Soil on (a little bit of)Drugs

Evidence against linear dose-response models and the implications for sustainability in agroecysostems

November 13, 2013

Stephanie DeVries

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Outline

- Experimental Overview
- Antibiotics in the environment
- Dose-Response Models
- Methods
- Results
- Conclusions
- Future Directions

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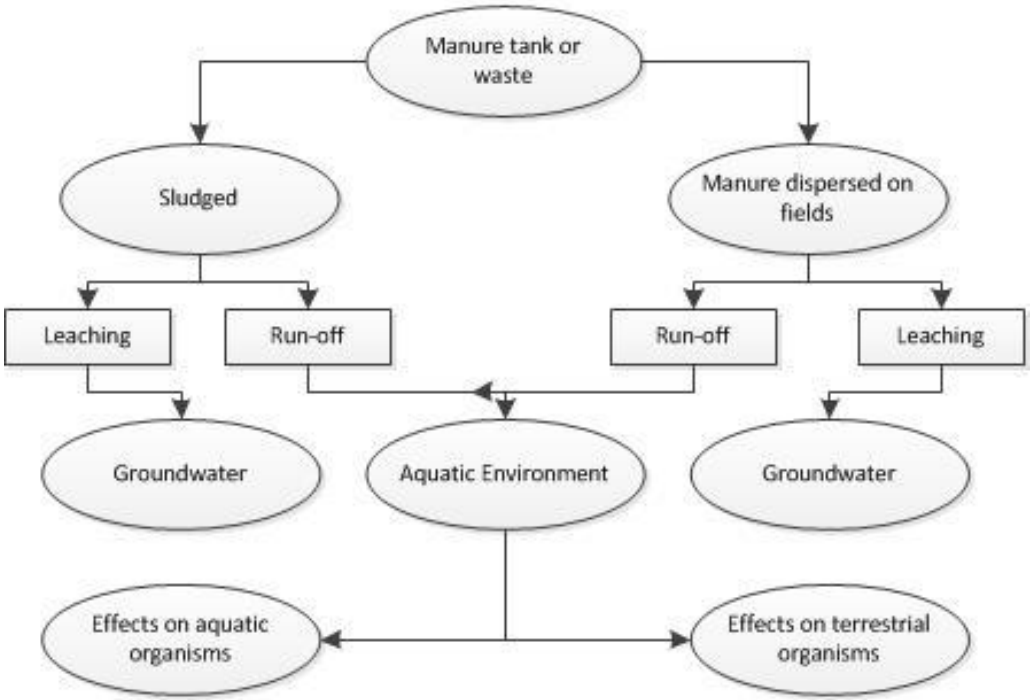
Antibiotics in the Environment: Pathways



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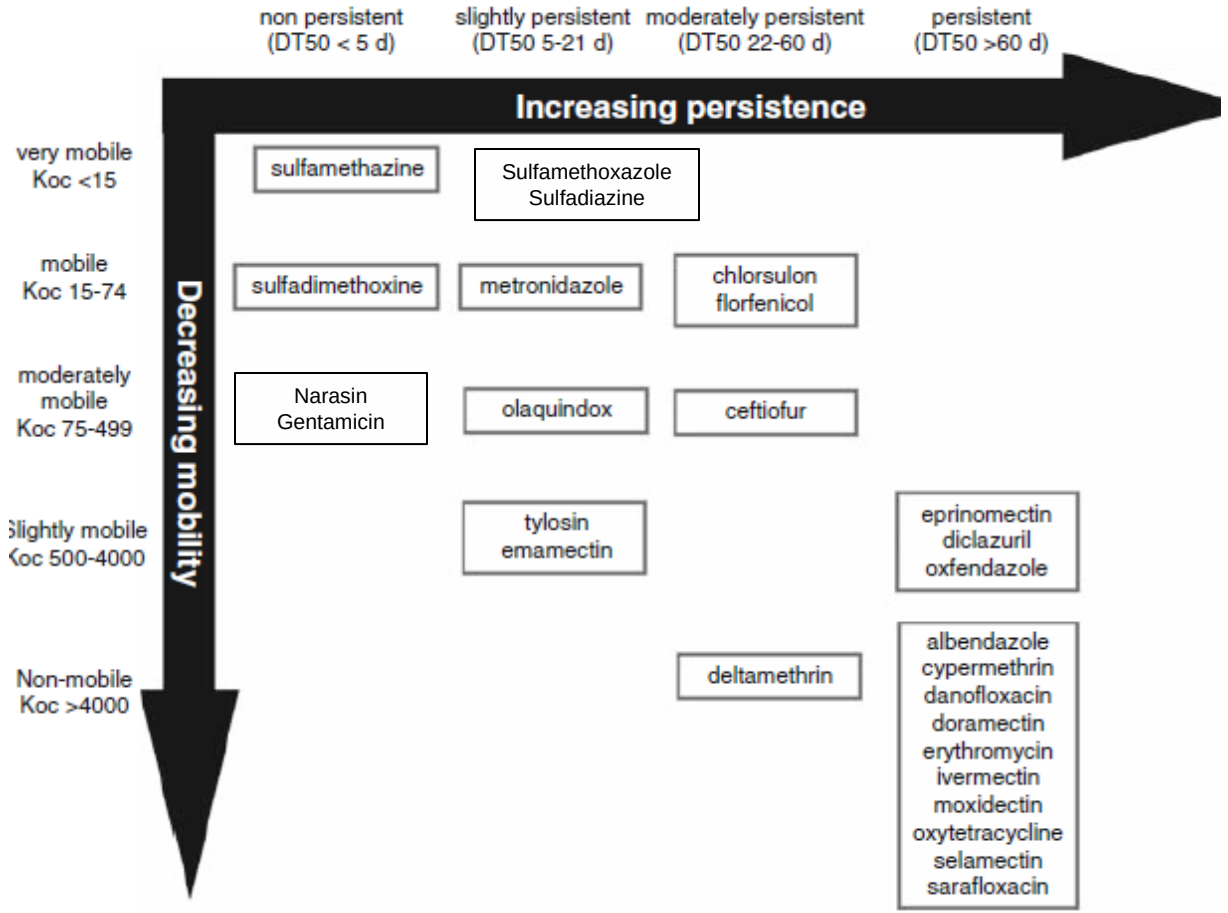
Antibiotics in the Environment:



Distribution of reported mobility (based on sorption coefficients) and persistence data for veterinary medicinal products (adapted from Boxall, 2010)

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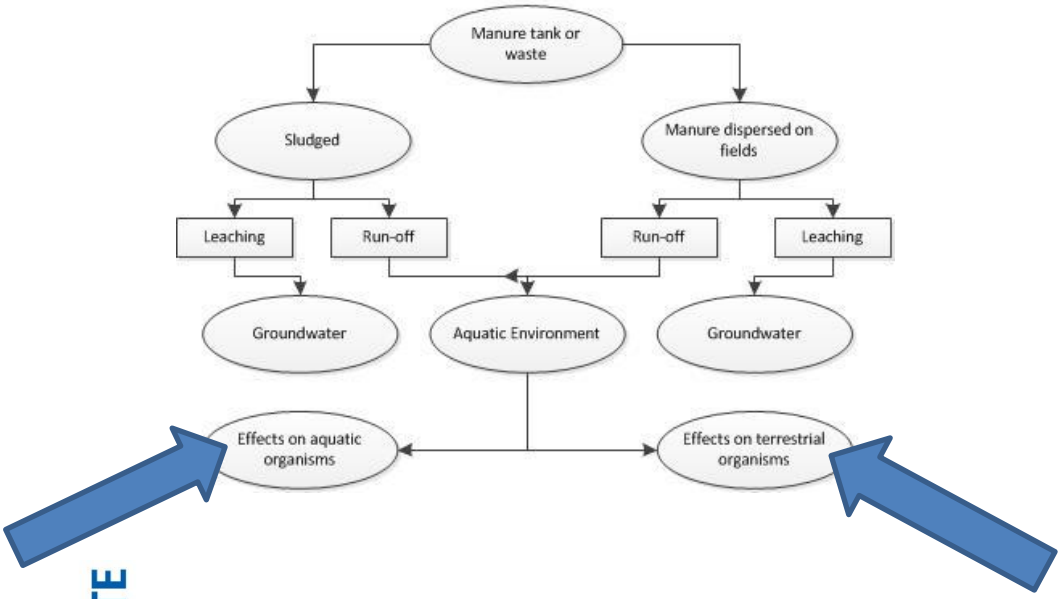
Antibiotics in the Environment: Risks



Potential risks include:

- Changes to biogeochemical cycling in soil and sediment.
  - Modified carbon mineralization
  - Modified nitrogen cycle, including production and removal of pollutant N species
  - Modified mineralization of parent bedrock (formation of soils).
- Development of antibiotic resistance that may spread via ground or surface water.

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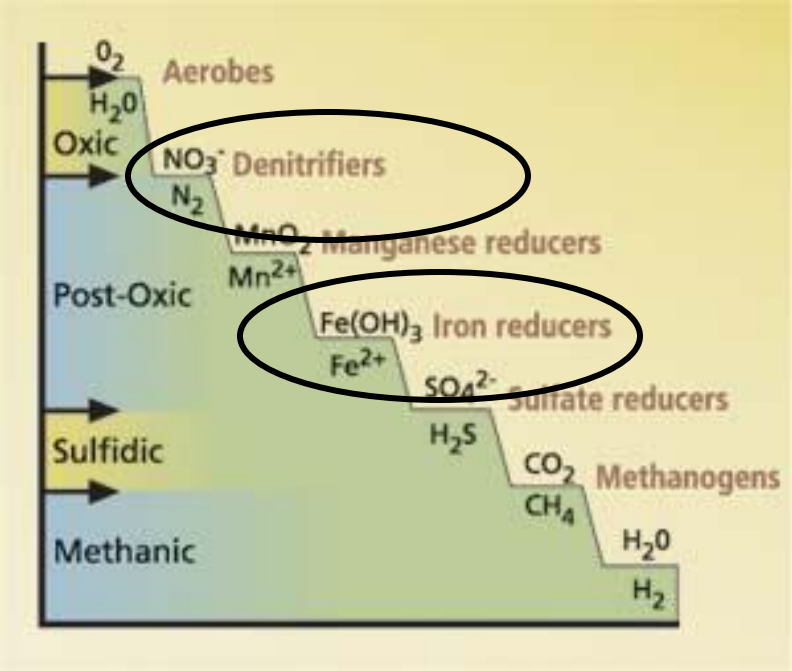
Antibiotics in the Environment: Consequences



http://ucanr.edu/repository/cao/landingpage.cfm?article=ca.v057n02p55&fulltext=yes

- Most investigations conducted to date have focused on acute toxicity tests to assess the risk of biogeochemical change in response to antibiotics.
- A few have emerged in the last 2-3 years in which environmentally relevant concentrations (µg – mg/kg_{soil}) were tested. Most report that there is no significant change or show modest inhibition of biogeochemical activity.

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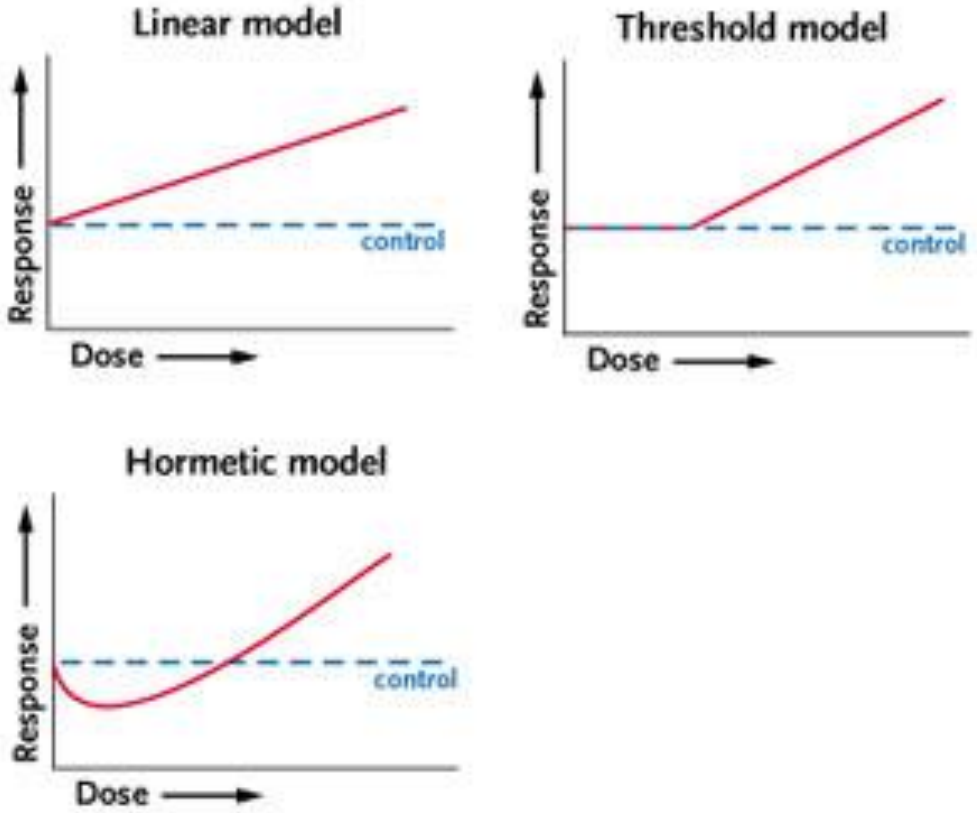
Antibiotics in the Environment: Consequences

- What happens in the months after application as the residual antibiotics degrade or are transported out of the soil?
  - Traditional dose-response models predict that there will be no observable effect, particularly if the dosages fall below those already tested as a result of transport and degradation.
  - If the response is hormetic or non-linear, the response might be quite significant.
- The primary objective of this research is to determine whether a non-linear dose-response model better describes the “antibiotic effect” in soils.

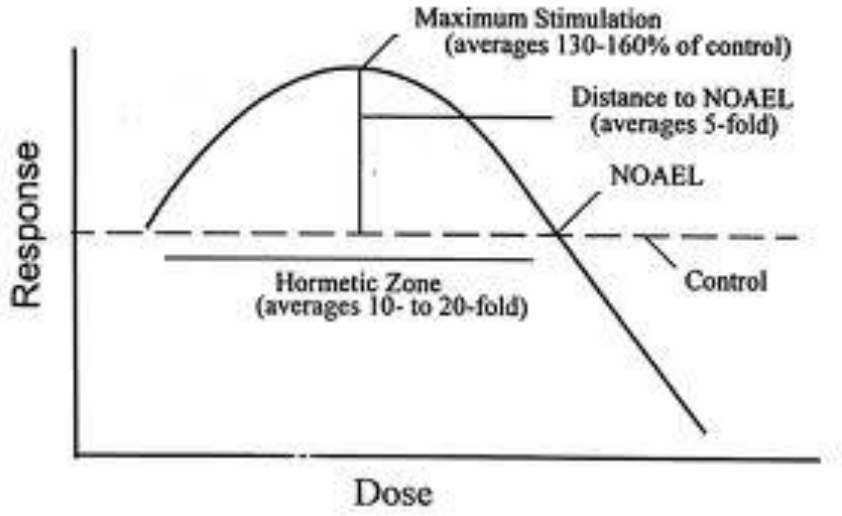
Dose-Response Models: Introduction



Calabrese, E. (2005) Challenging Dose-Response Dogma - The central pillar upon which toxicological assessments are built is the dose-response relationship. http://www.the-scientist.com/?articles.view/articleNo/16218/title/Challenging-Dose-Response-Dogma/

Dose-Response Models: Hormesis

- Hormesis occurs when exposure to a toxin at levels below the No Observable Adverse Effect Limit (NOAEL) has a stimulatory or beneficial impact.
- Hormetic behavior can often be overlooked because dosages below the NOAEL are simply not evaluated.



Hans-Jürgen Jäger, Sagar V. Krupa, Chapter 6 Hormesis—Its Relevance in Phytotoxicology, In: Allan H. Legge, Editor(s), Developments in Environmental Science, Elsevier, 2009, Volume 9, Pages 137-152.

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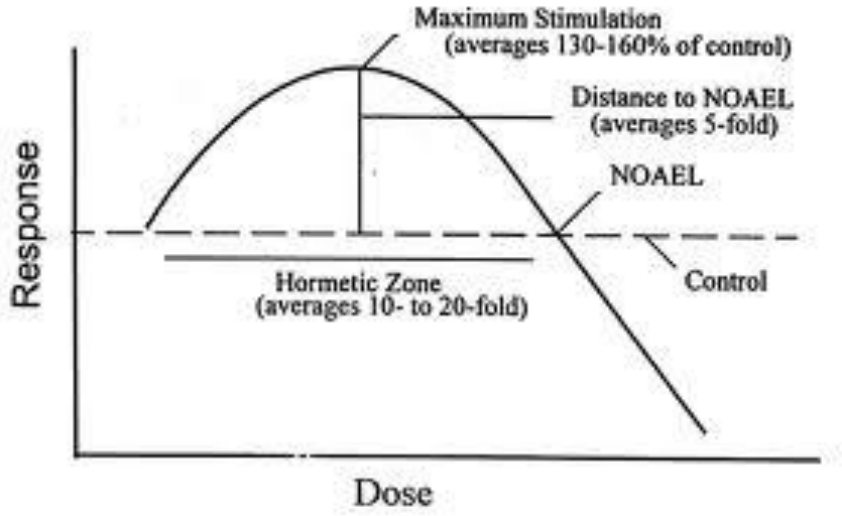

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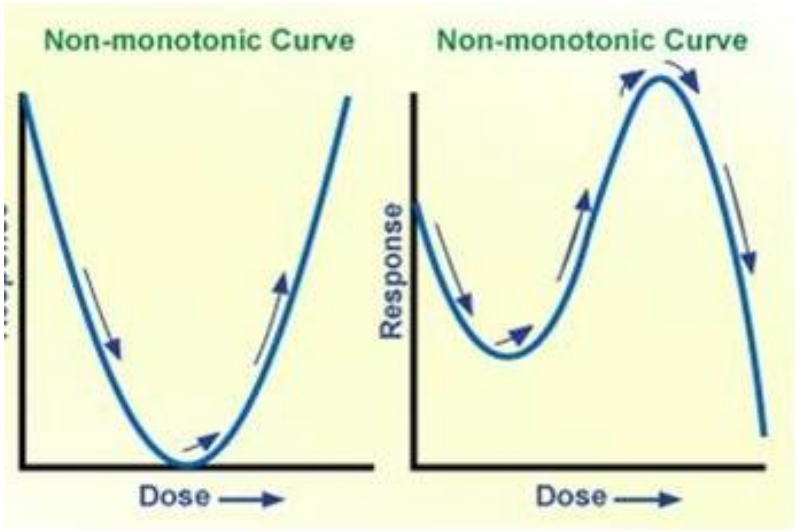
Dose-Response Models: Non-monotonic Curves

- Non-monotonic curves are used to describe non-linear behavior.
- It is possible for a dose-response curve to reverse direction multiplies times (several curves) and include a region in which the hormetic effect is observed.
- Again, hormesis is frequently overlooked because doses below the NOAEL are simply not tested.



http://epa.gov/ncct/edr/non-monotonic.html

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Experimental Methods

- Soils were treated with by 0, 1, 10, 100, or 1000 ng/kg_{soil} doses of commonly administered veterinary antibiotics to test for evidence of hormetic behavior.
- Separately, 15 cm columns of aquifer sand received a nitrate/glucose nutrient mix over a period of several weeks. To three of the columns, 1 ng/L Sulfamethoxazole was added and the effluent nitrate concentrations were monitored over time.

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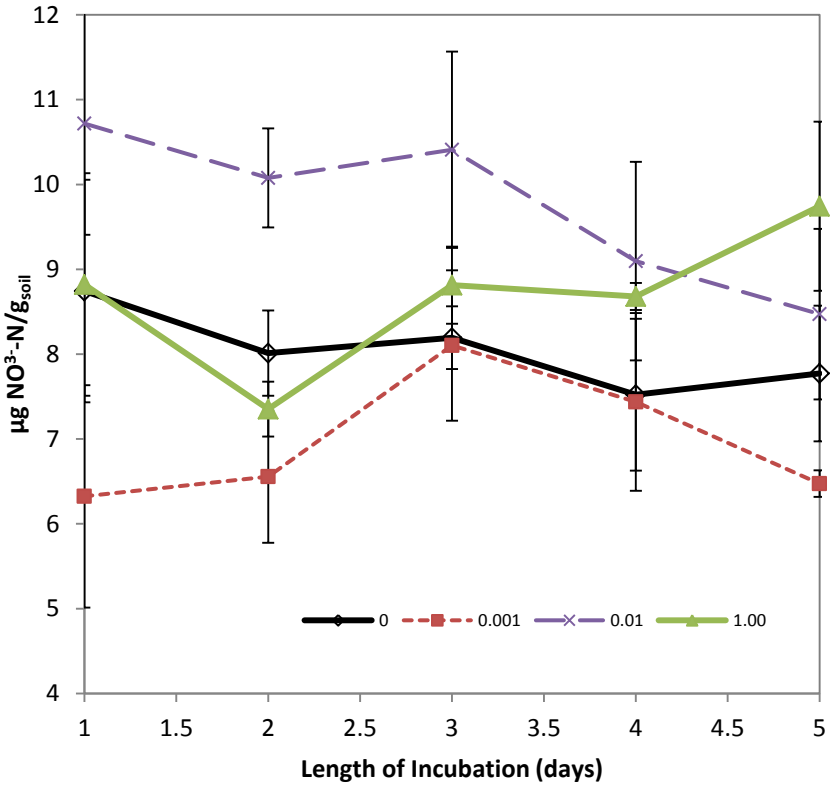
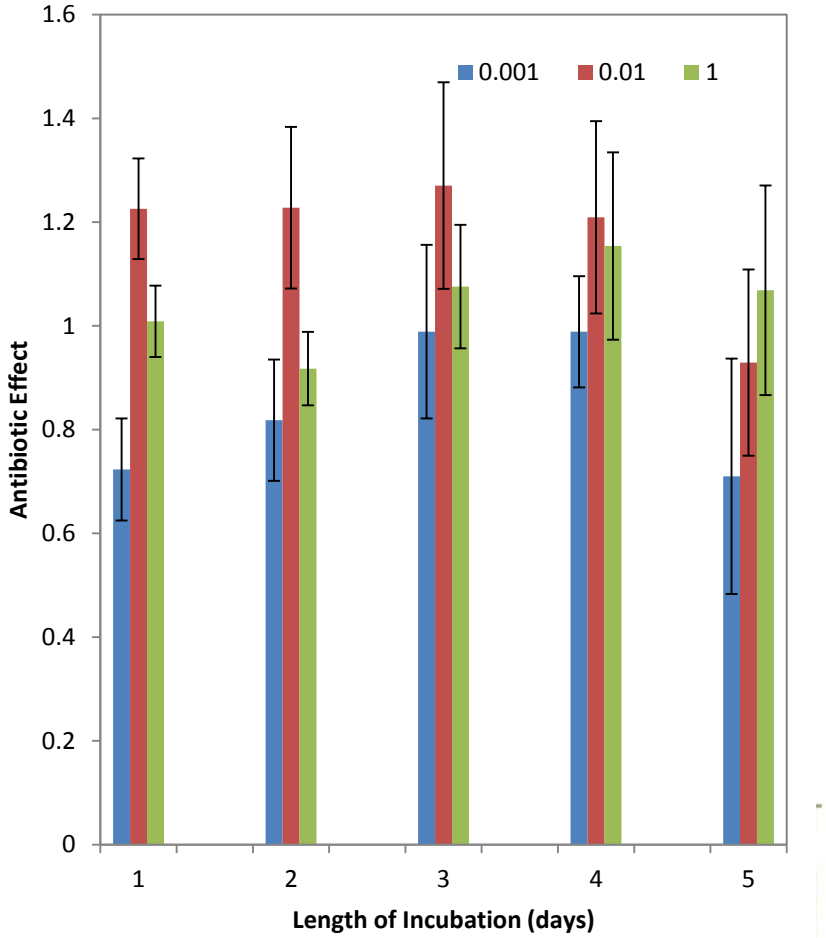
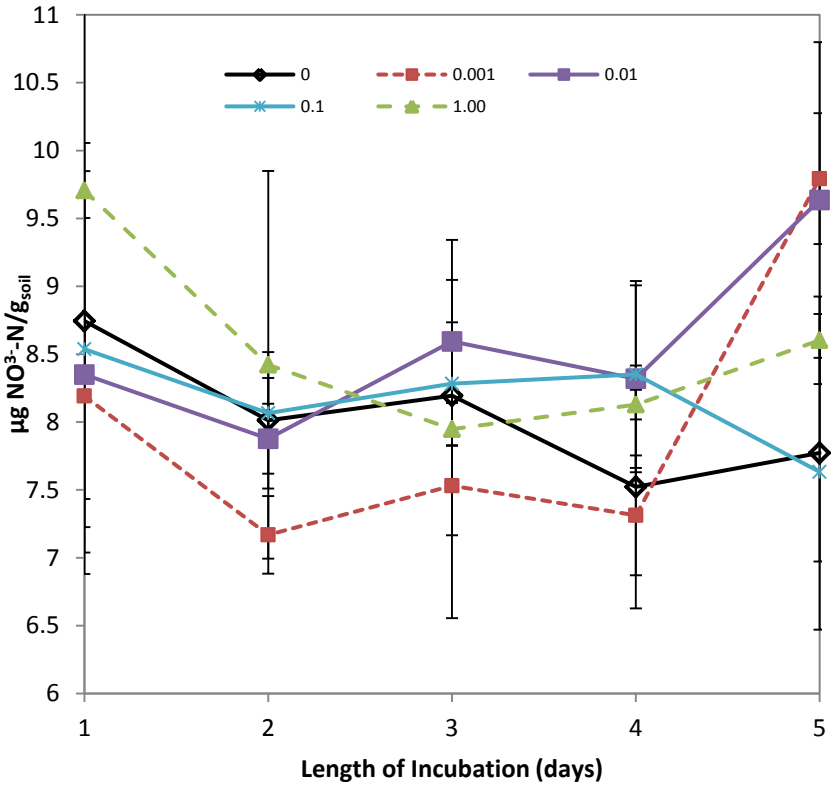
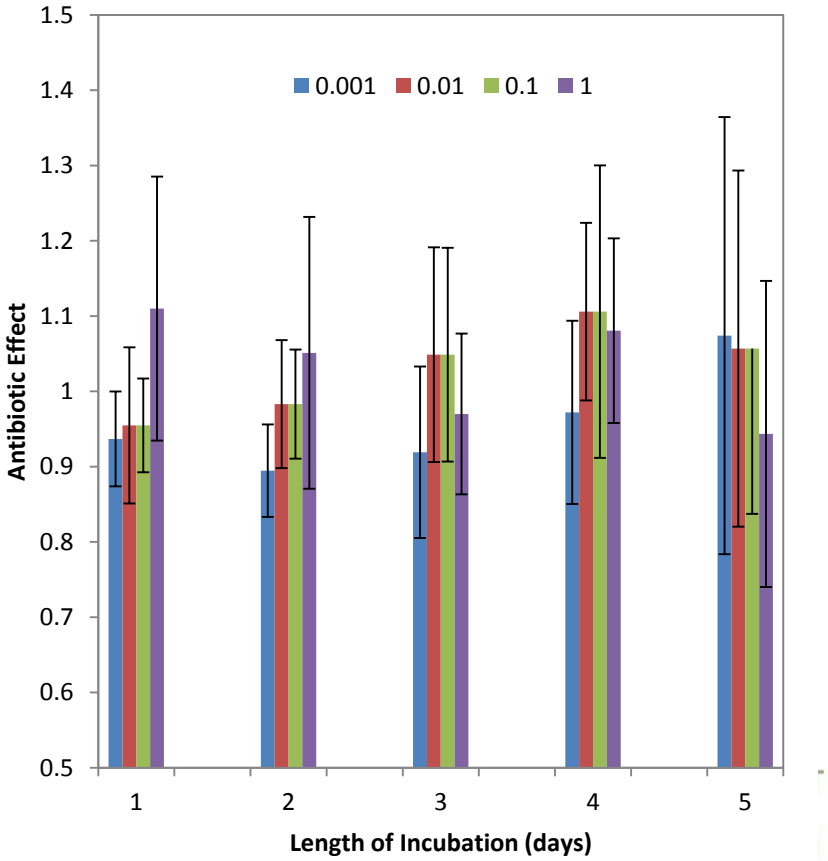
Results: Sulfamethoxazole





Results: Sulfadiazine





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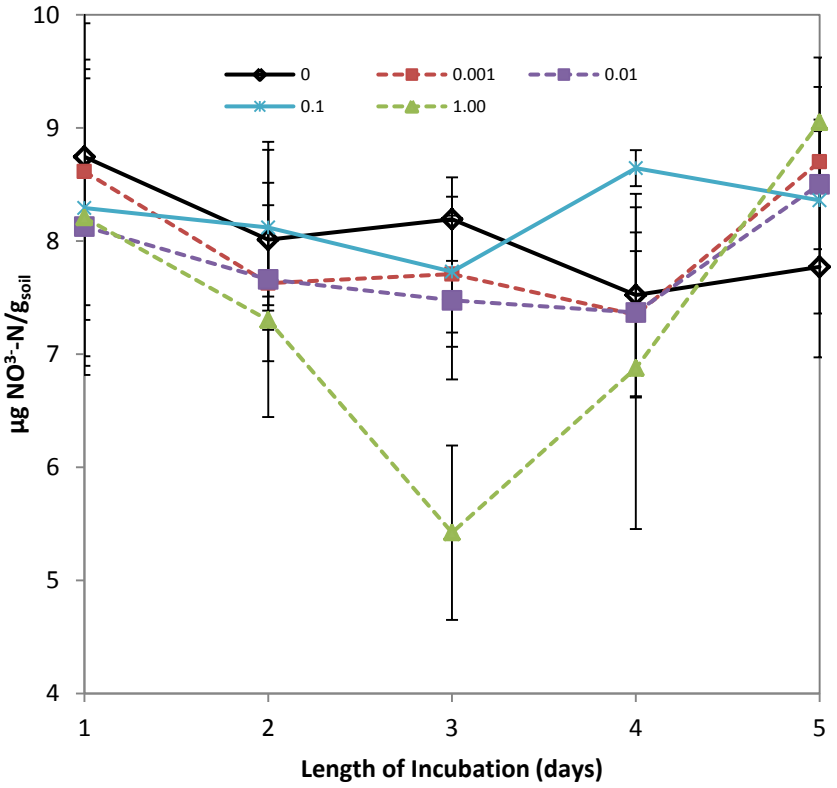
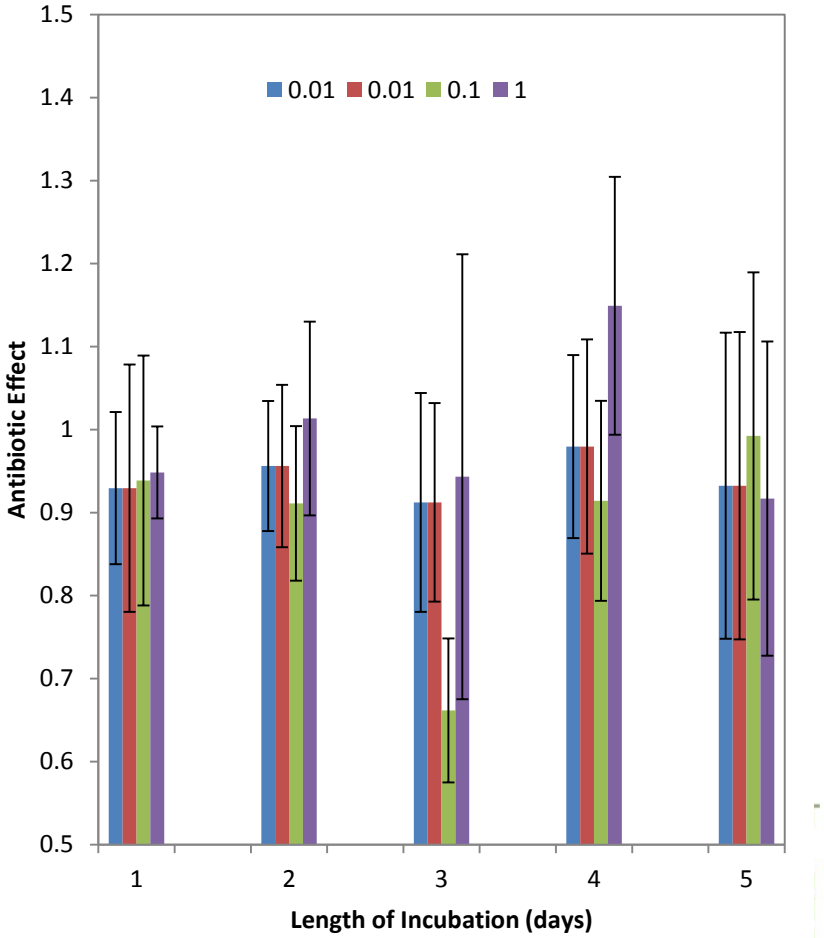
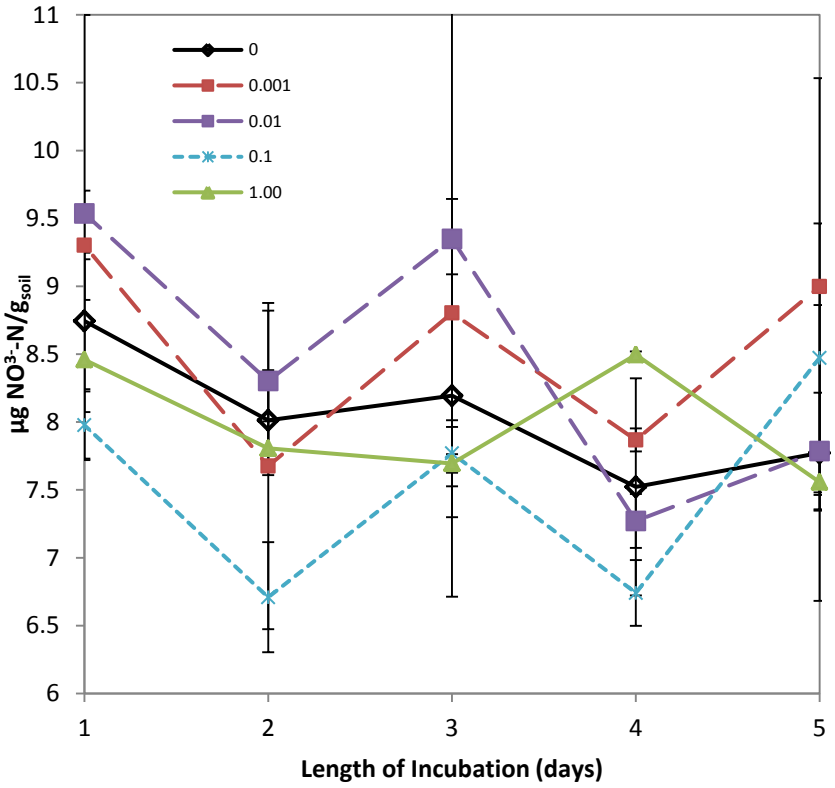
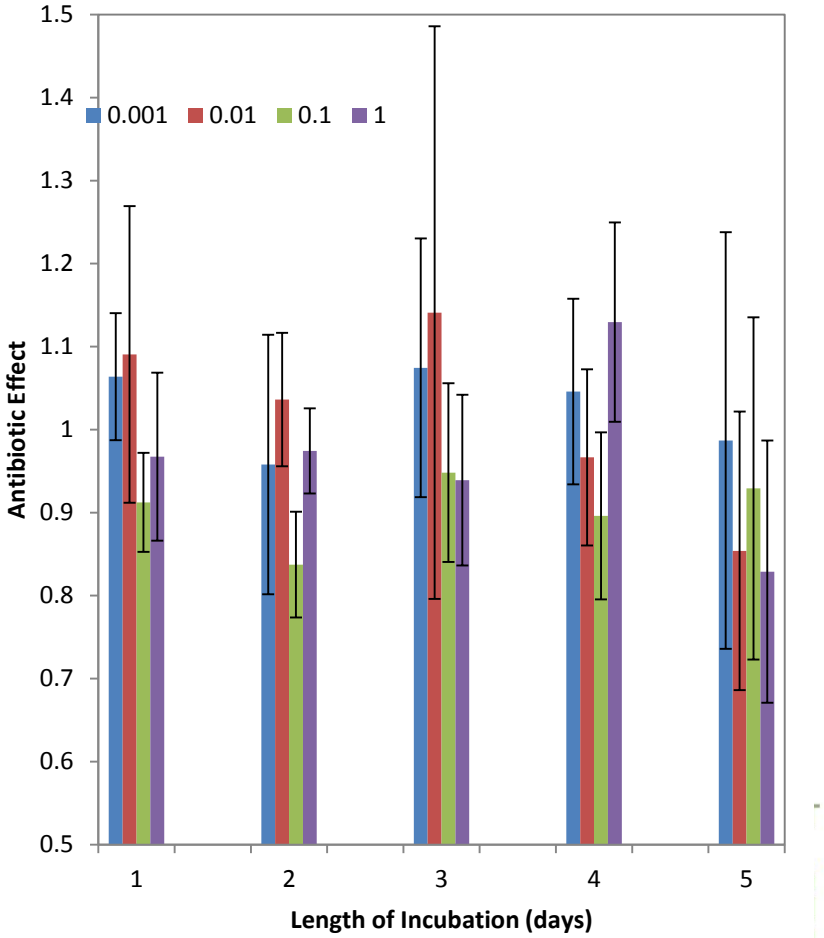
Results: Narasin



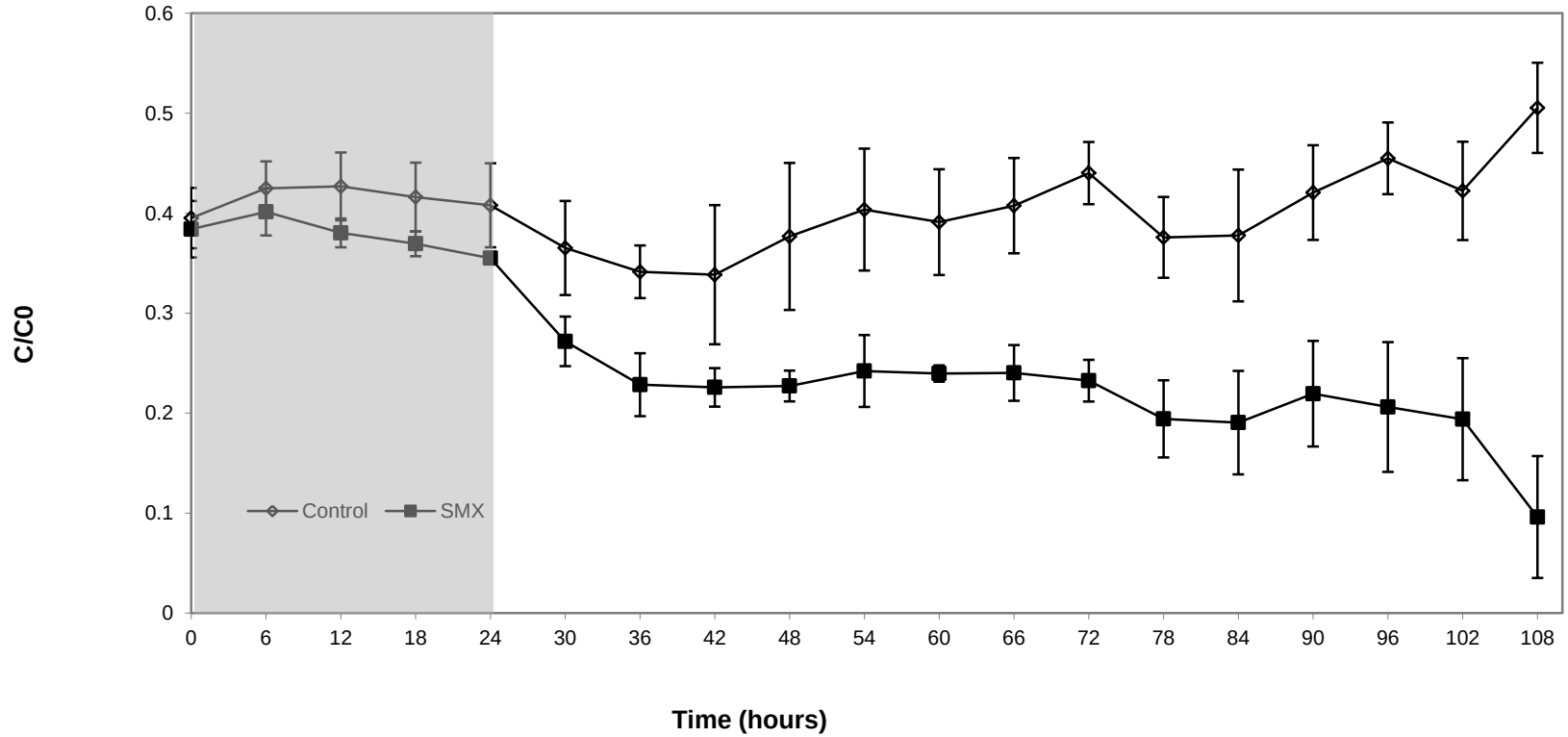


Results: Gentamicin





More evidence for Sulfamethoxazole



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Summary of Results

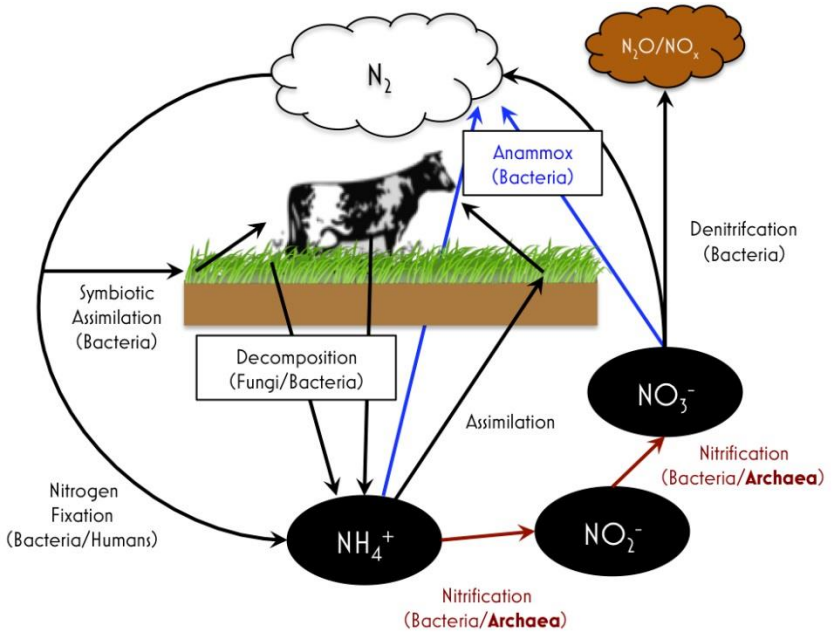
- Using 2-way ANOVA, it was determined that when considered over the 5 day sampling period, all but Gentamicin resulted in a strong correlation (>99%) between nitrate reduction and antibiotic dosage.
- In three of the four experiments, the lowest dosage, 0.001 ng/g_{soil}, showed evidence of stimulated nitrate removal (relative to the control), which is indicative of hormesis.
- In the fourth experiment, Gentamicin, the lowest doses were inhibitory and higher doses had a stimulant effect.
- Results from sulfadiazine indicate a simple hormetic curve whereas those obtained from narasin and sulfamethoxazole are less distinct, possibly multi-modal.

Conclusions

- The results of these experiments provide strong evidence that biogeochemical activity in soils will respond to antibiotic exposure levels not predicted by traditional linear or linear-threshold dose-response models.
- Further confirmation should be sought via development of a more thorough dose-response test obtained from bacterial cultures.
- Additionally, PLFA analyses will help to identify shifts in the microbial community structure that may account for some of the observed changes in reductive activity.

Future Considerations

- How are pollutant N species impacted by hormetic behavior?
  - NO_3^- leaching
  - N_2O production
- How might stimulated activity affect sediment mineralization?
  - Methane production?



http://lancaster.chem.cornell.edu/mission.html

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