Exploiting Omics Data to Advance Predictive Ecotoxicology.



Workshop on implementing EC Roadmap on phasing out animal testing in pesticides and biocides.

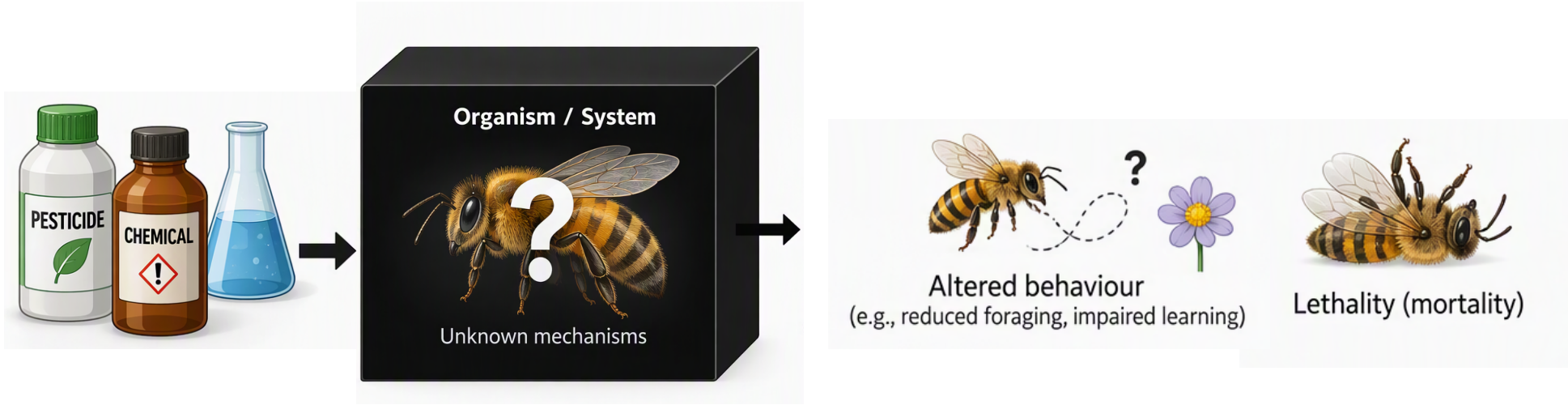
Stephen Short

21/10/2026

UKCEH

Our planet.
Decoded.

Moving from ‘black box’ to ‘mechanistic’: a particular challenge for environmental protection.



‘Non-animal chemical safety assessments will mostly <u>rely on a mechanistic understanding of toxicity</u> rather than on observing adverse effects in animals. This entails determining whether molecular-level changes predict adverse outcomes, and can, if necessary, describe them quantitatively.’

EC Roadmap towards phasing out animal testing for chemical safety assessments, 2026

Chemical diversity (so, many mechanisms) is an issue – this is true for human and environmental health.

For the environment, the scale of biological diversity dramatically increases the mechanistic challenge.

For the environment, our (sub-organismal) NAM will need to predict population consequences.

We're thinking about how to exploit expanding omic data (genomic and transcriptomic) to advance predictive ecotoxicology – a philosophy that aligns with the roadmap.



Environmental Science & Technology

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Critical Review

Exploiting Omic Data to Advance Predictive Ecotoxicology

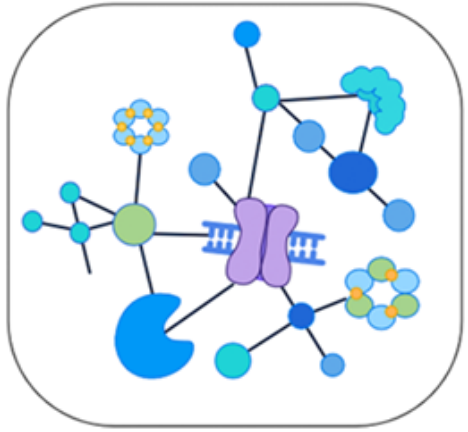
Stephen Short,* Amaia Green Etxabe, Elmer Swart, Claudia Rivetti, Bruno Campos, Rama Krishnan, Peter Kille, and David J. Spurgeon

Cite This: *Environ. Sci. Technol.* 2026, 60, 23642–23660

Read Online

Details the current state of play. Also, what gaps in fundamental knowledge, sequence data, and bioinformatic challenges prevent us exploiting omic resources.

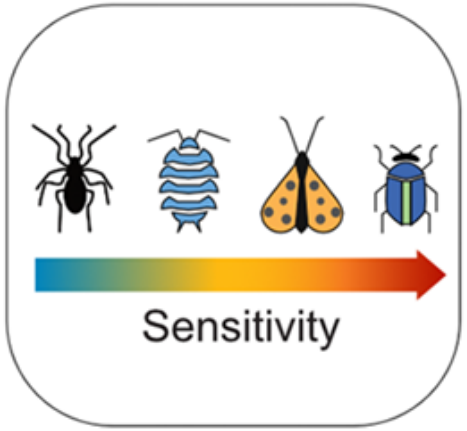
Omic-based Predictive Ecotoxicology



Understand how molecular difference underpins sensitivity.



Compare ‘omic’ data across untested species to find pertinent differences.



Predict species sensitivity.

The promise: we could have flagged the danger of neonics to bees:

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Review Article

The molecular determinants of pesticide sensitivity in bee pollinators

Chris Bass [a,*], Angela Hayward [a], Bartlomiej J. Troczka [a], Julian Haas [b], Ralf Nauen [b,*]

[a] Centre for Ecology and Conservation, University of Exeter, Penryn, Cornwall, United Kingdom
[b] Bayer AG, Crop Science Division, Alfred Nobel-Strasse 50, Monheim, Germany

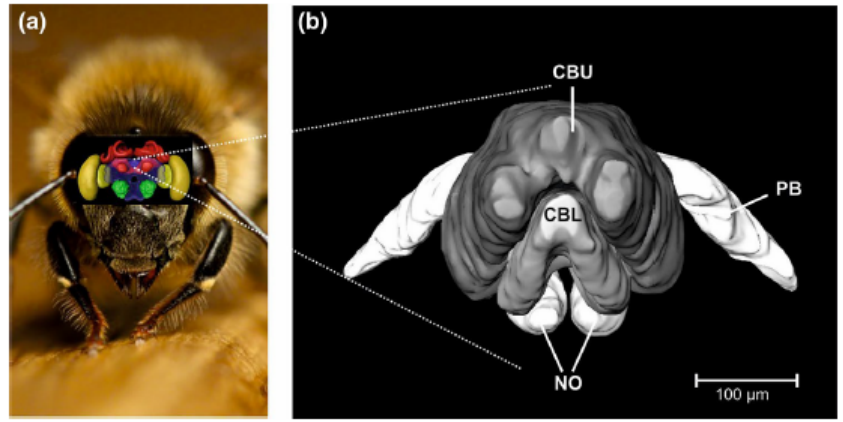


Review Article | Published: 19 October 2012

The honeybee as a model for understanding the basis of cognition

Randolf Menzel

Nature Reviews Neuroscience **13**, 758–768 (2012) | Cite this article



Taken from Giugra 2019: Journal of Comparative Physiology A (2019) 205:439–450 https://doi.org/10.1007/s00359-019-01344-2

PNAS

Cofactor-enabled functional expression of fruit fly, honeybee, and bumblebee nicotinic receptors reveals picomolar neonicotinoid actions

Makoto Ihara[a,1], Shogo Furutani[a,1], Sho Shigetou[a], Shota Shimada[a], Kunihiro Niki[a], Yuma Komori[a], Masaki Kamiya[a], Wataru Koizumi[a], Leo Magara[a], Mai Hikida[a], Akira Noguchi[a], Daiki Okuhara[a], Yuto Yoshinari[b], Shu Kondo[c], Hiromu Tanimoto[d], Ryusuke Niwa[e], David B. Sattelle[f], and Kazuhiko Matsuda[a,g,2]

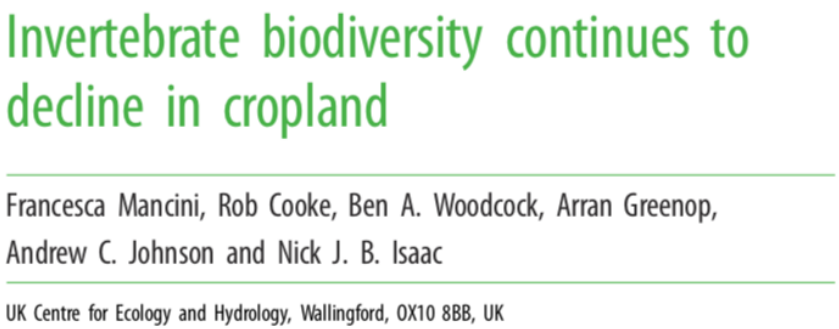
Combine MIE knowledge, 'omics', AI docking tools and neuroanatomy to flag bee sensitivity.

EC Roadmap alignment: exploiting 'omic' data expands the species we consider?

Answers the too many species problem – now is time.



Improved risk assessment - tackling invertebrate declines.

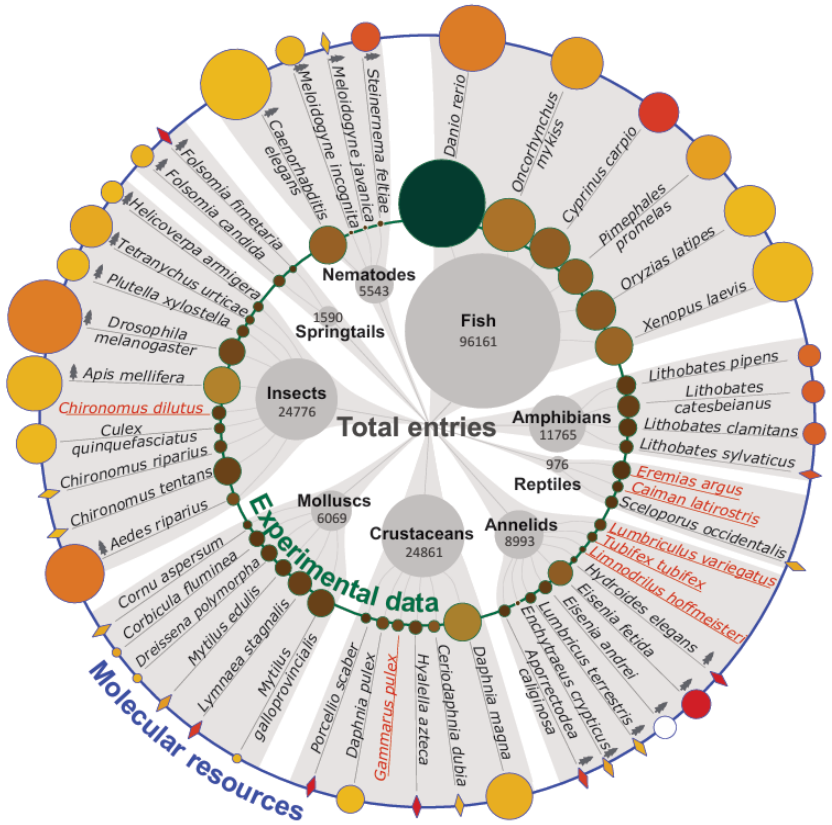

Invertebrate biodiversity continues to decline in cropland

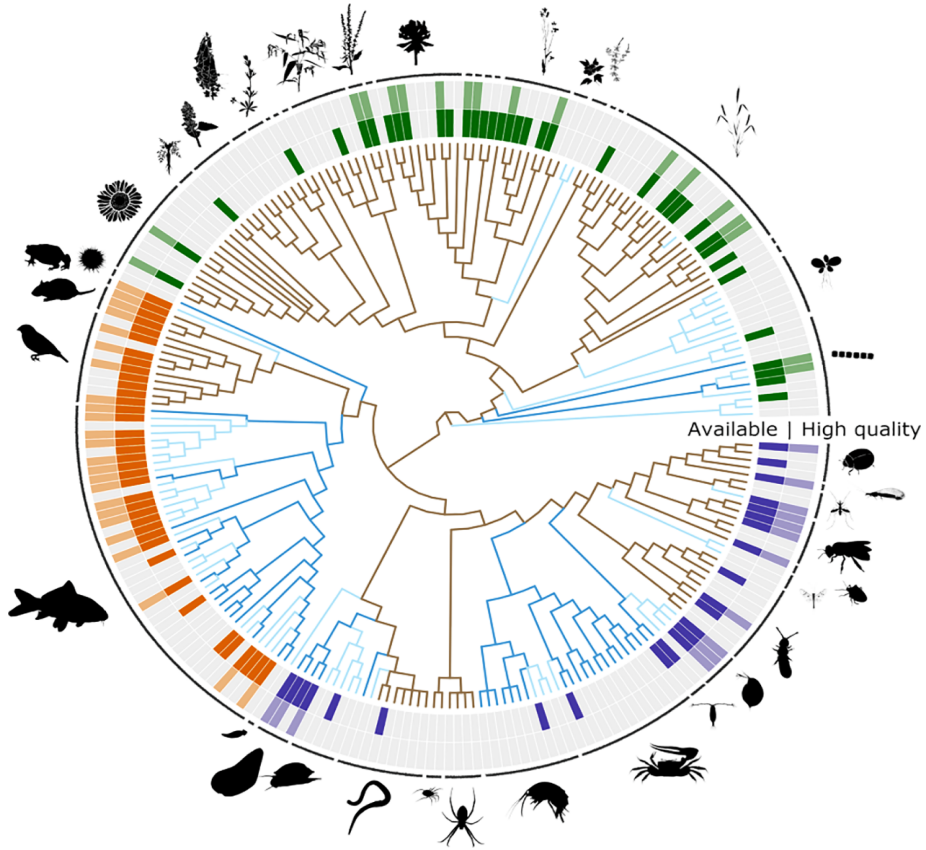
Francesca Mancini, Rob Cooke, Ben A. Woodcock, Arran Greenop, Andrew C. Johnson and Nick J. B. Isaac

UK Centre for Ecology and Hydrology, Wallingford, OX10 8BB, UK

EC Roadmap alignment: omic can incorporated into regulatory decisions - based increasingly on integrated evidence from multiple sources.

Genomes and ecotoxicology: data gaps inhibiting progress.





From: Short et al 2026. Exploiting omic data to advance predictive ecotoxicology.

Environ. Sci. Tech, *60*(34): 23642-23660.

From: Roell et al 2024 Missing Genomic Resources for the Next Generation of Environmental Risk Assessment.

Environ. Sci. Technol, 58(4):1877-1881.

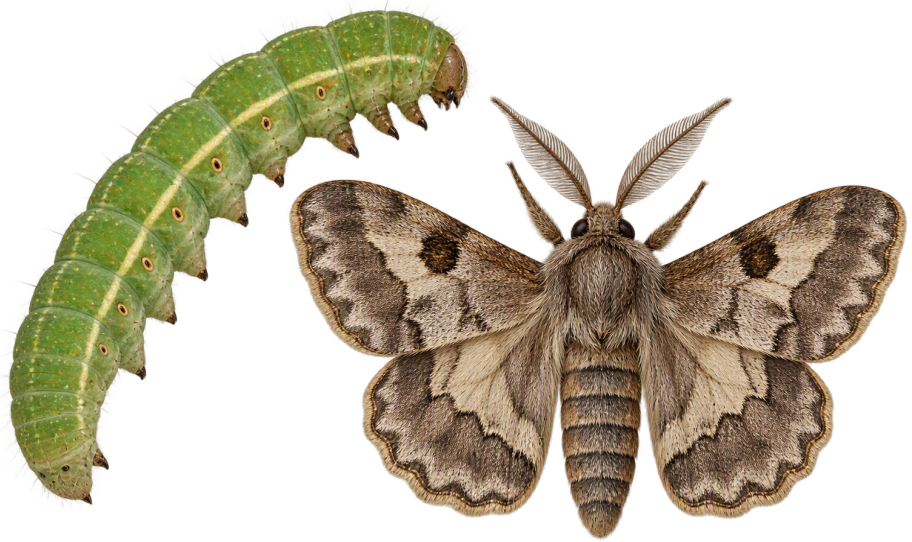
Recommendation: ecotoxicologists/risk assessors must lobby to fill gaps.

Genomes and transcriptomes: what can be exploited?

EARTH BIOGENOME PROJECT

1 domains
3 kingdoms
32 phyla
120 classes
464 orders
1,557 families
4,174 genera
6,282 species
54 subspecies

Two animals, one genome: expression of sensitivity-relevant genes at critical life-stages.



Recommendation: be proactive. Strategically generate gene expression profiles for the most vulnerable species/life stages.

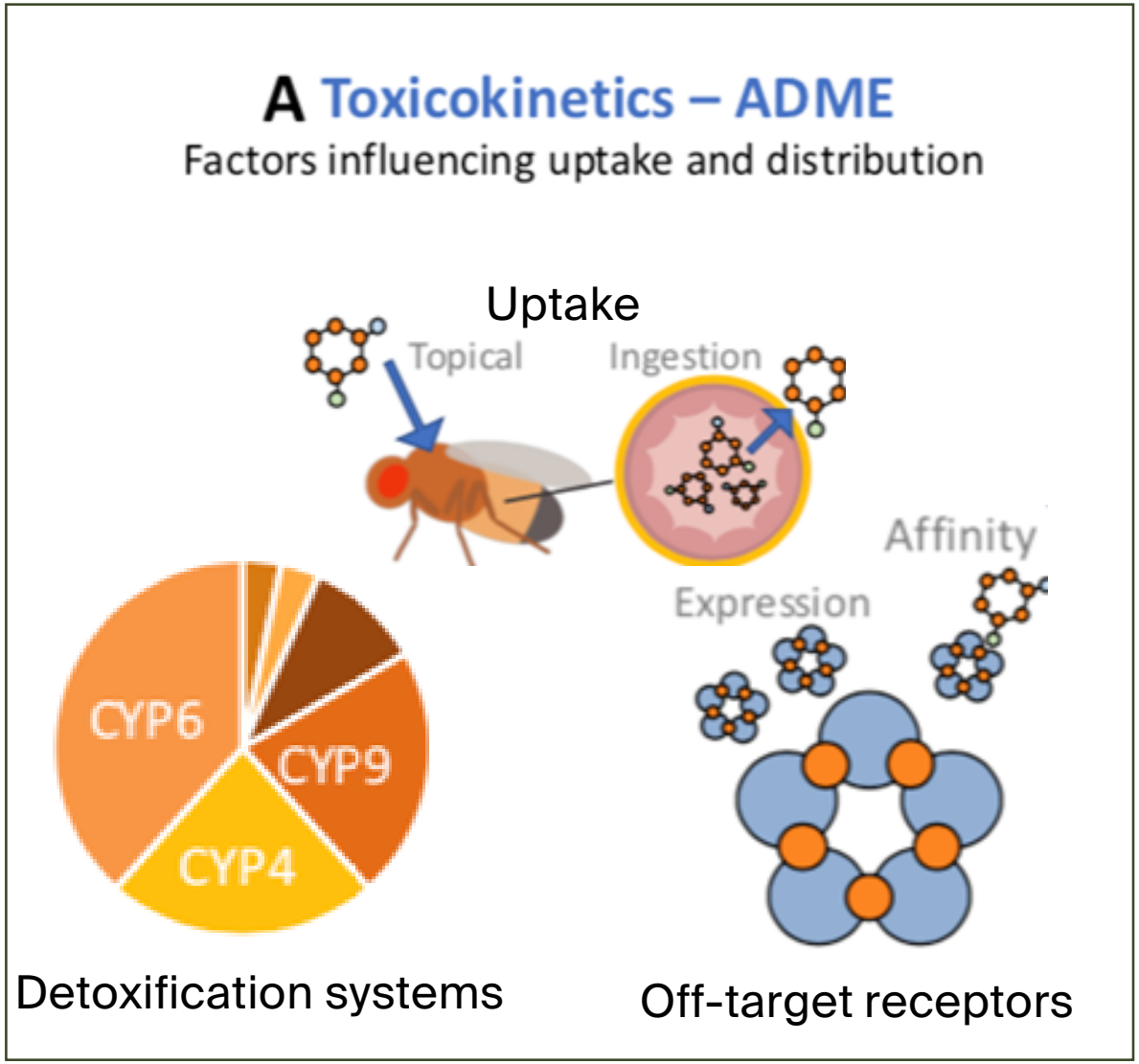
The role of other of ‘omics’

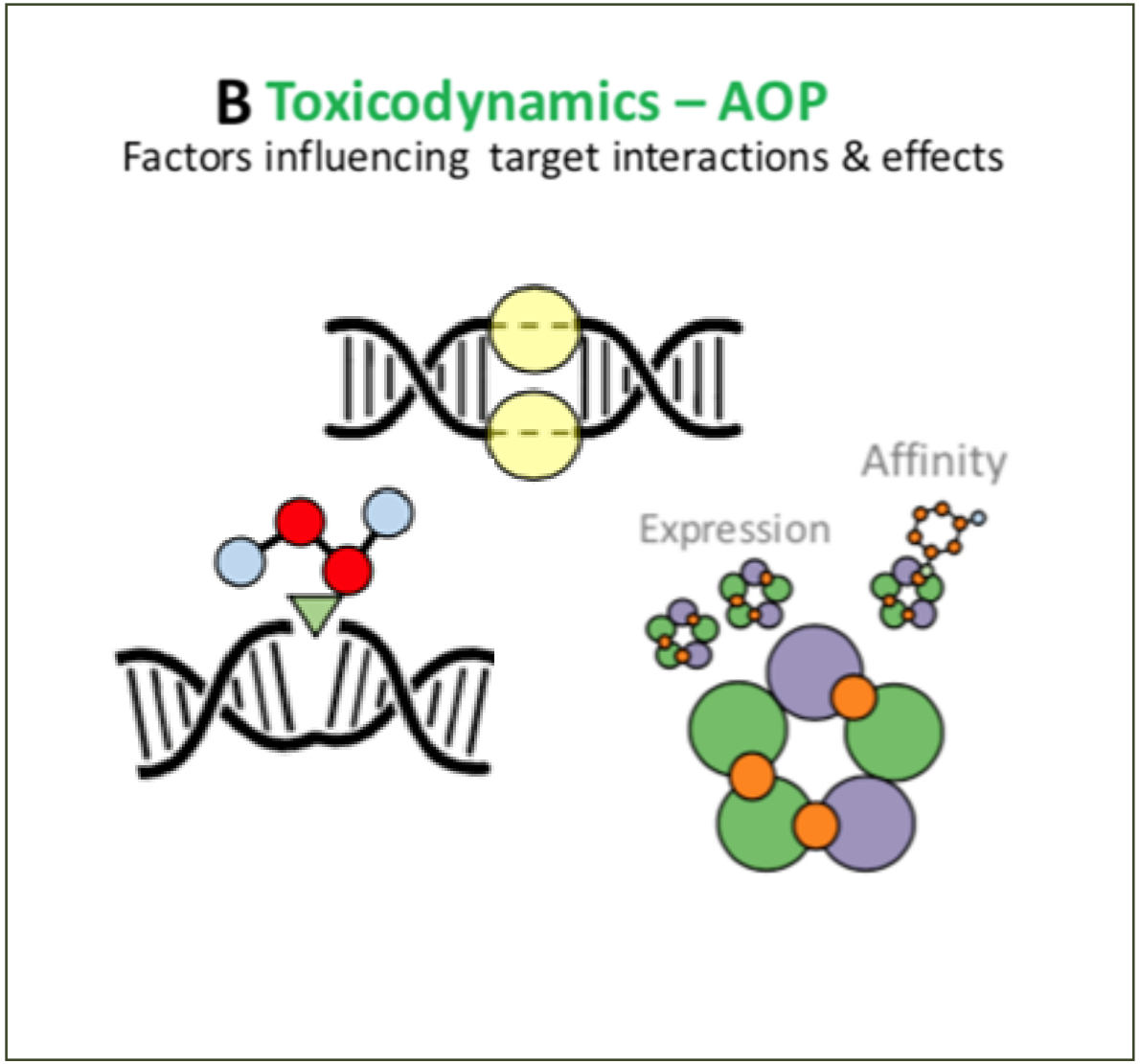
Proteomics
Metabolomics
Lipidomics
Peptidomics
Ionomics

↓

Critical for understanding sensitivity but not broad taxonomic prediction.

How 'omic' data inform us about sensitivity-relevant differences.





Fundamental research – knowledge allowing us to exploit omic data.

Research area	Data needed to predict	Example
- Reveal chemical receptors and MoAs	- Genomes	- Voltage-gated sodium channels and nematode insensitivity to pyrethroids.



Neurobiology of the *Caenorhabditis elegans* Genome

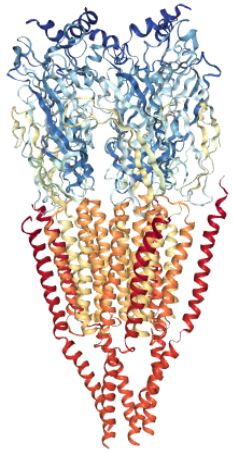
CORNELIA I. BARGMANN Authors Info & Affiliations

SIMILARITY, INDEPENDENCE, OR INTERACTION FOR BINARY MIXTURE EFFECTS OF NERVE TOXICANTS FOR THE NEMATODE *CAENORHABDITIS ELEGANS*

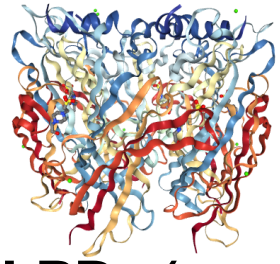
CLAUS SVENDSEN,* PIA SIANG, LINDSAY J. LISTER, ANNABEL RICE, and DAVID J. SPURGEON

Recommendation: Close the receptor gap – (e.g., PFAS and fungicides). Bad assumptions undermine current predictive approaches (SeqAPASS/AOP-based prediction), as well as future NAMs based on receptor-activation assays.

Research area	Data needed to predict	Example
- Off-target receptors	- Genomes and transcriptomes	- High expression of affinity binding proteins with high affinity for neonics drives earthworm sensitivity.

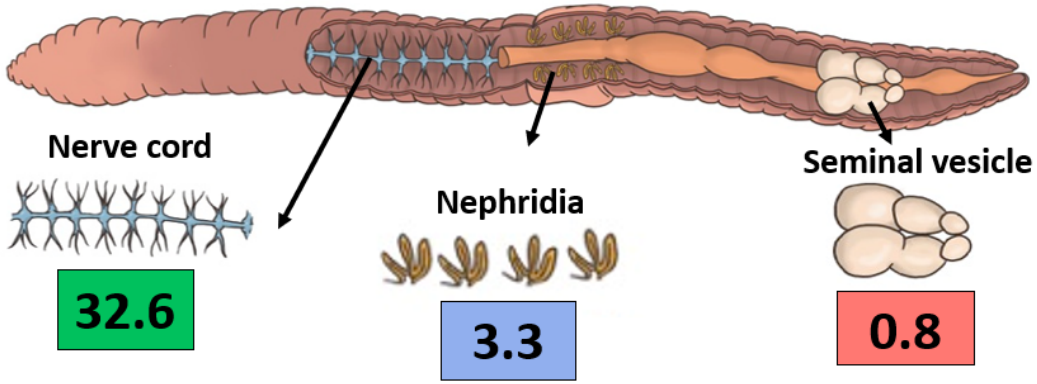


nAChR - target



AChBP – 'sponge'





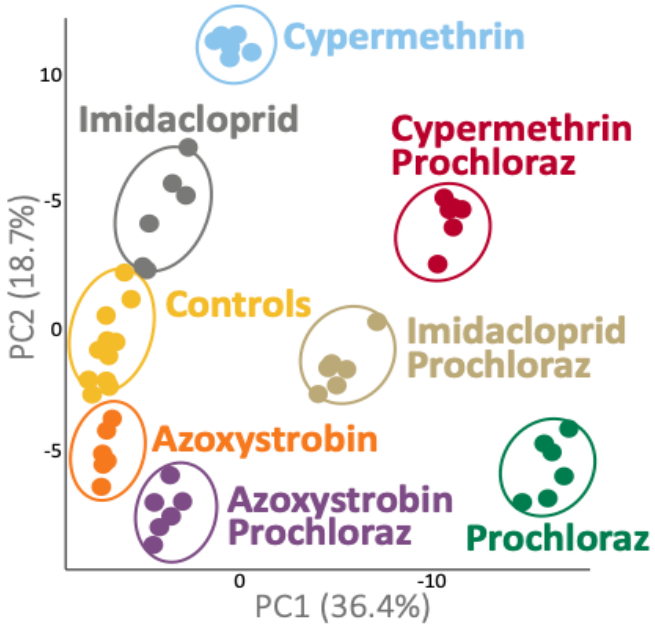
- High v low affinity 'sponge' in the nervous system aligns with 30x difference in sensitivity.

Recommendation: this is not a unique example. We must explore the role of off-targets for the chemicals presenting the highest environmental toxic burden.

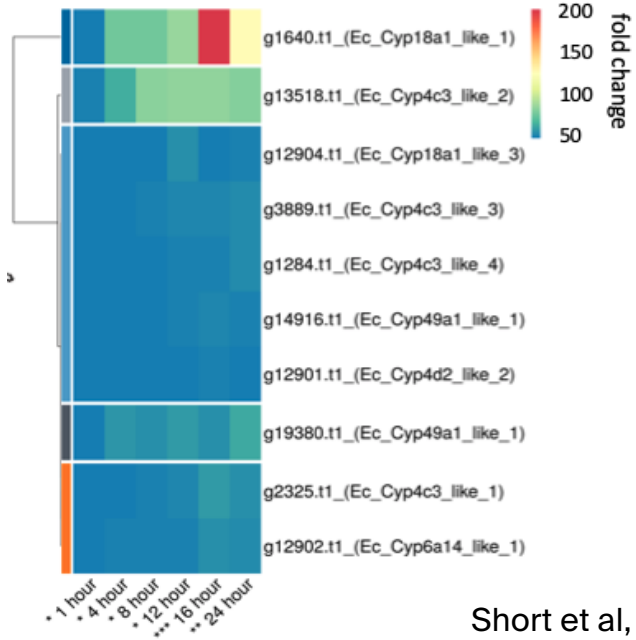
Finding genes that drive detoxification across critical invertebrates.

- What's the equivalent of human CYP3A4 genes in annelids?

RNASeq to sub-lethal exposures.



Finding CYP450 gene up-regulated across compounds: CYP18a1_like_1.



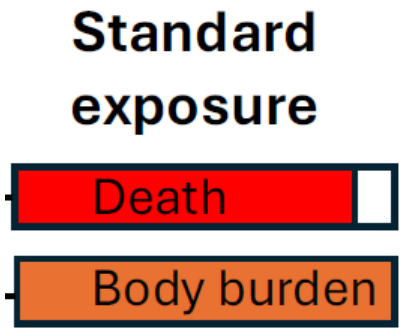


Short et al, paper in prep

Recommendation: make genomes more predictive: find genes driving detoxification across diverse taxa (we are doing this with insects).

The predictive power of knowledge: how to exploit CYP18a1.



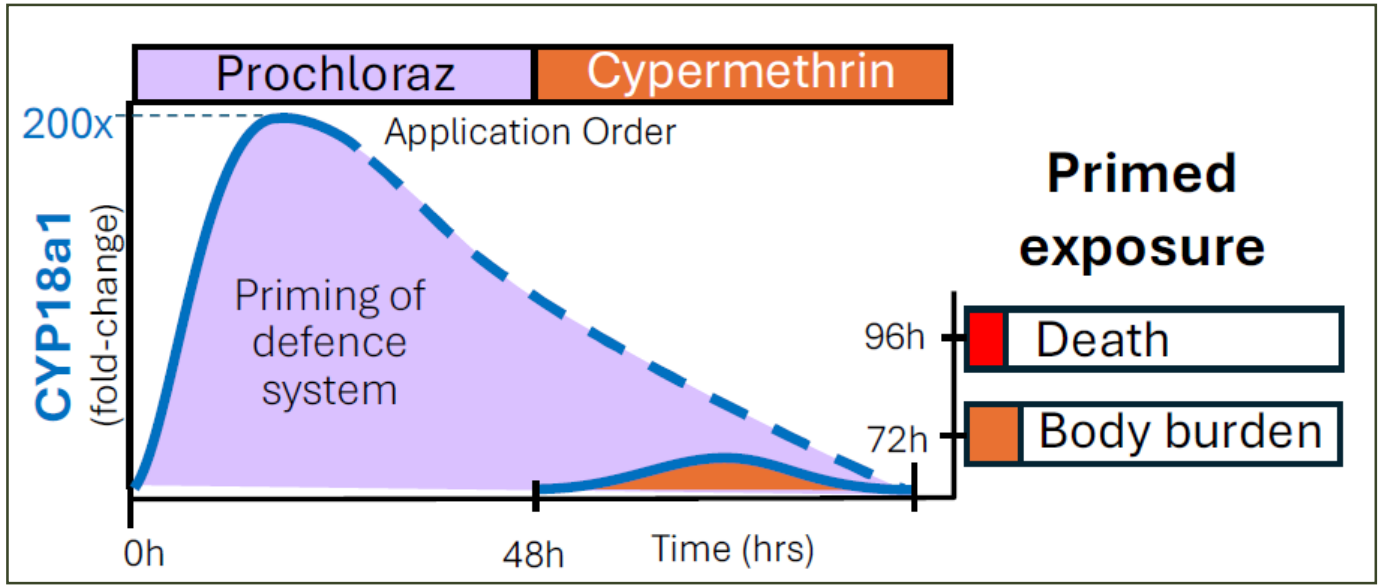


Cypermethrin - highly toxic insecticide that induces (~30x) expression of the CYP18a1.

Prochloraz (low toxicity) inhibits CYP450s, co-exposure increases cypermethrin toxicity (synergy).

But prochloraz also massively induces (100x fold) CYP18a1. <u>But this induction takes hours</u>.

<u>Hypothesis</u>: prochloraz pre-exposure (allowing CYP18a1 induction) protects against cypermethrin.



Data generated by Emily Eagles (UKCEH).

Close sequencing gaps - lobby for genomes (and basal transcriptomes) for ‘environmental species’.

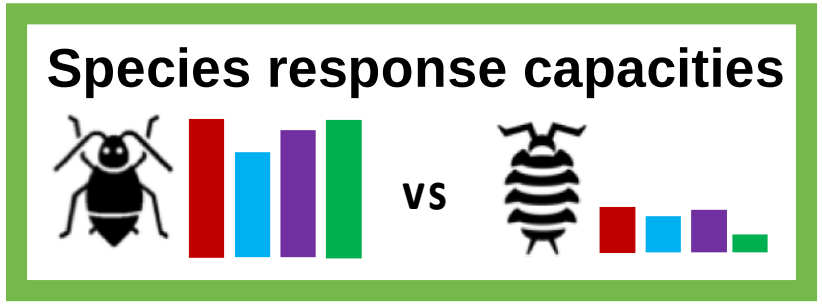
Expand and develop bioinformatic (user friendly) tools, turning knowledge/data into predictions.

Test mechanisms of action (i.e., target receptor) assumptions - increasing power of (current and future) receptor-chemical interaction prediction software, and (by extension) genomes.

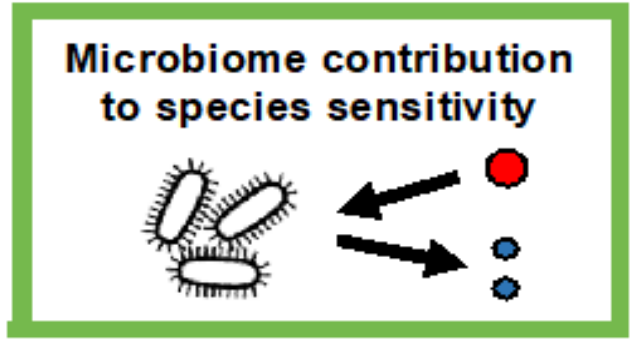
Identify off-target receptors and characterize roles in mediating toxicity.

Identify ‘core set’ of xenometabolic genes across invertebrates.

Further functional knowledge of sensitivity: unexplored mechanistic insights.



Stanton-Geddes et al (2016) Thermal reactionomes reveal divergent responses to thermal extremes in warm and cool-climate ant species. BMC Genomics 2016, 17, 171.



Theys et al (2025) The Gut Microbiome Causally Contributes to Interspecific Differences in Pesticide Sensitivity. Environ Sci Technol 2025, 59 (22), 10879–10890.

If we are to *'mostly rely on a mechanistic understanding of toxicity'*, we must do more than validate (nearly) existing NAMs.

Recommended actions for human health and environmental assessments

1. **Short-term actions** – *available approaches for which the process of implementation into regulatory practice, including by omitting redundant tests, can be launched immediately or within a short timeframe.*

2. **Medium-term actions** – *approaches for which further steps for validation or regulatory adaptation are required. After finalising required steps, approaches will be implemented immediately when deemed acceptable for wider use in a given regulatory context.*

3. **Long-term actions** – *redefining scientific safety assessment frameworks and performance criteria for future non-animal approaches. Long-term actions include the need to develop further approaches, to be implemented in a given regulatory context when deemed acceptable. Work on a new scientific safety assessment framework will start immediately as a core activity for implementing this roadmap.*

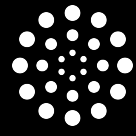
Opinion: For invertebrates (at least), realising the roadmap requires notable 'grass roots' research into mechanistic chemical sensitivity – to feeding ever improving NAMs/omic prediction from the bottom up.

For the environment, NAMs will need validating against population consequences – that's if NAMs need to improve on currently established methods. So, if NAMs are to be truly protective of the environment, they will require a somewhat different development/validation process.

Thank you for listening.

The data presented represents the hard work of many people:

Amaia Green Etxabe	UK Centre for Hydrology and Ecology
Emily Eagles	UK Centre for Hydrology and Ecology
Ivy Ng'iru	UK Centre for Hydrology and Ecology
Melanie Gibbs	UK Centre for Hydrology and Ecology
Alex Robinson	UK Centre for Hydrology and Ecology
Dave Spurgeon	UK Centre for Hydrology and Ecology
Bruno Campos	Unilever PLC
Claudia Rivetti	Unilever PLC
Rama Krishnan	Cardiff University, UK
Peter Kille	Cardiff University, UK
Angela Marchbank	Cardiff University, UK



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