# *Effects of pharmaceuticals in aquatic environments – bridging the gap between lab and field*

Prof. Tomas Brodin - Chair of Aquatic Ecology
Department of Wildlife, Fish, and Environmental Studies - SLU, Umeå, Sweden

@DrBrodin

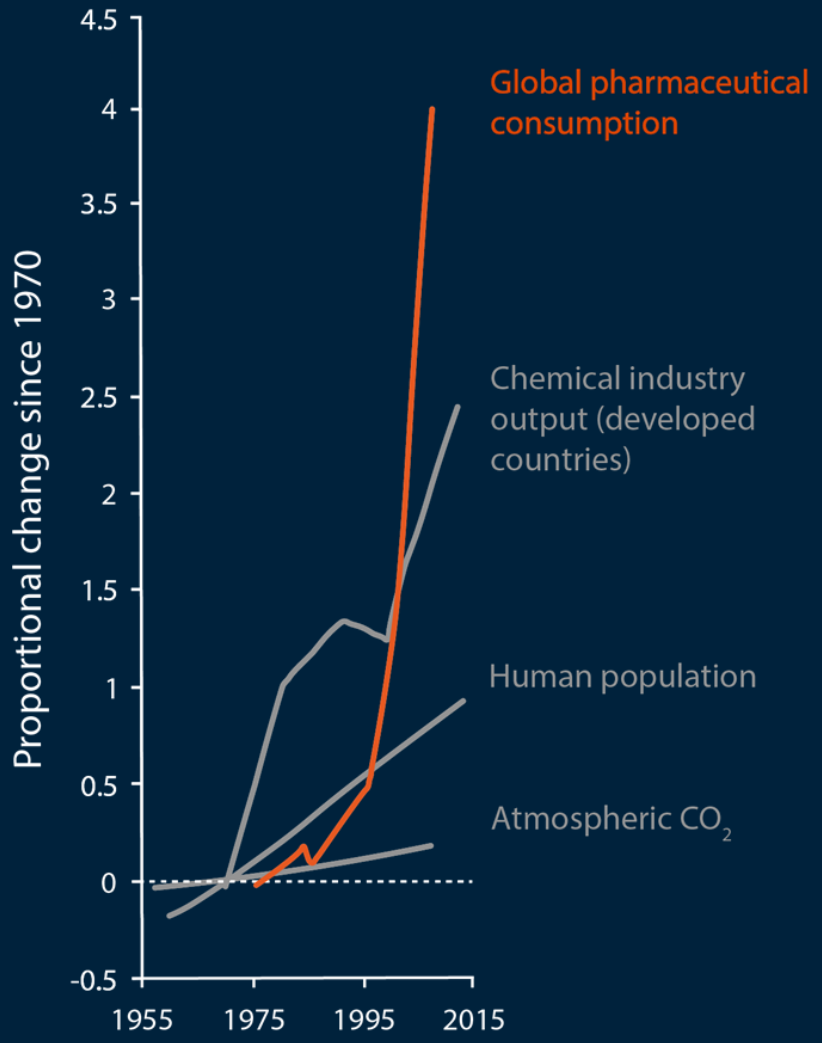
# Pharmaceutical pollution
## poses a global threat


104 countries

Only **2 rivers** had no detections

**25 %** had **harmful levels** of **pharmaceuticals**

Wilkinson et al. 2022 Proc Nat Acad Sci



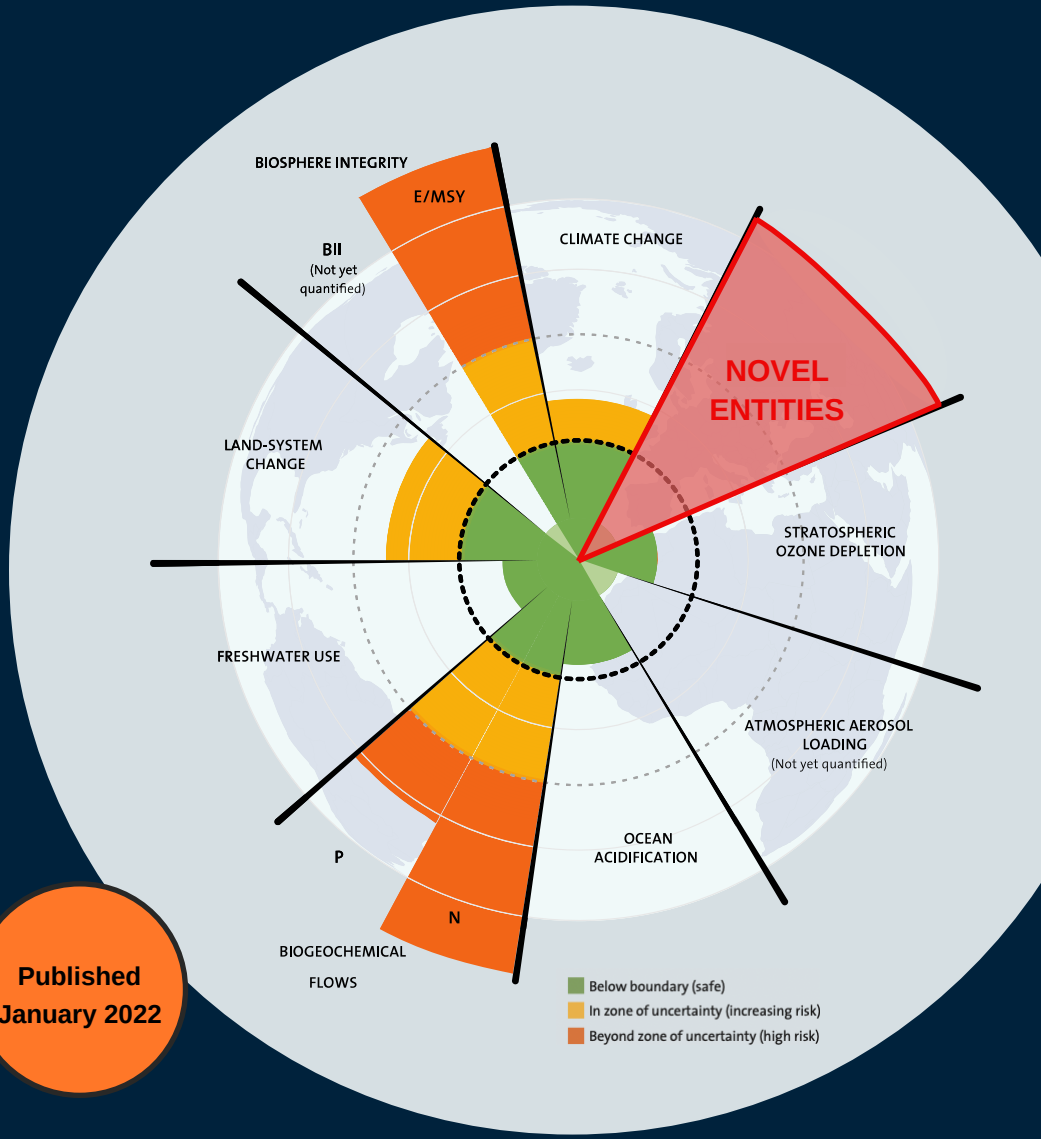

# Rate of production & release far outpacing ability to assess safety

Bernhardt et al. 2017 Front Ecol Env

# Planetary boundary passed

Recently proposed that the safe operating space for the planetary boundary of novel entities is exceeded

Annual production and releases are increasing at a pace that outstrips the global capacity for assessment and monitoring



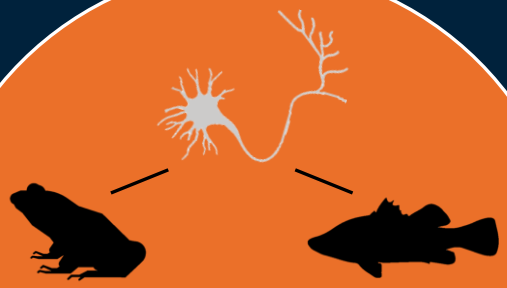

**Published January 2022**

(Persson et al. *Environ. Sci. Technol.* 2022)

SLU
Sveriges lantbruksuniversitet
Swedish University of Agricultural Sciences

Designed to have biological effects at low doses

Persistent in the environment



Drug targets evolutionarily conserved across phyla

Bioaccumulate in organisms and can biomagnify in food chains

# Ecological effects

Oriental white-backed vultures (*Gyps bengalensis*) scavenged livestock carcasses contaminated with diclofenac in India and Pakistan

Population decline of ~99.7%, beginning in the 1990s

(Oaks et al. *Nature* 2004)

Sveriges lantbruksuniversitet
Swedish University of Agricultural Sciences

# Ecological effects

Intersexuality in wild populations of riverine roach (*Rutilus rutilus*) throughout the UK due to hormonally active pharmaceuticals in wastewater

~1/4 of roach in UK rivers show signs of sex-reversal

(Jobling et al. *Environ. Sci. Technol.* 1998; Tyler and Jobling *BioScience* 2008)

Complete sex-reversal (masculinisation) of zebrafish (*Danio rerio*)

(Larsen and Baatrup *Environ. Toxicol. Chem.* 2010)

Depressed reproductive behaviour in female eastern mosquitofish (*Gambusia holbrooki* )

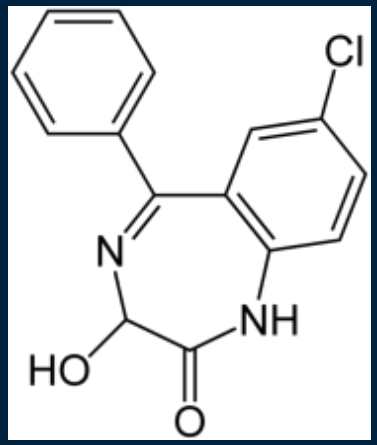
(Saaristo et al. *PLoS ONE* 2013)

Altered mating tactics in male guppies (*Poecilia reticulata*)

(Bertram et al. *Horm. Behav.* 2015)

# Benzodiazepines

- Discovered in 1955, sold since 1960
- Class of 20-25 pharmaceuticals
- Approx. 300 tonnes/year globally
- Used to treat anxiety, muscle cramps, sleeping disorders and used as a sedative.




Oxazepam

# Ecological effects

Wild European perch (*Perca fluviatilis*) exposed to field-realistic levels of the anti-anxiety drug oxazepam

Increased activity, reduced sociality, increased feeding

(Brodin et al. *Science* 2013)

# Ecological effects

Wild European perch (*Perca fluviatilis*) exposed to field-realistic levels of the anti-anxiety drug oxazepam

Increased activity, reduced sociality, increased feeding

What does this mean?

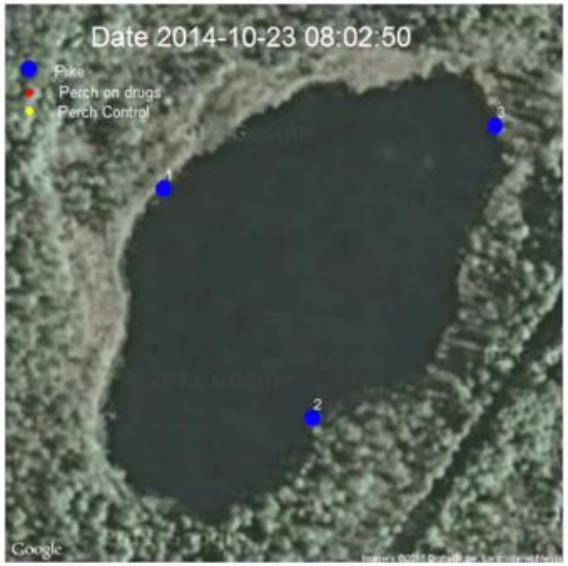
Growth increased with 16% over summer

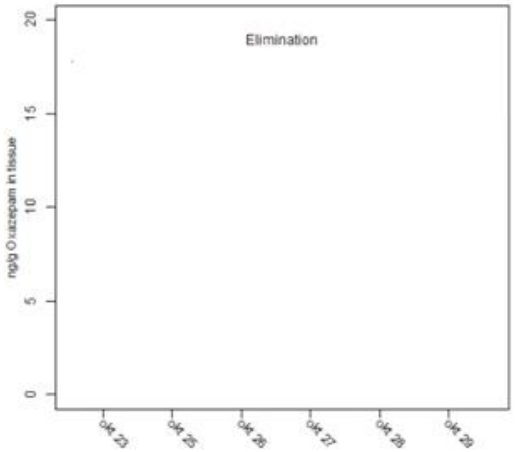
Risk of being eaten increased

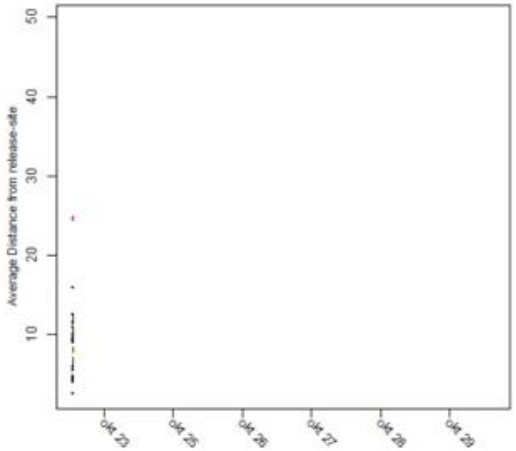
(Brodin et al. *Science* 2013)

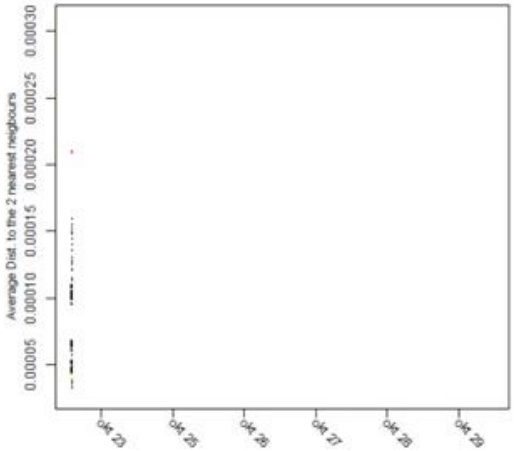
Oxazepam

Control



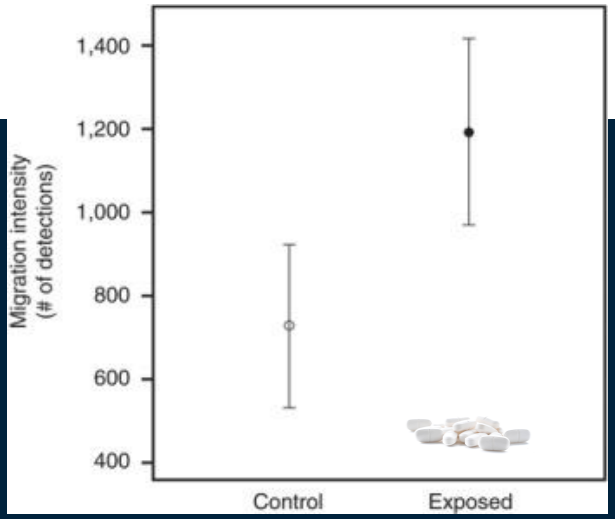



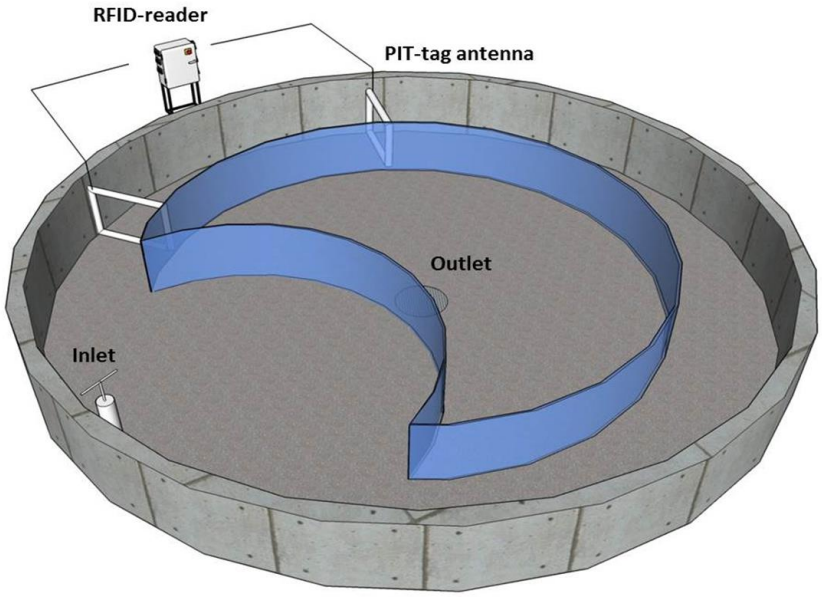




Klaminder et al. 2016

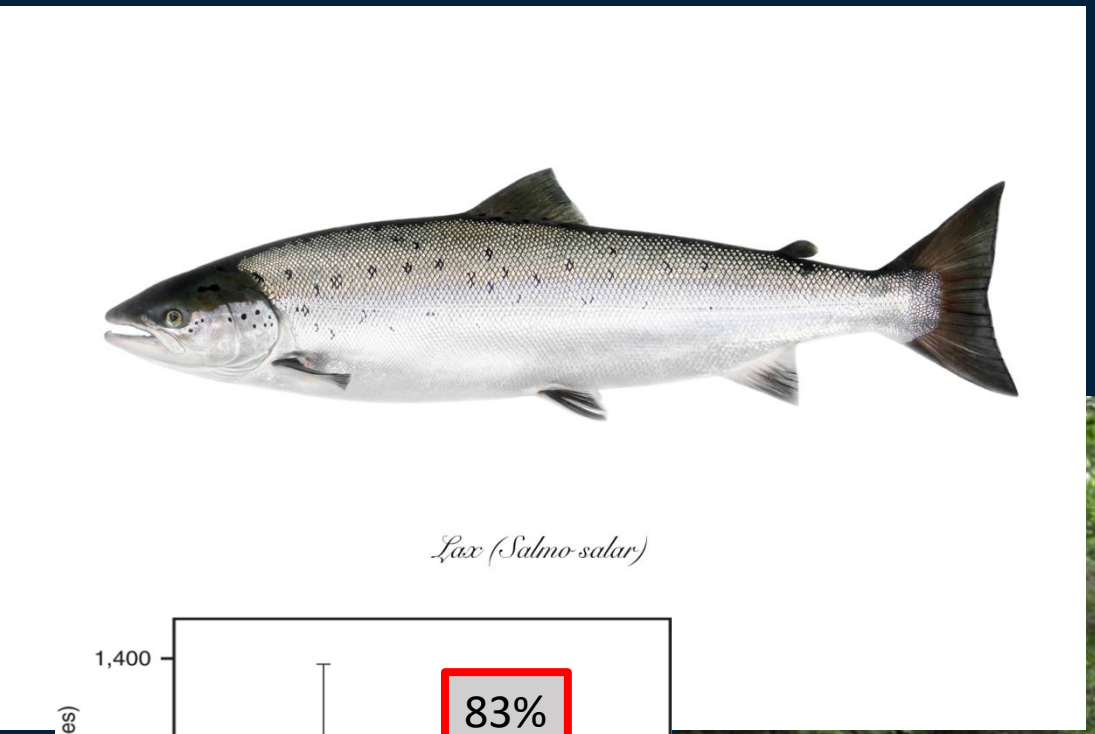
# Effects on salmon migration - lab

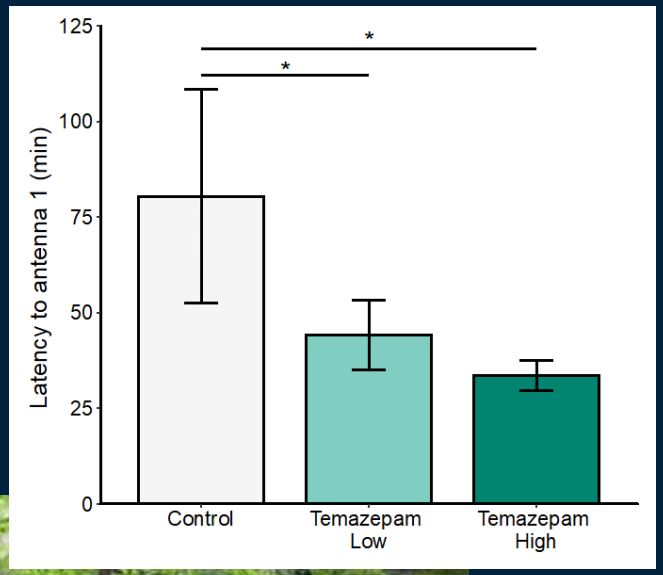
*Lax (Salmo salar)*

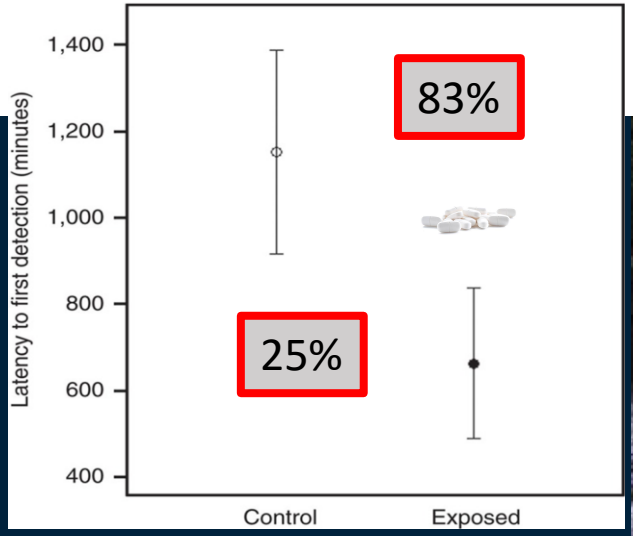


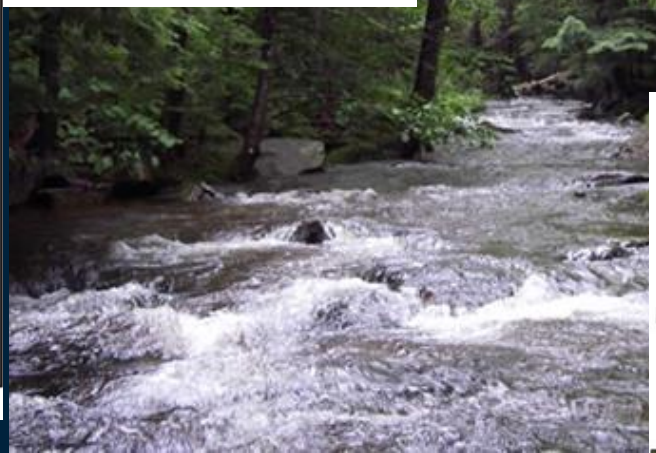



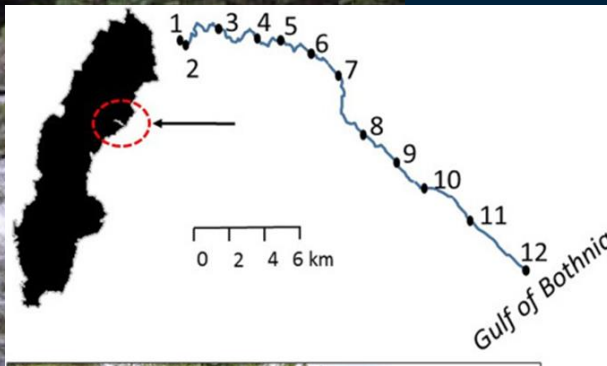
# Effects on salmon and trout migration - field



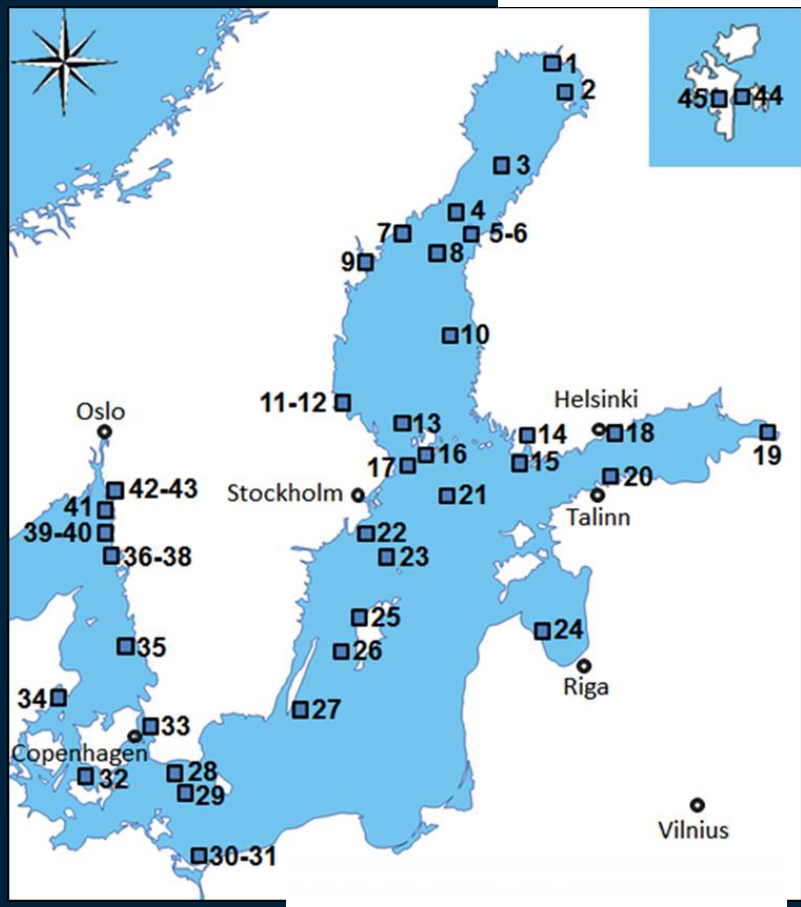


# Where do exposed salmon end up?

Eaten by pike and large perch in the river.

# Where in the environment?

Bonefish


Cod

100% of bonefish, average = 7

53 pharmaceuticals:
Heart, psychoactive & antihistamines

52.7% exceed human threshold

Present in remote areas

N = 134

94% of redfish, average = 2

17 pharmaceuticals:
Heart, pain killers & psychoactive

25.7% exceed human threshold

Present in small cities

N = 103

# Ecological effects of pharmaceuticals

- Direct mortality – e.g. diclofenac
- Changed reproductive physiology – all female populations due to EDC
- Behavioural effects – activity, sociality, boldness, migration
- Ecological effects – larger home-range, changed habitat use
- Secondary effects – reduced growth, reduced reproduction, higher mortality
- Ecosystem effects – changed productivity, stability

**Thank you for listening**

**and thanks to:**

Vetenskapsrådet

**Kempestiftelserna**

formas The Swedish Research Council Formas

WALLENBERGSTIFTELSERNA
*stödjer svensk forskning*

Bonefish & Tarpon TRUST

Nobelmuseet

Stiftelsen för Strategisk Forskning

# This is us!

Tomas Brodin

Gustav Hellström

Jerker Fick

Erin McCallum

Michael Bertram

Marcus Michelangeli

Johan Fahlman
Johan Leander

Jonatan Klaminder

Daniel Cerveny

Aneesh Bose

Jake Martin

Sara Gronlund

# Pharmaceuticals in the environment

~6.3 trillion doses p.a.

~5000 products on the market

>600 pharmaceutical substances detected in the environment

Reported across 104 countries spanning all continents

Sveriges lantbruksuniversitet
Swedish University of Agricultural Sciences

# Issues with lab-bred model organisms

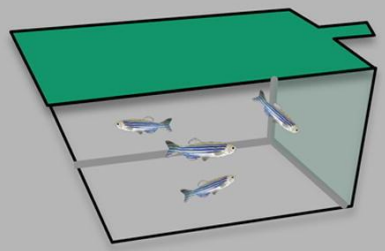
wild-caught zebrafish

Response to alarm pheromone:

control: strong response
exposed: reduced response

oxazepam 7 days

laboratory zebrafish



control: no response
exposed: no response

Vossen et al. 2020

Environmental Science & Technology

pubs.acs.org/est

Perspective

# The Role of Behavioral Ecotoxicology in Environmental Protection

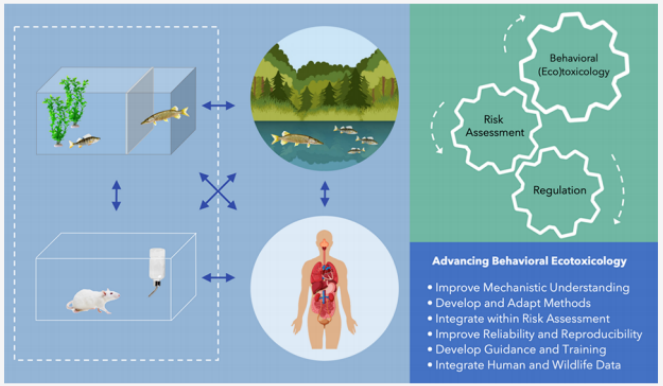
Alex T. Ford,* Marlene Ågerstrand, Bryan W. Brooks, Joel Allen, Michael G. Bertram, Tomas Brodin, ZhiChao Dang, Sabine Duquesne, René Sahm, Frauke Hoffmann, Henner Hollert, Stefanie Jacob, Nils Klüver, James M. Lazorchak, Mariana Ledesma, Steven D. Melvin, Silvia Mohr, Stephanie Padilla, Gregory G. Pyle, Stefan Scholz, Minna Saaristo, Els Smit, Jeffery A. Steevens, Sanne van den Berg, Werner Kloas, Bob B.M. Wong, Michael Ziegler, and Gerd Maack

Cite This: https://doi.org/10.1021/acs.est.0c06493

Read Online

ACCESS | Metrics & More | Article Recommendations

**ABSTRACT:** For decades, we have known that chemicals affect human and wildlife behavior. Moreover, due to recent technological and computational advances, scientists are now increasingly aware that a wide variety of contaminants and other environmental stressors adversely affect organismal behavior and subsequent ecological outcomes in terrestrial and aquatic ecosystems. There is also a groundswell of concern that regulatory ecotoxicology does not adequately consider behavior, primarily due to a lack of standardized toxicity methods. This has, in turn, led to the exclusion of many behavioral ecotoxicology studies from chemical risk assessments. To improve understanding of the challenges and opportunities for behavioral ecotoxicology within regulatory toxicology/risk assessment, a unique workshop with international representatives from the fields of behavioral ecology, ecotoxicology, regulatory (eco)toxicology, neurotoxicology, test standardization, and risk assessment resulted in the formation of consensus perspectives and recommendations, which promise to serve as a roadmap to advance interfaces among the basic and translational sciences, and regulatory practices.



# Pharmaceutical pollution and behaviour

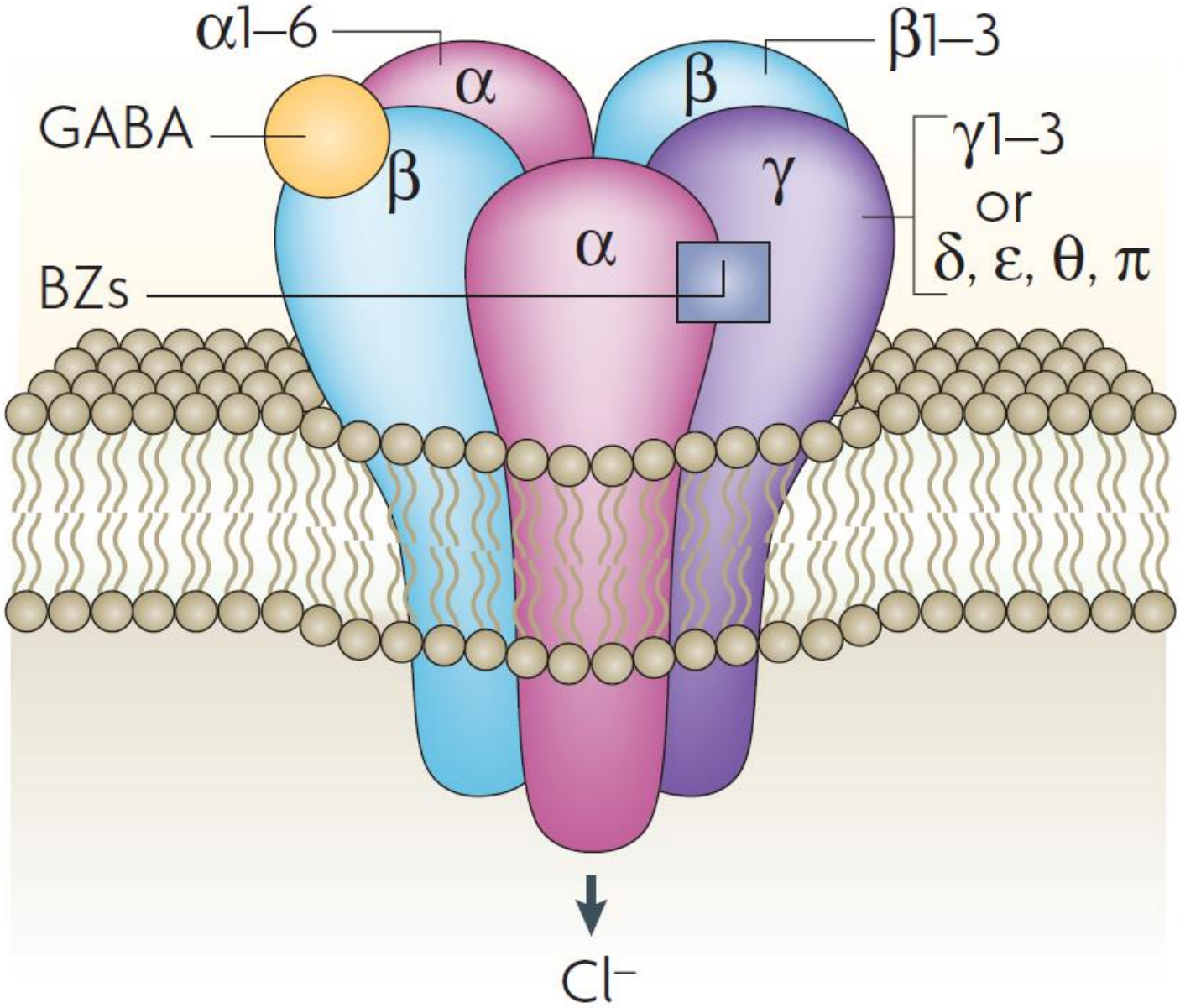
Generally, more sensitive than conventional endpoints

Link between physiological processes and the environment

Fundamental to the ecology of individuals, and the evolution of populations and species

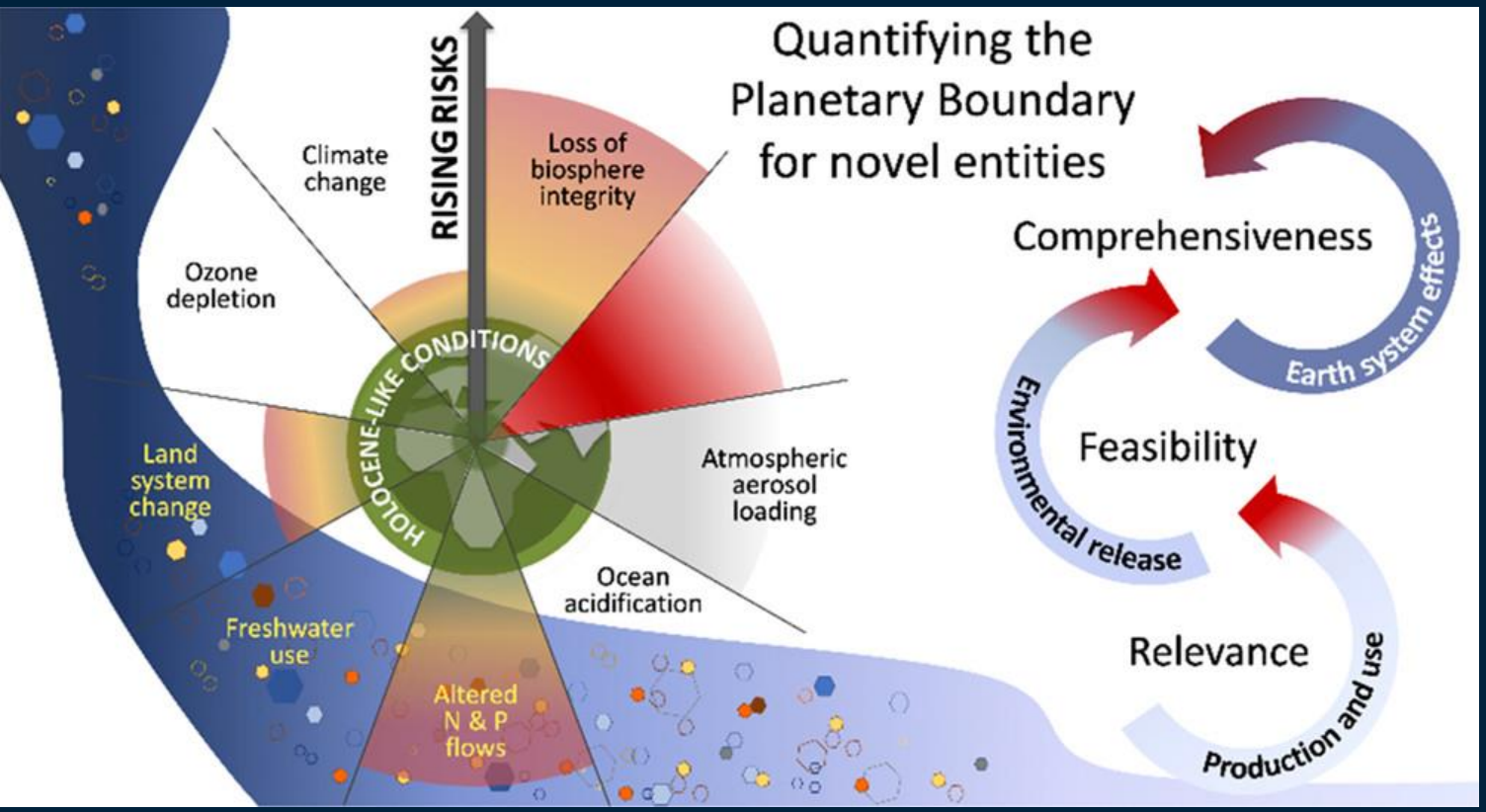
Has received relatively little attention

SLU
Sveriges lantbruksuniversitet
Swedish University of Agricultural Sciences




Jacob et al NRN 2008

# Safe operating space for novel entities is exceeded




Persson et al. 2022
Environ Sci Technol