What are systematic reviews and what can we learn from them?

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Mistra EviEM, Stockholm Environment Institute

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Overview

- What do we mean by ‘systematic review’?
- What are systematic reviews?
- What are they useful for?
- What can we learn from systematic reviews?

What do we mean by ‘Systematic Review’?

- Typology:
  - Primary research (‘simple’ evaluations)
  - Systematic reviews (evaluations by aggregation & collating)

eLIFE

RESEARCH ARTICLE

A bacterial sulfonolipid triggers multicellular development in the closest living relatives of animals

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Abstract Bacterially-produced small molecules exert profound influences on animal health, morphogenesis, and evolution through poorly understood mechanisms. In one of the closest living relatives of animals, the choanoflagellate *Salpingoeca rosetta*, we find that rosette colony development is induced by the prey bacterium *Algoriphagus machipongonensis* and its close relatives in the Bacteroidetes phylum. Here we show that a rosette inducing factor (RIF-1) produced by *A. machipongonensis* belongs to the small class of sulfonolipids, obscure relatives of the better known sphingolipids that play important roles in signal transmission in plants, animals, and fungi. RIF-1 has extraordinary potency (femtomolar, or 10^{-15} M) and *S. rosetta* can respond to it over a broad dynamic range—nine orders of magnitude. This study provides a prototypical example of bacterial sulfonolipids triggering eukaryotic morphogenesis and suggests molecular mechanisms through which bacteria may have contributed to the evolution of animals.

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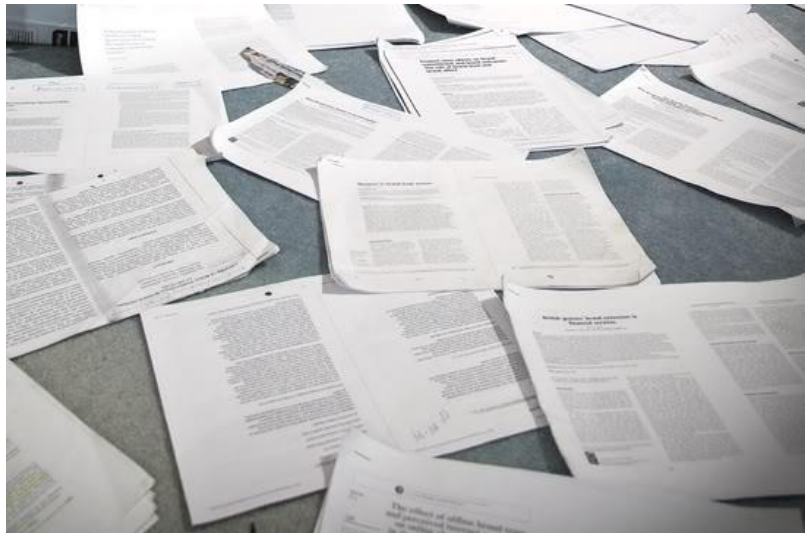
Introduction

Eukaryotes evolved in a world filled with bacteria and throughout their shared history these two branches of life have developed a complex set of ways to compete and cooperate with each other. While research on these interactions has historically emphasized bacterial pathogens, bacteria also regulate the biology of eukaryotes in many other ways (*McFall-Ngai 1999*; *Koropatnick et al. 2004*; *Maansarian et al. 2005*; *Falkow 2006*; *Hughes and Sperandio 2008*; *Desbrosses and Stougaard 2011*) and may have exerted critical influences on animal evolution. Choanoflagellates, microscopic bacteria-eating eukaryotes that are the closest living relatives of animals (*James-Clark 1868*; *Saville Kent 1880*; *Hibberd 1975*; *Carr et al. 2008*; *King et al. 2008*; *Ruiz-Trillo et al. 2008*), could provide particularly important insights into the mechanisms underlying bacterial influences on animal biology and evolution. Moreover, some choanoflagellates have both solitary and multicellular stages in their life histories (*Leadbeater 1983*; *Karpov and Coupe 1998*; *Dayel et al. 2011*) and understanding the environmental cues that regulate choanoflagellate colony formation could provide a molecular model for animal multicellularity.

Results

In the choanoflagellate *Salpingoeca rosetta*, rosette-shaped multicellular colonies develop when a single founder cell undergoes multiple rounds of incomplete cytokinesis, leaving neighboring cells physically attached by fine intercellular bridges (*Fairclough et al. 2010*; *Dayel et al. 2011*). Although the original stock of *S. rosetta* (ATCC50818) was established from a rosette colony (*Dayel et al.*



What do we mean by ‘Systematic Review’?

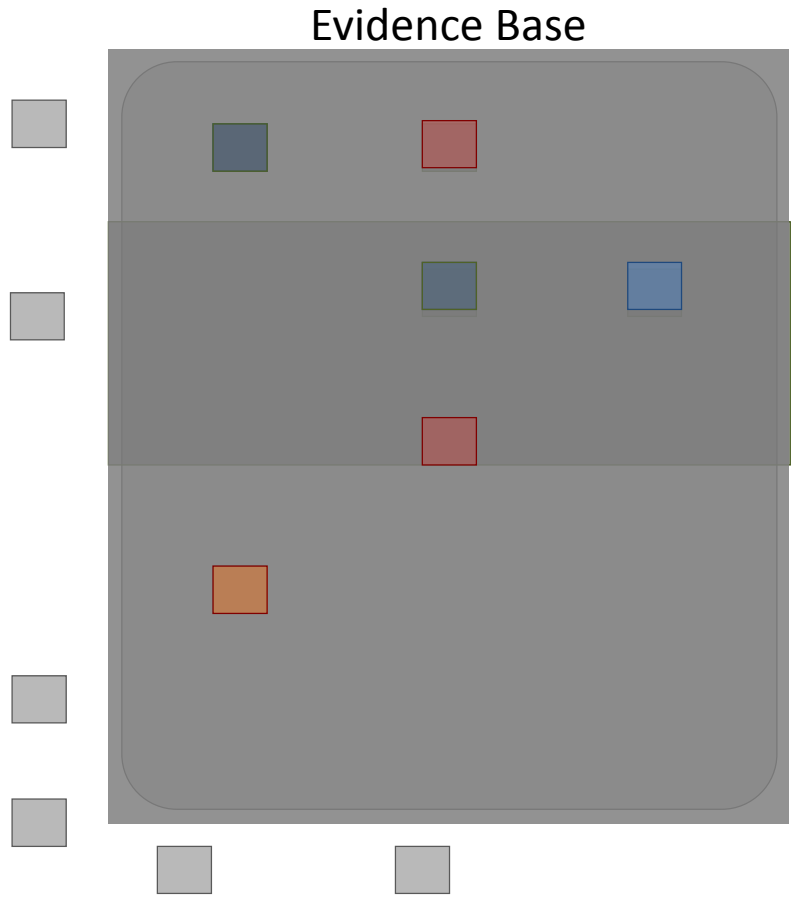
- Systematic reviews are about:
  - effectiveness

- efficacy

- impact

What's wrong with traditional reviews?

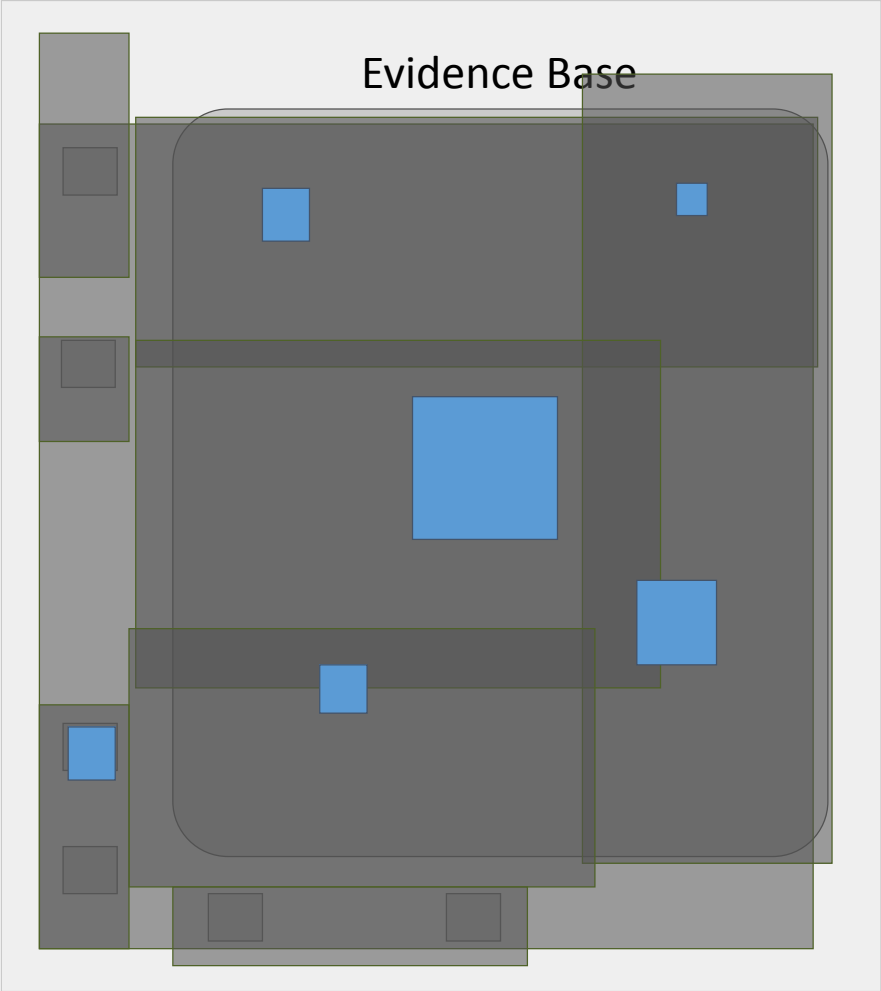
- Selection bias
- Lack of comprehensiveness
- Publication bias
- No transparency
- Vote-counting/quality bias
- Discussion bias



➢ **Haddaway, N. R.**, Woodcock, P., Macura, B., and Collins, A. (2015) Making literature reviews more reliable through application of lessons from systematic reviews. Conservation Biology, DOI: 10.1111/cobi.12541.

What's right with systematic reviews?

- Exhaustive searching
- Comprehensiveness
- Grey literature
- Transparent methods
- Weight studies
- Synthesis of all relevant studies

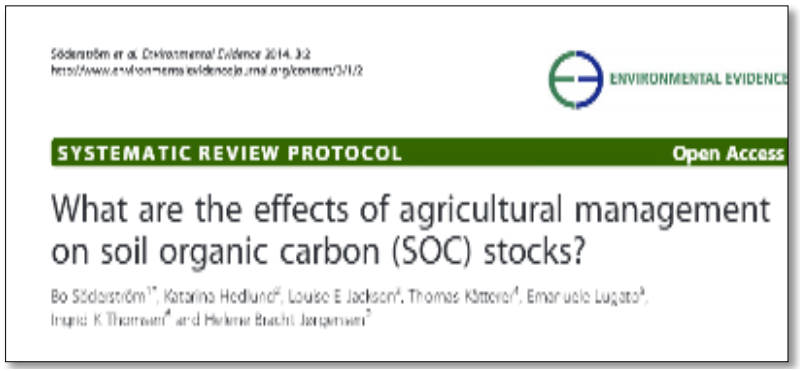


Methodology

Photo: Claes Bernes, EviEM

Photo: Bo Söderström

Identify **Question** (with stakeholder engagement) → Generate & publish **Protocol** → **Search** studies → **Include** relevant evidence → Critically **appraise** → **Extract** & **Synthesise** → Syst. **review report**



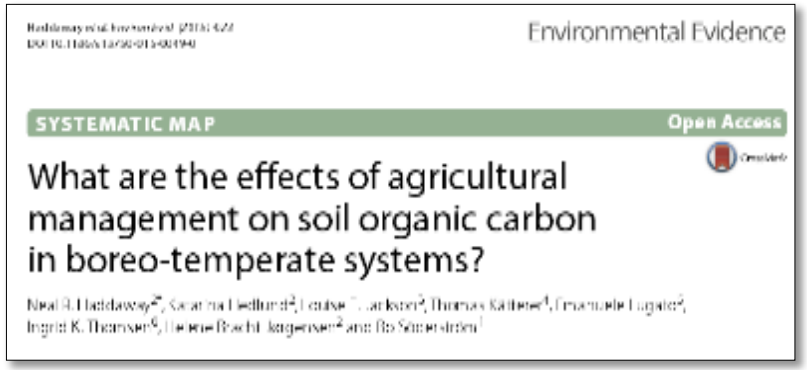
Söderström et al. Environmental Evidence 2014, 3:2
http://www.environmentalevidencejournal.org/content/3/1/2

ENVIRONMENTAL EVIDENCE

SYSTEMATIC REVIEW PROTOCOL Open Access

What are the effects of agricultural management on soil organic carbon (SOC) stocks?

Bo Söderström[1*], Katarina Hedlund[2], Louise E Jackson[3], Thomas Kätterer[4], Emanuele Lugato[5], Ingrid K Thomsen[6] and Helene Bracht Jørgensen[7]



Environmental Evidence

SYSTEMATIC MAP Open Access

What are the effects of agricultural management on soil organic carbon in boreo-temperate systems?

Neal R Haddaway[2*], Sarah Gardner Hedlund[2], Louise E Jackson[3], Thomas Kätterer[4], Emanuele Lugato[5], Ingrid K Thomsen[6], Helene Bracht Jørgensen[7] and Bo Söderström[1]

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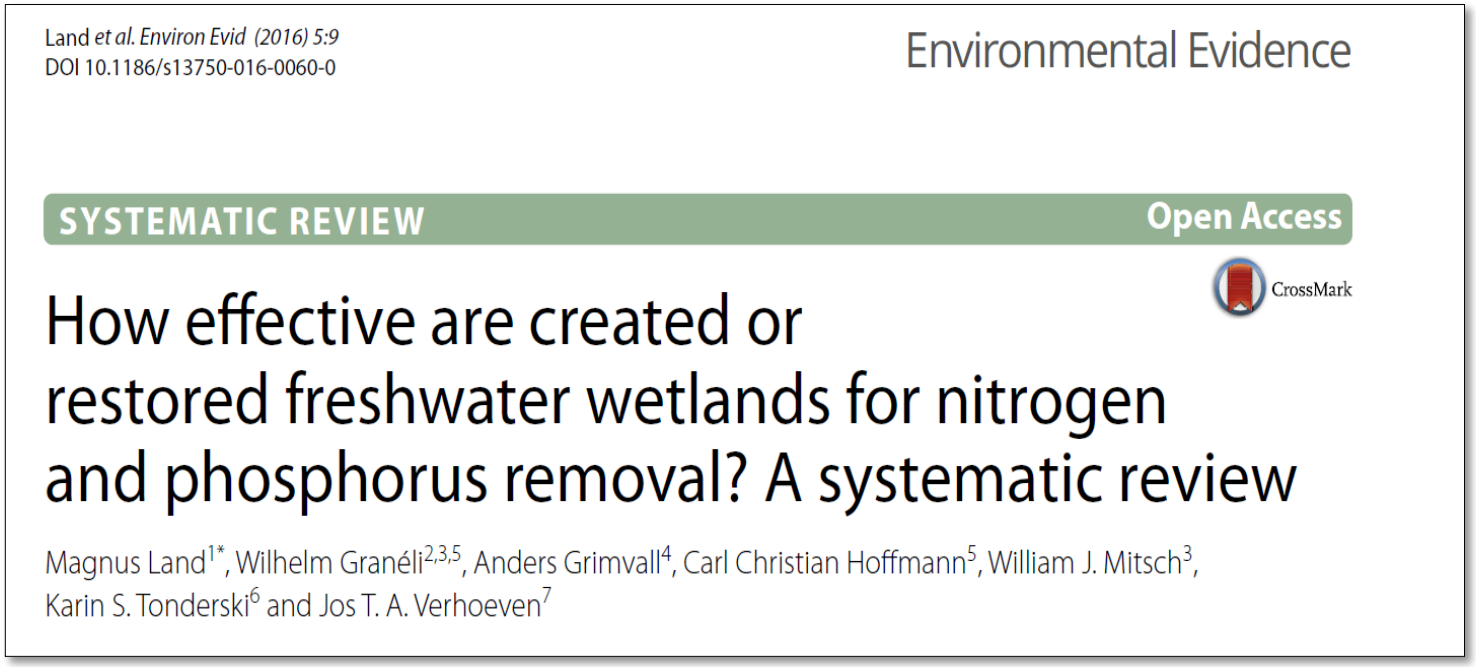
Example from environmental management



Land *et al. Environ Evid (2016) 5:9*
DOI 10.1186/s13750-016-0060-0

Environmental Evidence

SYSTEMATIC REVIEW Open Access

How effective are created or restored freshwater wetlands for nitrogen and phosphorus removal? A systematic review

Magnus Land[1*], Wilhelm Granéli[2,3,5], Anders Grimvall[4], Carl Christian Hoffmann[5], William J. Mitsch[3], Karin S. Tonderski[6] and Jos T. A. Verhoeven[7]

- An intervention that works!
- Wetlands are generally highly efficient for removing nutrients (TF & TN) from run-of
- Efficient if inlet concentration of the nutrients high & the hydraulic loading rate low

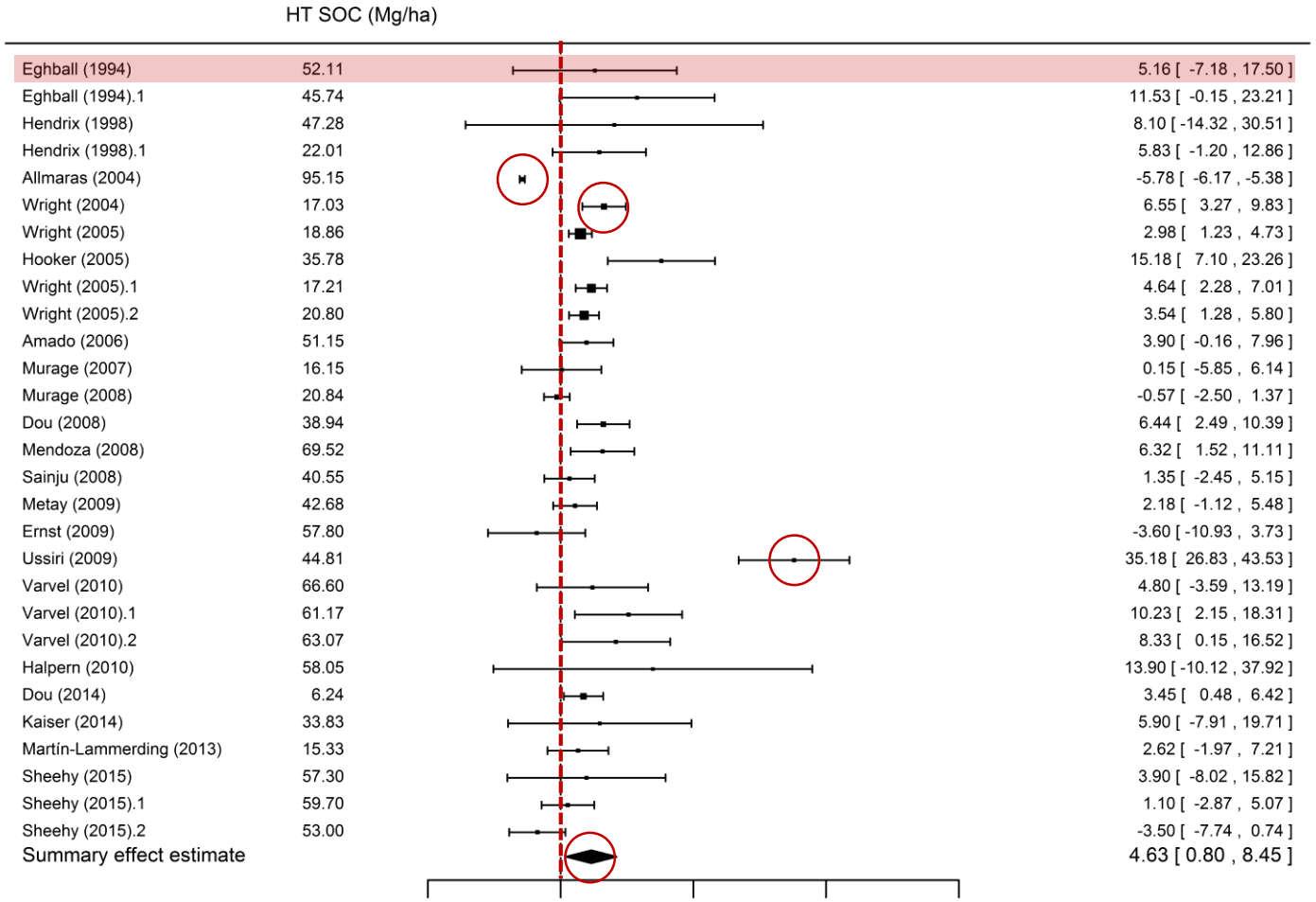
Systematic review coordinating bodies

- Collaboration for Environmental Evidence, Cochrane, Campbell

The value of systematic reviews

- SRs are more/just as valuable than a new evaluation
  - Increase statistical power
  - Reduce variability
  - Allow examination of context (sources of heterogeneity)

The benefits of aggregating studies



Other uses of systematic reviews

- Knowledge gaps

	Sweden	Norway	Finland	Denmark	Iceland	
Methane	10	15	18	21	5	*69*
Carbon dioxide	8	2	13	19	4	*46*
Nitrous oxide	11	17	20	23	7	*78*
	29	*34*	*51*	*63*	*16*	

- Methodological patterns in primary research
  - Best practices / gold standards
  - Poor methods (high risk of bias)
  - Range of methods available

Lessons from systematic review

- Full systematic review not always appropriate
  - Staff
  - Resources
- We can still learn from systematic review methods
  - Have we missed some vital evidence?
  - What have we done and how?
  - Have we been consistent?
  - Is evidence reliable? If not what do we do?

1. Comprehensiveness

- Academic literature AND grey literature (?)
  - Multiple academic sources useful
  - Impact of publication bias
  - Importance of availability of grey literature evaluations!

- Comprehensiveness vital for systematic reviews
  - May not be so vital for evaluations, but consider

2. Procedural transparency

- Vital for verifiability / accountability / repeatability
- What did you do?
  - Where did you search? What was the search string? When? What settings?
  - How did you decide what was relevant? Consistency checking?
  - How was data/information extracted? How was it dealt with?
  - How did you judge quality? Consistency checking?
  - How were studies combined? Which studies were excluded from analysis?
- Low resource requirement

3. Reporting

- Benefits
  - Ensure outputs are usable by others (implementation, further analysis)
  - Allows evaluation to be upgraded (scoping review -> systematic review)

- Practical advice
  - Be as transparent as possible
  - Include raw data (supplementary information)
  - Report all results in summary figures/tables (summarise again in text)
  - Avoid skipping challenging results
  - Mean + standard deviation + sample size

4. Procedural consistency

- Important where
  - Work is complex
  - Tasks completed over time
  - Tasks undertaken by multiple people

- What is it?
  - Check that work is done in the same way
  - Definitions, interpretations, enactment are consistent
  - Test with statistics (percentage agreement, formal Kappa test)
  - Discuss all disagreements and refine definitions

5. Critical appraisal

- Assess quality of studies or evaluation designs
- Use formal ‘tool’ (series of questions)
  - Sufficient replication?
  - Appropriate intervention?
  - Appropriate measurement methods?
  - Possible confounding factors?
- Useful in choosing an evaluation design (best methods to use)
- Useful in reviewing evidence (not all evaluations are equal!)

Summary

- Systematic reviews as gold standard
- Not always appropriate (staff and resource)
- Many lessons to be learned: primary research (evaluations) and traditional reviews

Thank you

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