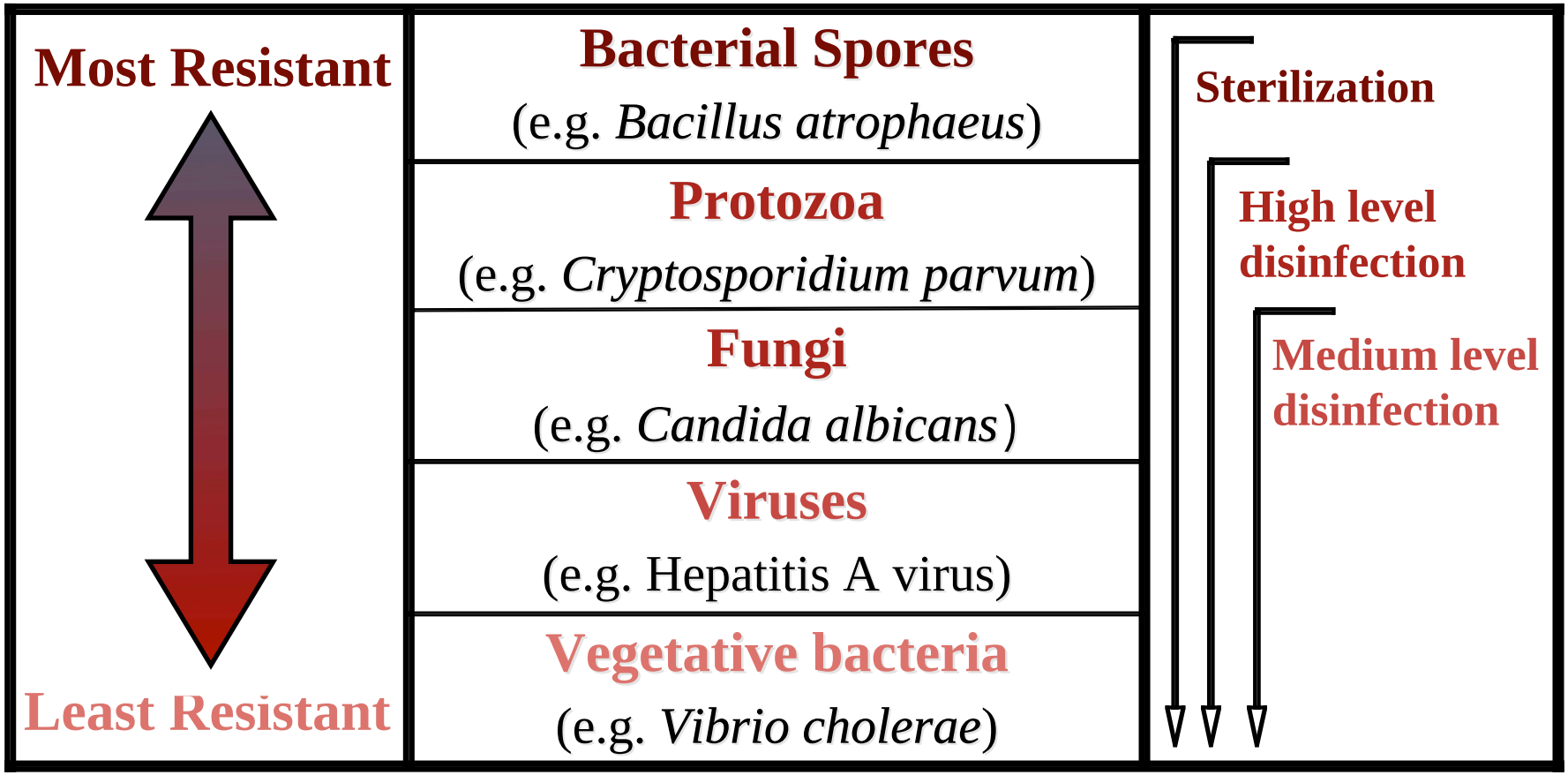
Incubations with a municipal wastewater sample (obtained prior to chlorination) resulted in >99% removal of estradiol as assessed by ELISA.

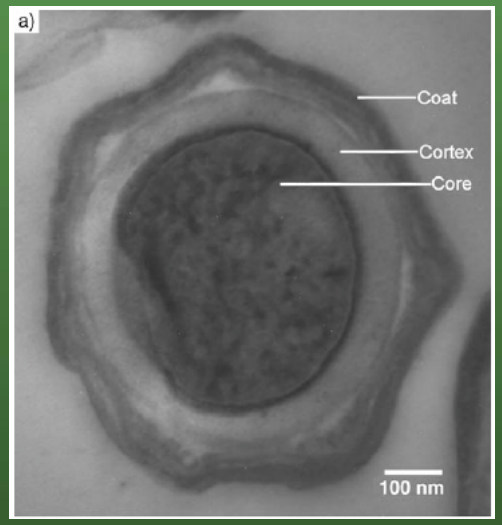


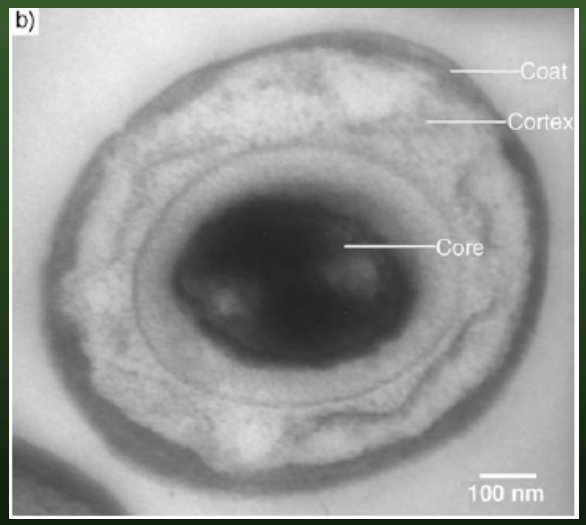
Green oxidation catalysis for rapid deactivation of bacterial spores

Angew. Chem. Int. Edn. 2006, *45*, 3974–3977

Banerjee, D., A. L. Markley,
T. Yano, A. Ghosh,
P. B. Berget, E. G. Minkley Jr.,
S. K. Khetan, T. J. Collins,



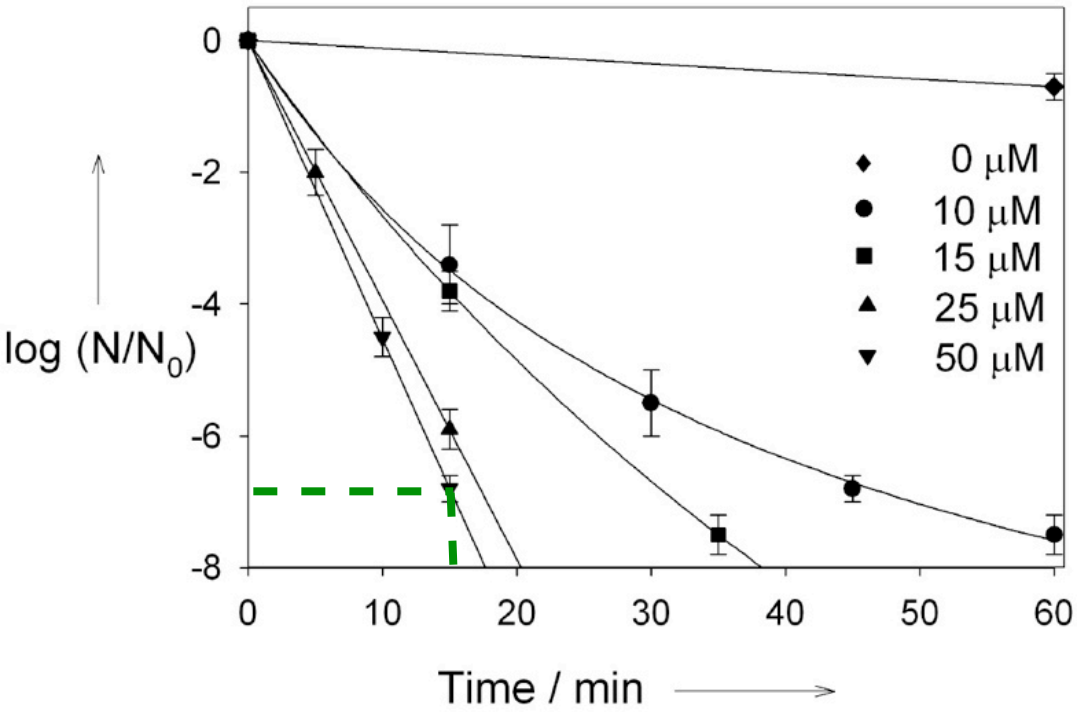




TEM images of *B. atrophaeus* spores **a)** before and, **b)** after treatment with Fe-TAML/TBHP (10 µM/0.5 M) and CTAB (0.03%) for 1 h

Conditions

- **start ca. 10^8 CFU/mL**
- **0.5 M TBHP**
- **0.03% CTAB (except for 50 µM Fe-TAML, [CTAB] = 0.05%)**



Pittsburgh in 1936

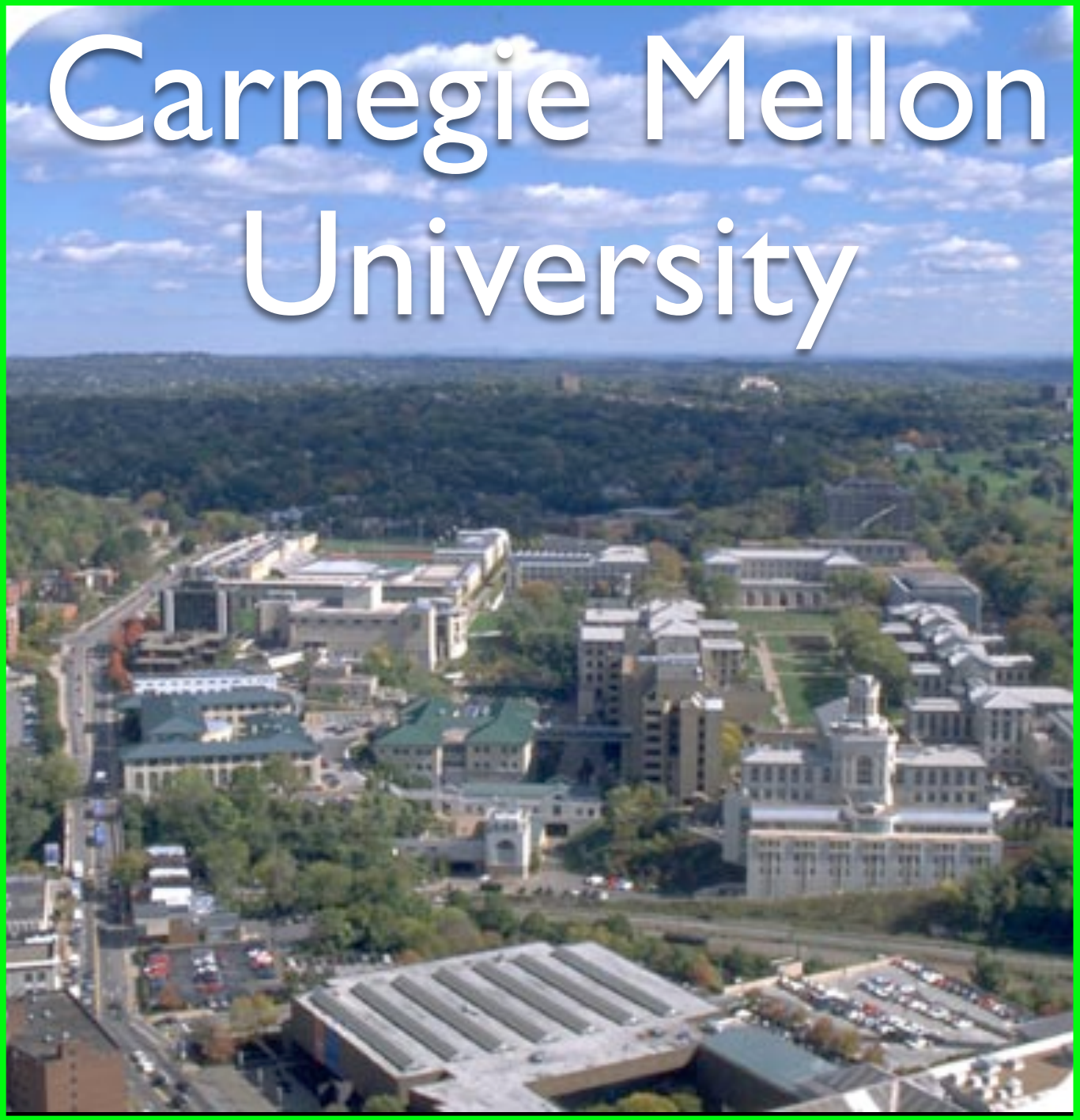
Photograph by Margaret Bourke-White, courtesy Life magazine.

THIS WAS PITTSBURGH—as Margaret Bourke-White saw it when she flew over the city in 1936 to photograph it for a new picture magazine which was launched in that year—*Life*.

Modern Pittsburgh:

an icon of our ability to clean up

Carnegie Mellon University



Carnegie Mellon
Institute for Green Science

Environmentally Safe Technologies

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