Endocrine Disruption in Wildlife

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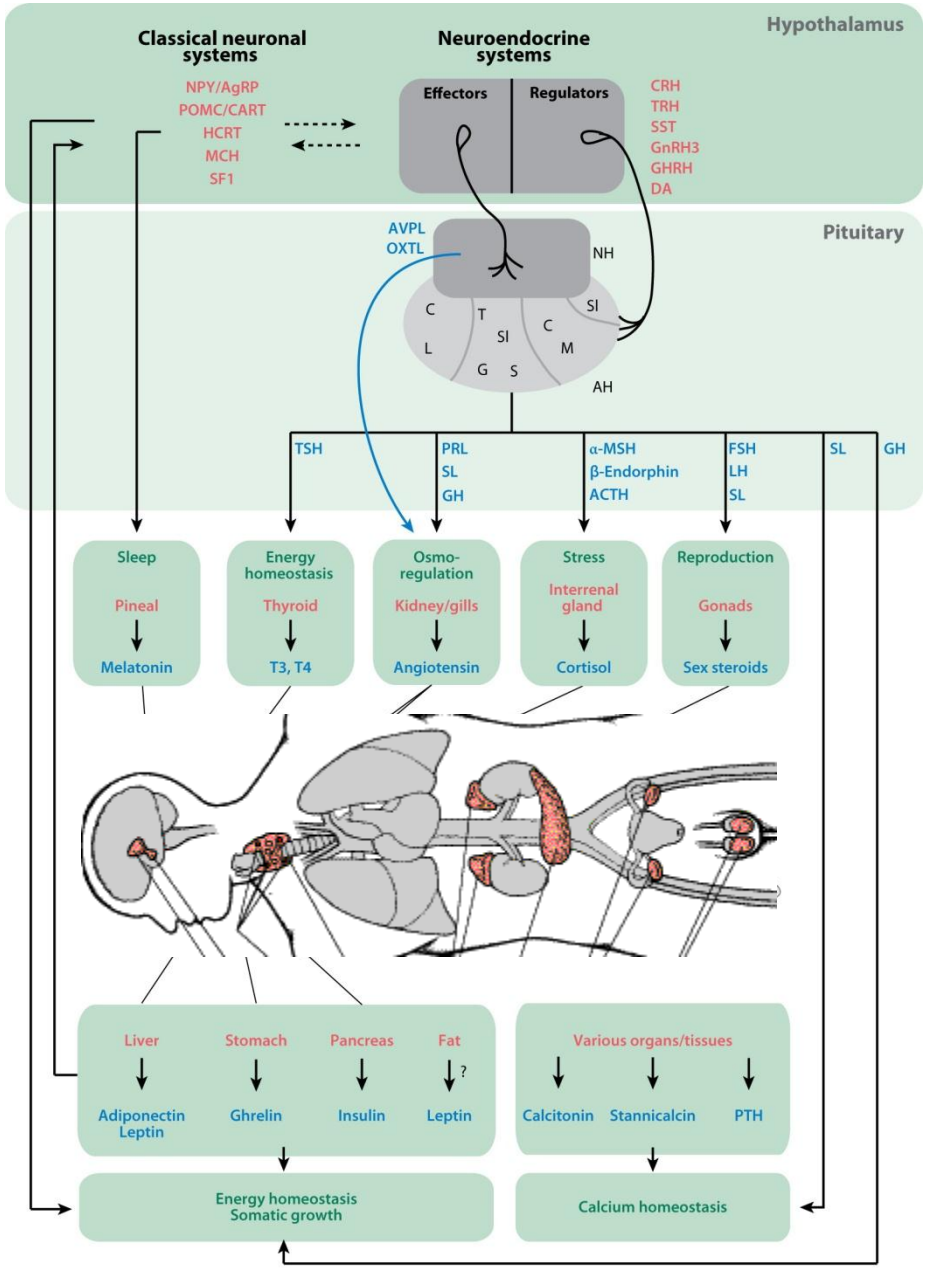
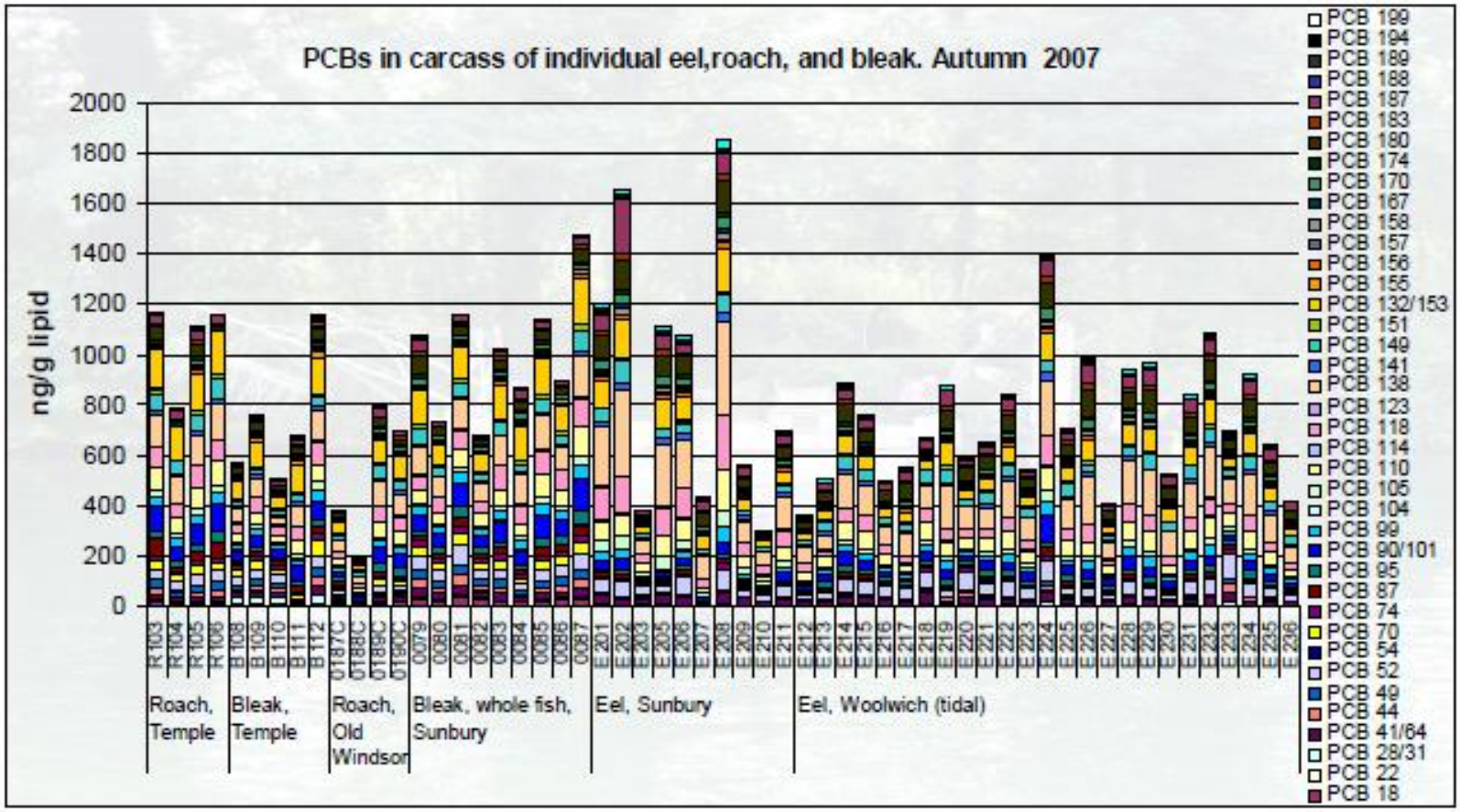
Comparative Endocrinology of Humans and Wildlife



Löhr H, Hammerschmidt M. 2011.
Annu. Rev. Physiol. 73:183–211

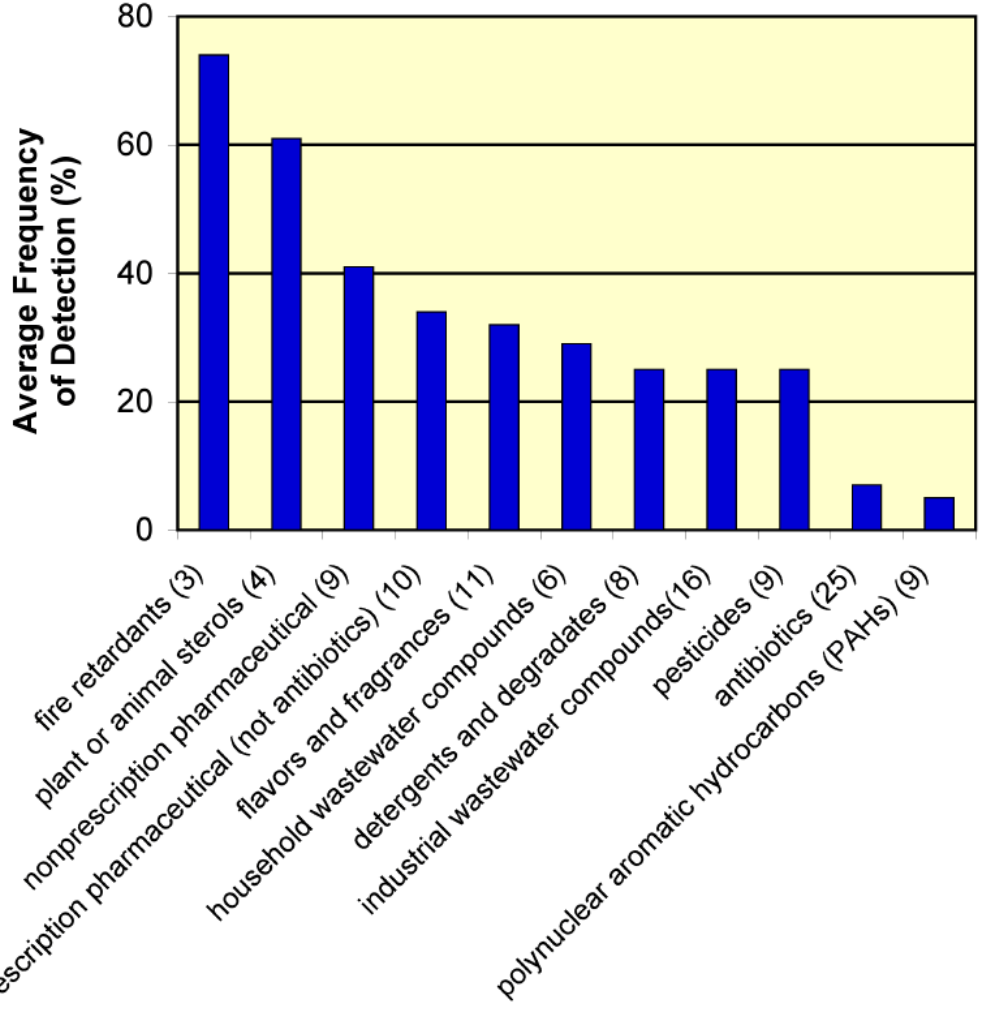
EDCs are found in Wildlife



Some of the first results from individual fish show PCBs, banned in the UK in 1981, can still be found in three species of fish collected from the River Thames in 2007

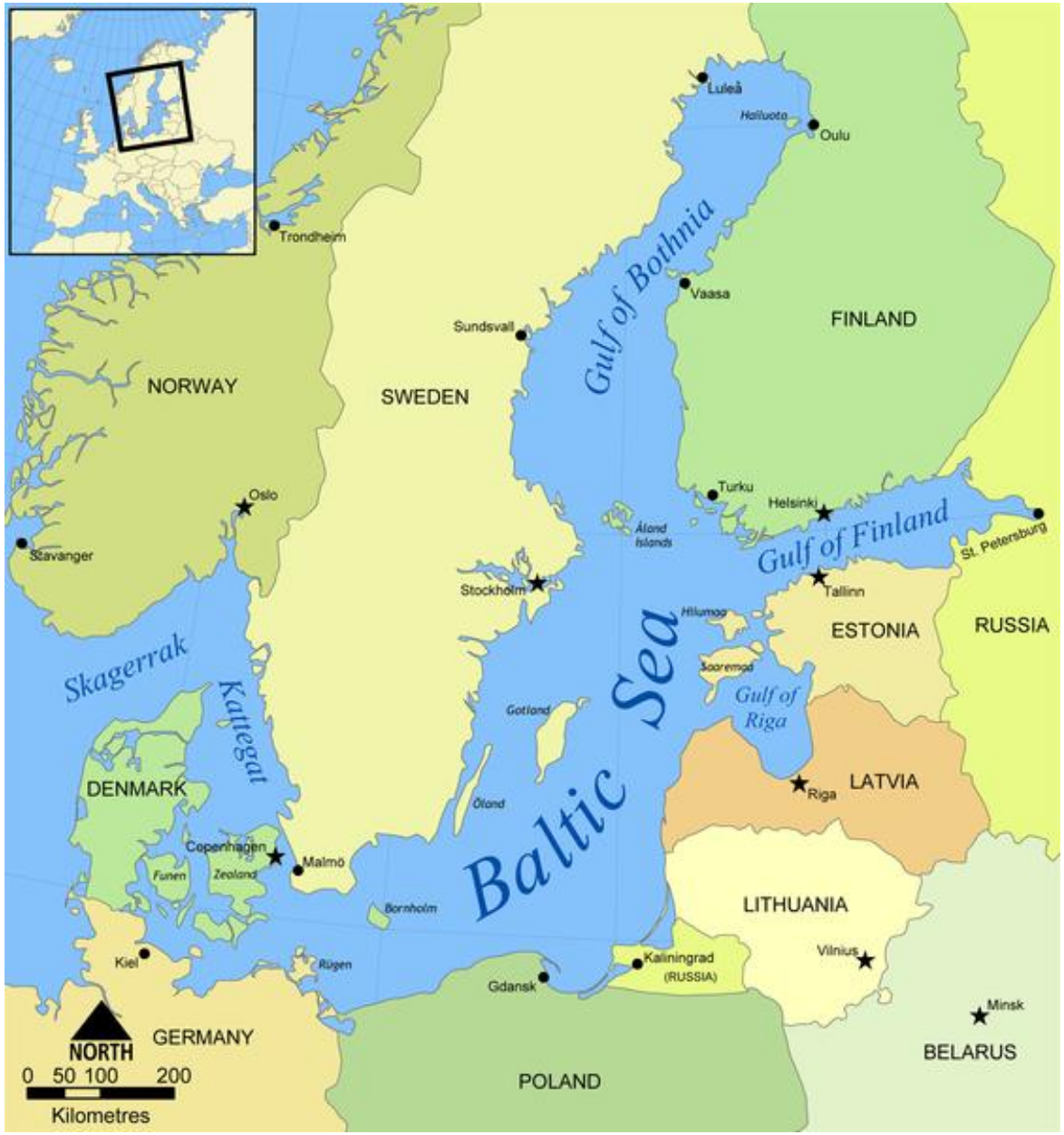
Fish Name	Maximum Servings That Can Be Safely Eaten Each Month				Health Risk
	WOMEN	MEN	OLDER KIDS	YOUNG KIDS	
Alewife	0	0	0	0	PCBs
Bass, striped (wild)	0	0	0	0	mercury, PCBs
Bluefish	0	0	0	0	mercury, PCBs
Croaker, white	0	0	0	0	PCBs
Eel, American	0	0	0	0	mercury, PCBs
Eel, European	0	0	0	0	PCBs
Shad	0	0	0	0	PCBs
Sturgeon, wild (imported)	0	0	0	0	mercury, PCBs
Tuna, bluefin	0	0	0	0	mercury, PCBs
Weakfish	0	0	0	0	mercury, PCBs
Mackerel, king	0	½	0	0	mercury
Marlin	0	1	0	0	mercury
Shark	0	1	0	0	mercury
Swordfish	0	1	0	0	mercury
Croaker, Atlantic	1	1	½	½	PCBs
Flounder, summer	1	1	½	½	PCBs
Flounder, winter	1	1	1	½	PCBs
Opah	1	1	1	½	mercury

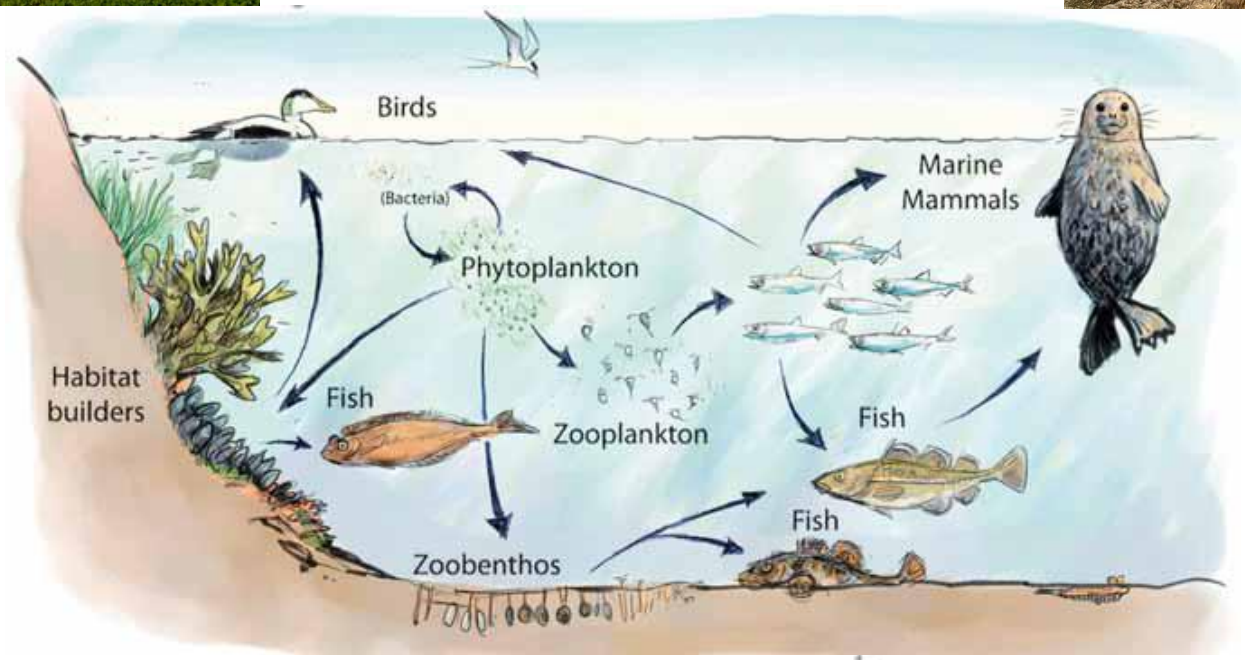
Chemicals in modern commerce in treated sewage effluents

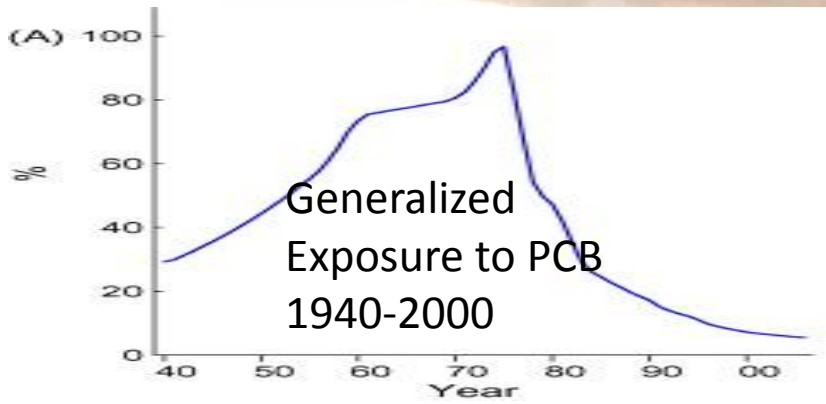


Evidence for effects of endocrine disrupting chemicals on wildlife populations

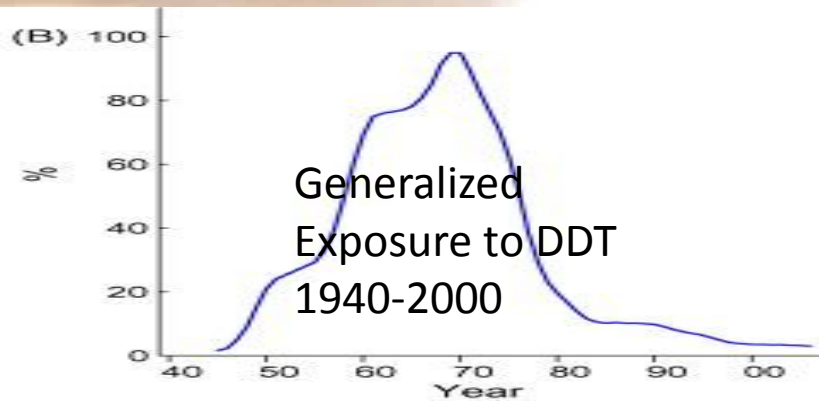
- Population declines in some wildlife populations associated with exposures to ecosystems contaminated with EDCs and other chemicals
- Endocrine disorders present in declining populations
- EDCs present in ALL populations
- Exposure to EDC chemicals in the laboratory caused endocrine disorders
- Body burdens of EDCs in some wildlife today at levels known to cause effects in lab studies or other wildlife


Luleå
Hailuoto
Oulu
Trondheim
Vaasa
FINLAND
Sundsvall
Gulf of Bothnia
NORWAY
SWEDEN
Turku
Helsinki
Oslo
Åland Islands
Gulf of Finland
St. Petersburg
Stavanger
Stockholm
Tallinn
Hiiumaa
ESTONIA
RUSSIA
Skagerrak
Kattegat
Saaremaa
Gulf of Riga
Gotland
Baltic Sea
DENMARK
Öland
Riga
LATVIA
Copenhagen
Malmö
Funen
Zealand
LITHUANIA
Bornholm
Kiel
Rügen
Kaliningrad (RUSSIA)
Vilnius
Gdansk
Minsk
BELARUS
NORTH
GERMANY
0 50 100 200
Kilometres
POLAND





Generalized
Exposure to PCB
1940-2000



Generalized
Exposure to DDT
1940-2000

Abnormalities of the uterus in the grey seal at the peak of PCB and DDT exposures

(Bergman and Olsson, 1986; Bergman, 1999; Backlin, Bredhult and Olovsson 2003).

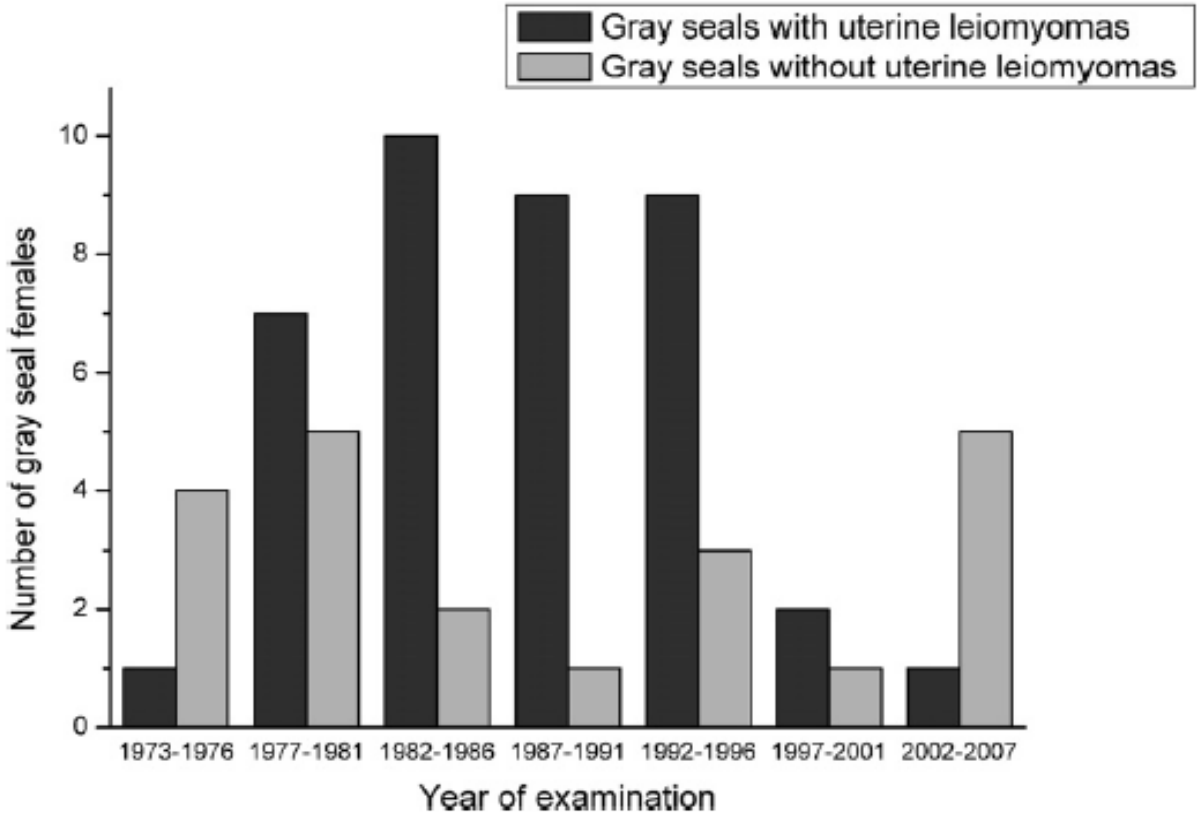
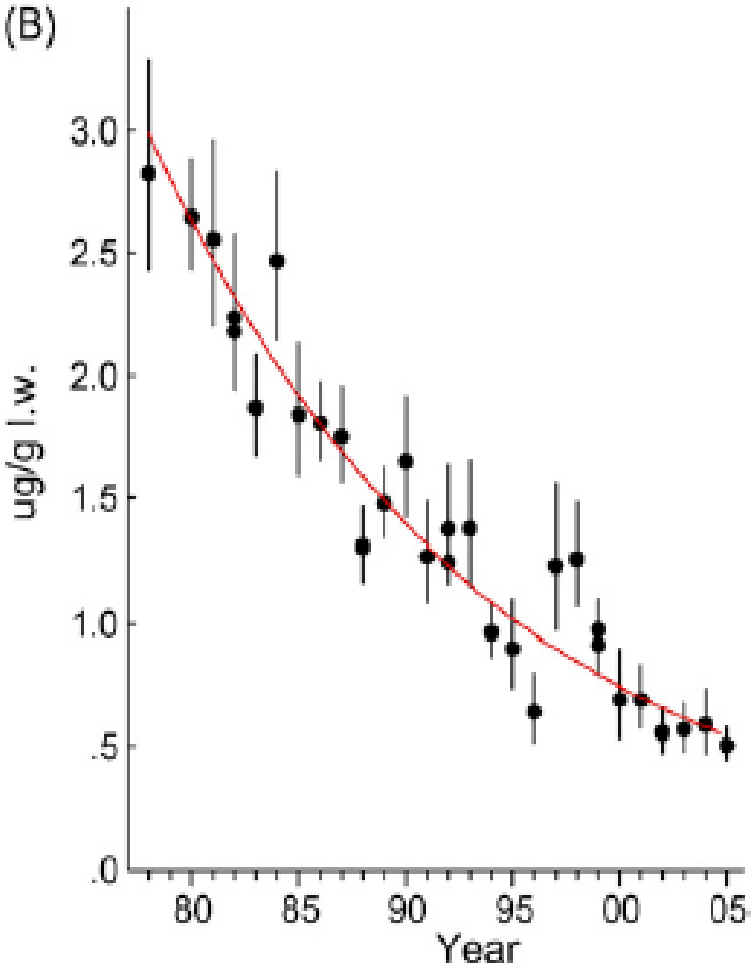
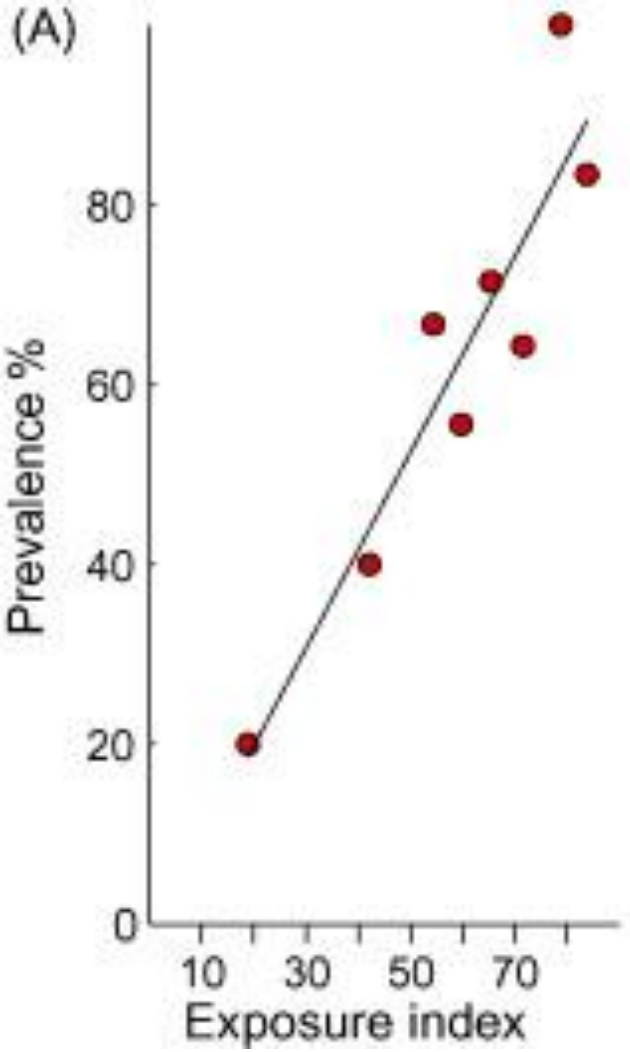


Fig. 2. Prevalence of uterine leiomyomas in Baltic gray seal females between 22 and 41 years of age.

Histology of Uterine Leiomyoma and Occurrence in Relation to Reproductive Activity in the Baltic Gray Seal (*Halichoerus grypus*)
B.-M. Bäcklin, L. Eriksson and M. Olovsson
Vet Pathol 2003 40: 175

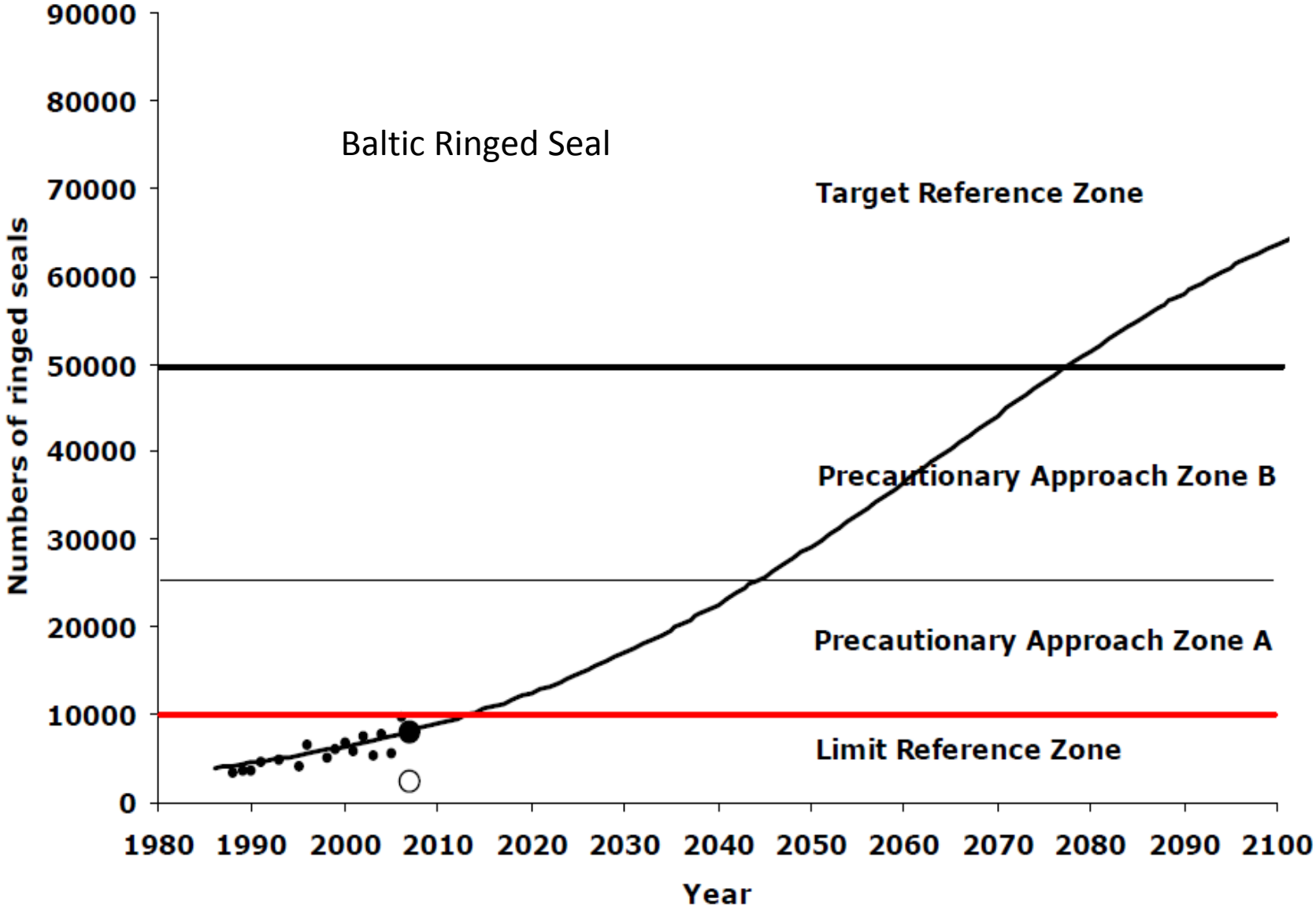




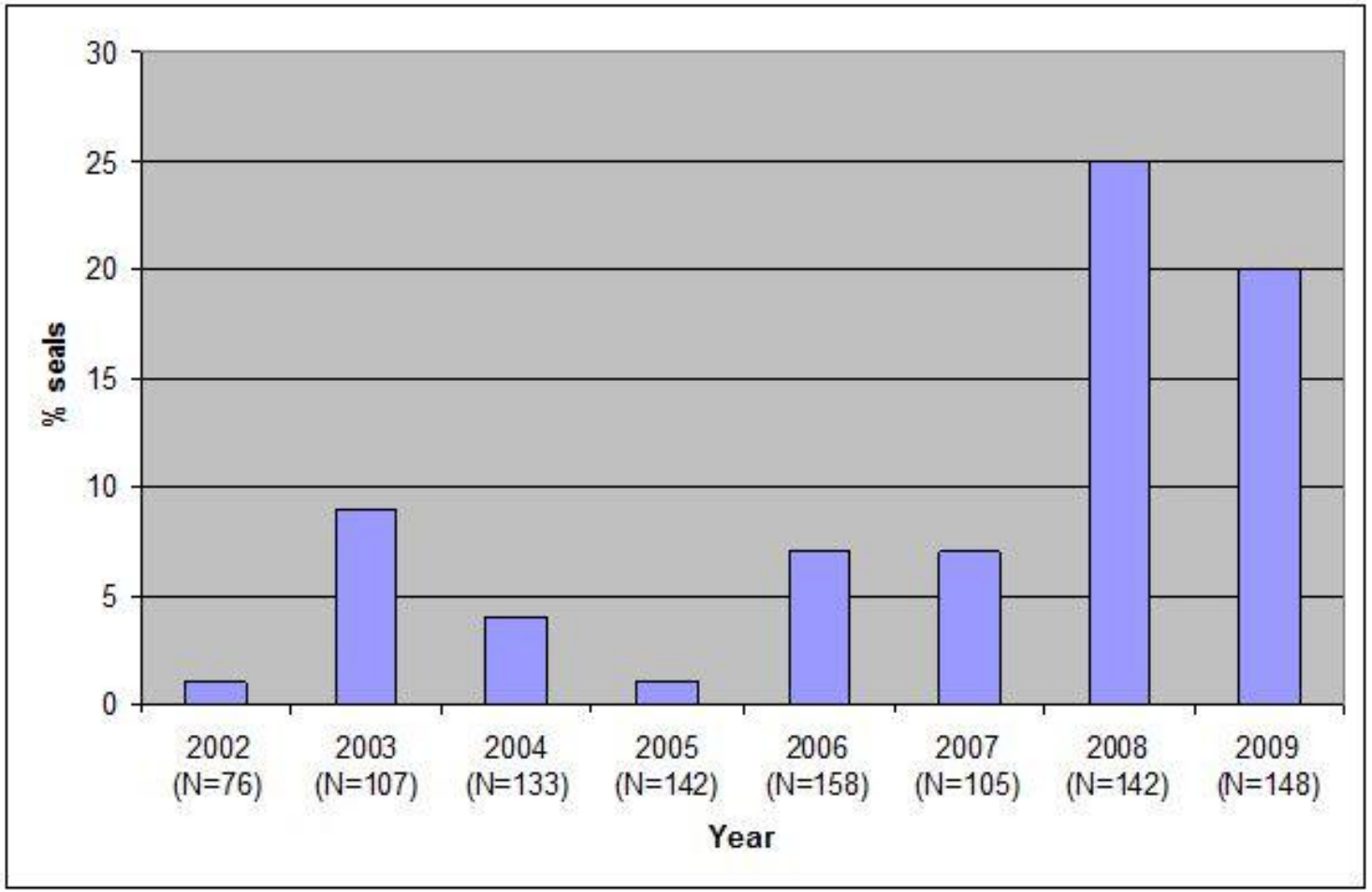
Study of the relation between the incidence of uterine leiomyomas and the concentrations of PCB and DDT in Baltic gray seals

Carolina Bredhult[a]. Britt-Marie Bäcklin[b]. Anders Bignert[b]. Matts Olovsson[a,*]

Reproductive Toxicology 25 (2008) 247–255


Baltic Ringed Seal
Target Reference Zone
Precautionary Approach Zone B
Precautionary Approach Zone A
Limit Reference Zone
Numbers of ringed seals
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
1980
1990
2000
2010
2020
2030
2040
2050
2060
2070
2080
2090
2100
Year

Liver flukes in “recovering seals”



Breeding success of white-tailed sea eagle 1964-2006

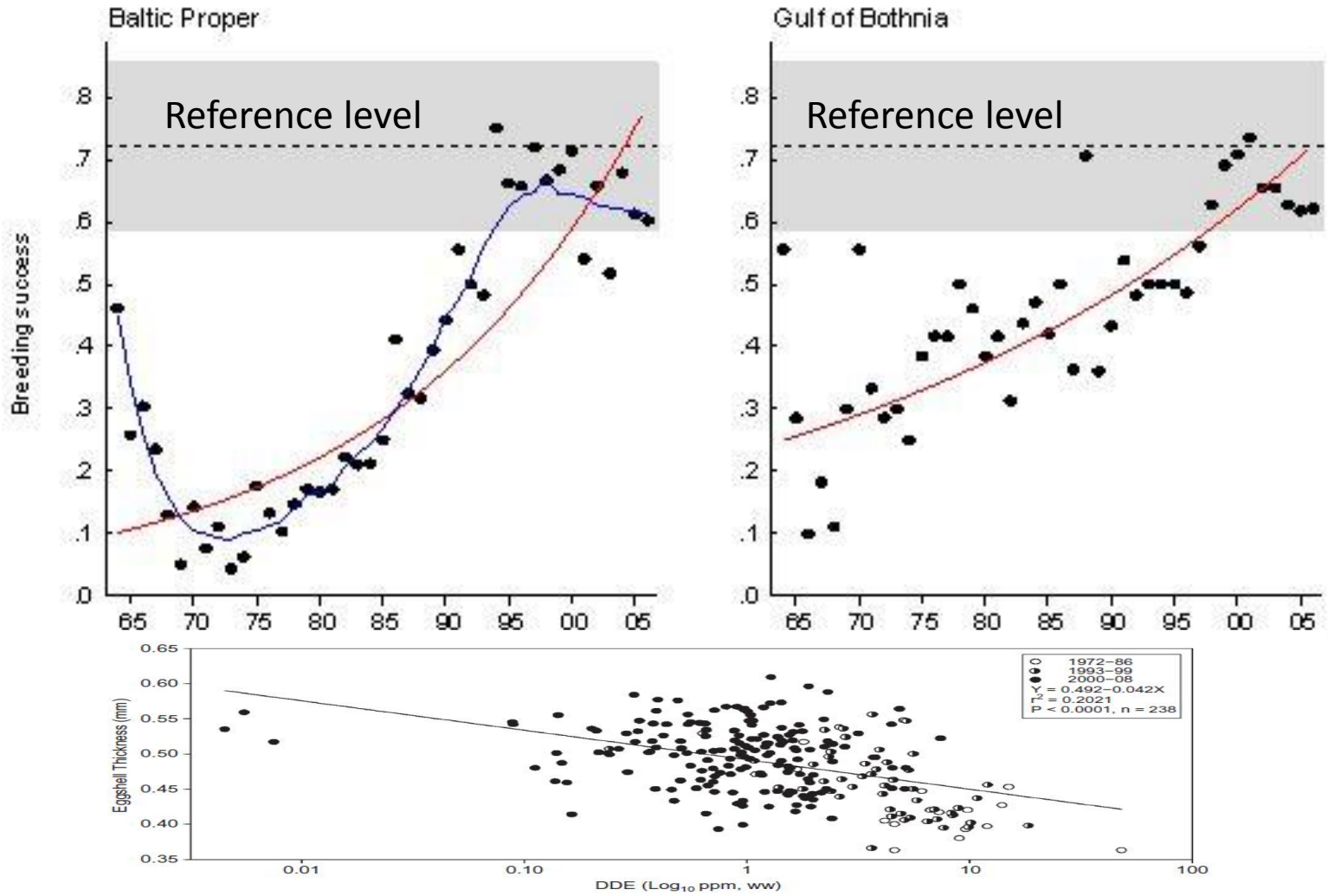


FIGURE 5. Semi-log relationship between DDE (ppm) and eggshell thickness (mm) using osprey eggs collected from the Pacific Northwest (OR, WA, ID), 1972–2008.

Recent advances strengthen the evidence for endocrine disrupting mechanism; e.g. egg shell thinning

- ***Eggshell thinning caused by exposure of adults through inhibition of prostaglandin synthesis in the shell gland mucosa and, as a consequence, calcium and bicarbonate transport is reduced (Lundholm 1993, 1997).***
- **Eggshell thinning results from a DEVELOPMENTAL structural and functional malformation in the shell gland and disrupted expression carbonic anhydrase (Berg et al.2001, Holm et al. 2001; Berg et al., 2004, Holm et al., 2006; Kamata et al., 2010; Kamata-Ryo et al., 2009) ALSO IN MICE**
- **Involvement of the estrogen receptor (Mattson et al ., 2011)**
- **Developmental effects occur at LOWER doses than the effects on adults**

Recent advances strengthen the evidence for endocrine disrupting mechanism; e.g. baltic seals

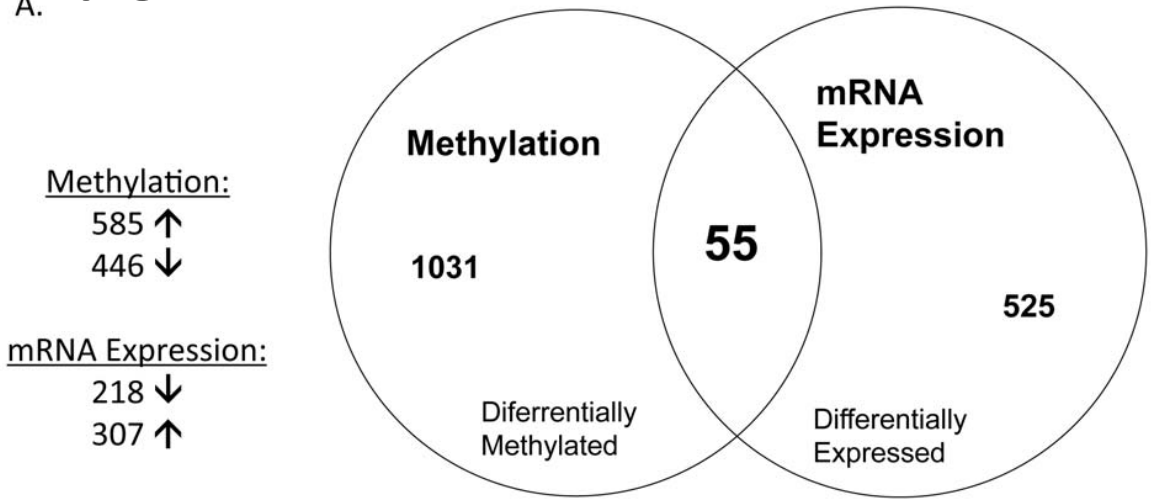
- PCB induced proliferation of myometrial cells **in seals** in vitro was INCONSISTENT (Backlin , Eriksson and Olovsson, 2003)
- Non reproducing seals …high levels of PR and ER, therefore more vulnerable
- **In humans:** In vitro proliferation in response to estrogen (othman and Al-hendy, 2008) and progesterone (Ishikawa et al., 2010) and EDCs Crain et al., 2008, Hodges et al., 2000, 2001)
- Steroid hormone levels the same **BUT** estrogen receptor concentrations higher in women with fibroids and normal women (Blake 2007; Okolo et al, 2008)
- CD-1 mice and Eker rats foetal exposures lead to increased risk in adulthood (Newbold et al.2007, Crain 2008)

2007- : integrated analysis of DNA microarray studies with human tissue, thirty-eight genes were found to be differentially expressed , twelve of which were identified as estrogen-regulated

5 receptors involved : ER,RAR, RXR, NR4A1, PPAR gamma

2012…Epigenetics involved in fibroid induction

A.



Where are we now?

- Wildlife are exposed to many chemicals in modern commerce that are known to interfere with hormone action in a similar way to persistent legacy EDCs like PCBs and OC pesticides

Mixtures of similarly acting EDCs can act in combination

(2005) Brian, JV. et al, Accurate prediction of the response of freshwater fish to a mixture of estrogenic chemicals, Environmental Health Perspectives 113 (6) : 721-728

(2007) Brian, JV et al., Evidence of estrogenic mixture effects on the reproductive performance of fish, International Journal of Environmental Science and Technology 41 (1) : 337- 344

(2007) Sumpter, JP. and Brian, JV., Mixtures of chemicals in water: implications of chemical legislation and environmental policy, The Journal of Water Law 18 (2) : 62-65

Effects of ethinylestradiol and of an environmentally relevant mixture of xenoestrogens on steroidogenic gene expression and specific transcription factors in zebrafish

R. Urbatzka [a,*], E. Rocha [a,b], B. Reis [a], C. Cruzeiro [a], R.A.F. Monteiro [b], M.J. Rocha [a,b,c]

[a] *Laboratory of Cellular, Molecular and Analytical Studies (LECEMA), Interdisciplinary Centre of Marine and Environmental Research (CIIMAR), CIMAR Associated Laboratory (CIMAR LA), University of Porto (U.Porto), Rua dos Bragas 289, 4050-123 Porto, Portugal*

[b] *Laboratory of Histology and Embryology, Institute of Biomedical Sciences Abel Salazar (ICBAS), University of Porto (U.Porto), Portugal*

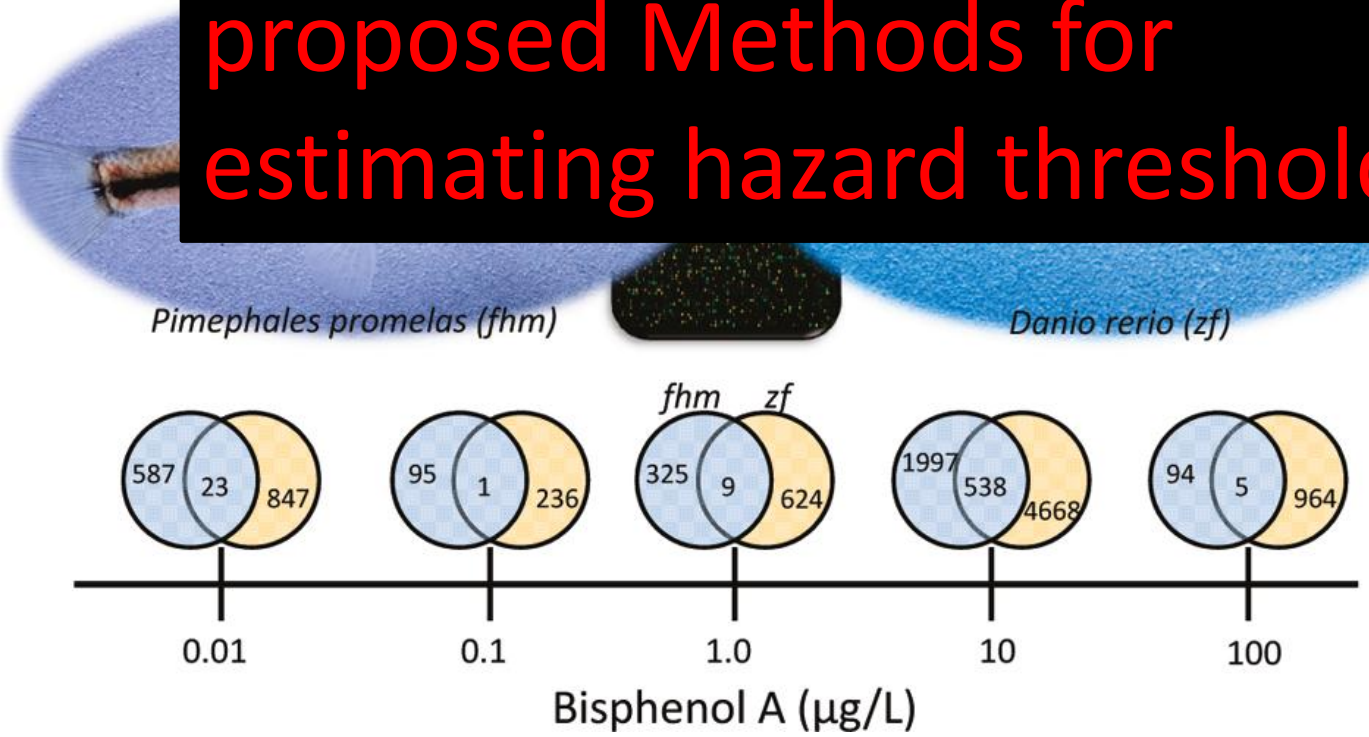
[c] *Department of Pharmaceutical Sciences, Superior Institute of Health Sciences-North (ISCS-N), Gandra-Paredes, Portugal*

Environmental Science & Technology

Ecotoxicogenomics to Support Ecological Risk Assessment: A Case Study with Bisphenol A in Fish

Daniel L. Ville
Jenna E. Caval
Linnea M. Tho

Violates assumptions of proposed Methods for estimating hazard thresholds



IN OVO EXPOSURE TO NONYLPHENOL AND BISPHENOL A RESULTED IN DOSE-INDEPENDENT FEMINIZATION OF MALE GONADS IN JAPANESE QUAIL (*COTURNIX JAPONICA*) EMBRYOS

ATSUSHI OSHIMA,*† RYO YAMASHITA,† KEIGO NAKAMURA,† MASARU WADA,‡ and KAZUMOTO SHIBUYA†
†Nippon Institute for Biological Science, Ome, Tokyo, Japan
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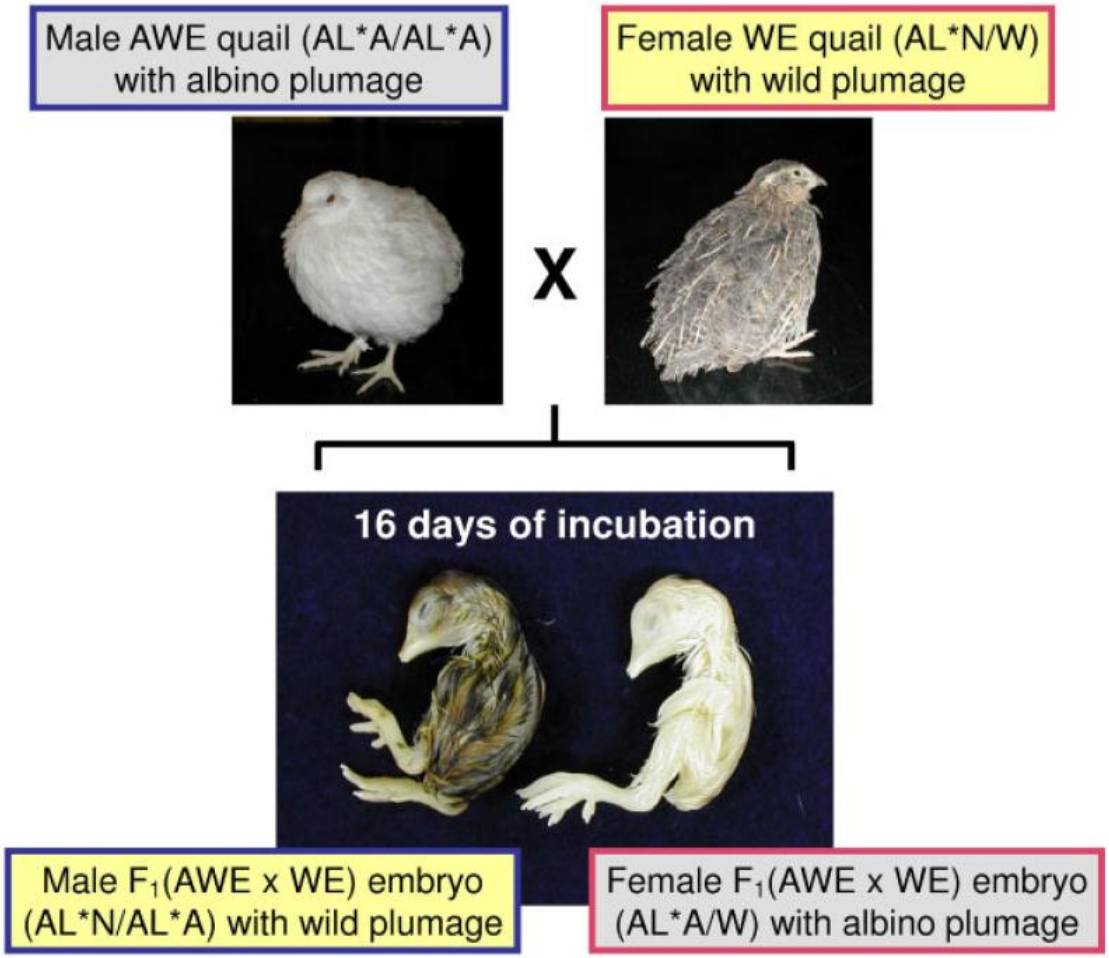
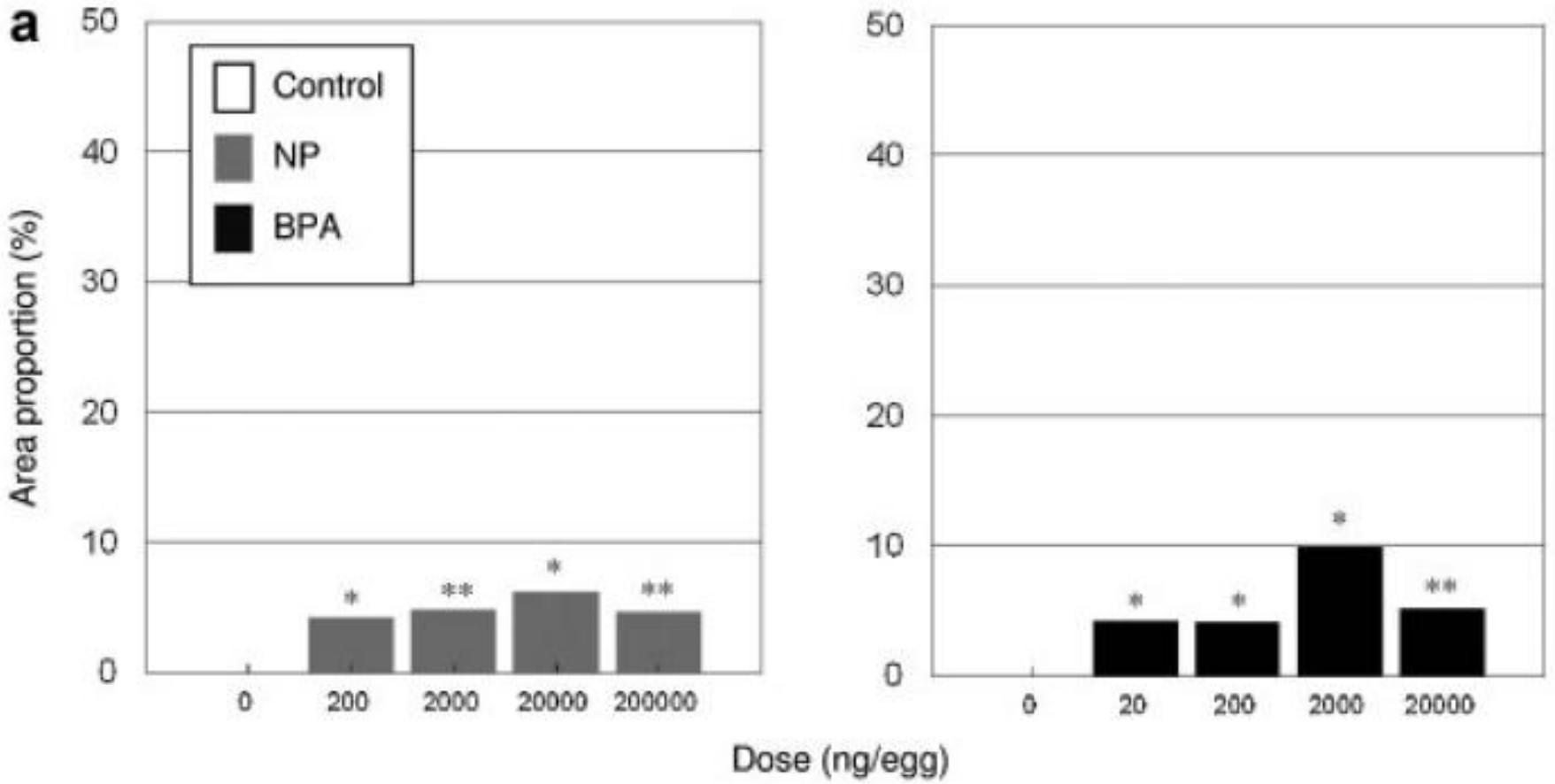
(*Submitted* 15 *September* 2011; *Returned for Revision* 27 *October* 2011; *Accepted* 12 *December* 2011)



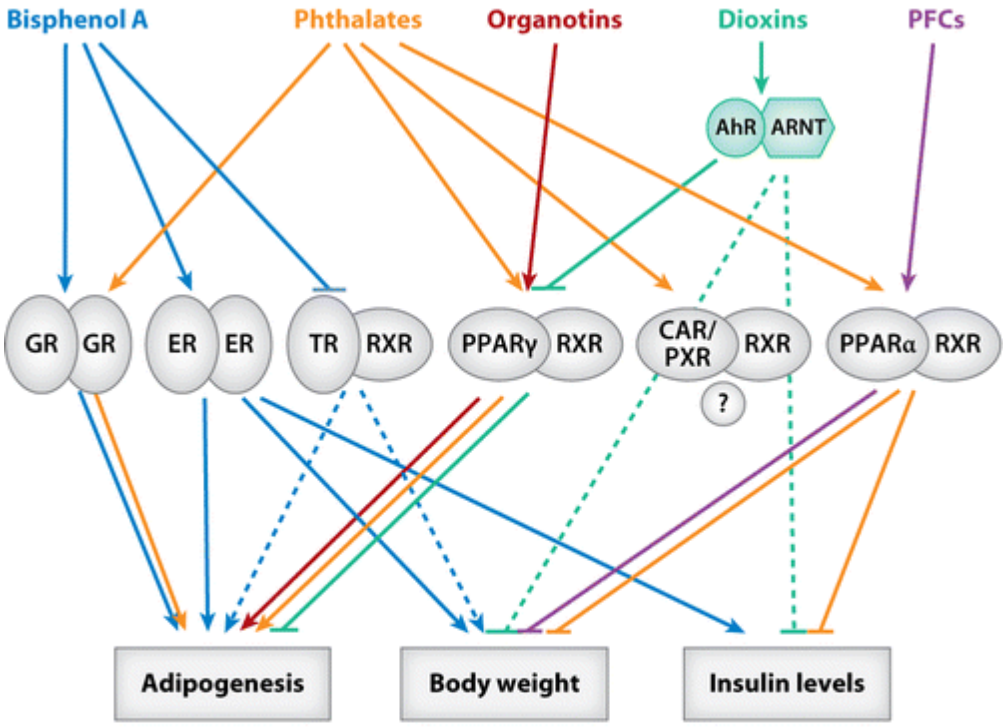


** $p < 0.01$ from the control group.

Summary of characteristics of recent studies on animals

- Tissue specific effects
- Non monotonic dose response curves
- Low dose effects
- Hormone or receptor concentration altered by EDCs early in development is a critical factor directing organ morphology and function
- Mismatches between exposure and effects occur
- Timing of exposure is of equal or greater importance than potency
- ED in wildlife not just about EAT disruption

Thee same molecular mechanism might influence different endpoints



Casals-Casas C, Desvergne B. 2011.
Annu. Rev. Physiol. 73:135–62

TBT and population declines in molluscs
Galante-Oliveira et al; 2011; Gibbs and bryan 1986; Ellis and Pattisina,1990

Organotins in North Sea brown shrimp (*Crangon crangon* L.) after implementation of the TBT ban

Y. Verhaegen [a,b], E. Monteyne [c], T. Neudecker [d], I. Tulp [e], G. Smagghe [b], K. Cooreman [a], P. Roose [c], K. Parmentier [a,*]

[a] Institute for Agricultural and Fisheries Research (ILVO), Animal Sciences Unit, Fisheries, Ankerstraat 1, 8400 Ostend, Belgium
[b] Department of Crop Protection, Faculty of Bioscience Engineering, Ghent University, Coupure Links 653, 9000 Ghent, Belgium
[c] Management Unit of the North Sea Mathematical Models, Royal Belgian Institute of Natural Sciences, 3rd and 23rd Linieregimentsplein, 8400 Ostend, Belgium
[d] Johann Heinrich von Thünen-Institut, Institut für Seefischerei, Palmaille 9, 22767 Hamburg, Germany
[e] Institute for Marine Resources and Ecosystem Studies (IMARES), P.O. Box 68, 1970 AB IJmuiden, The Netherlands

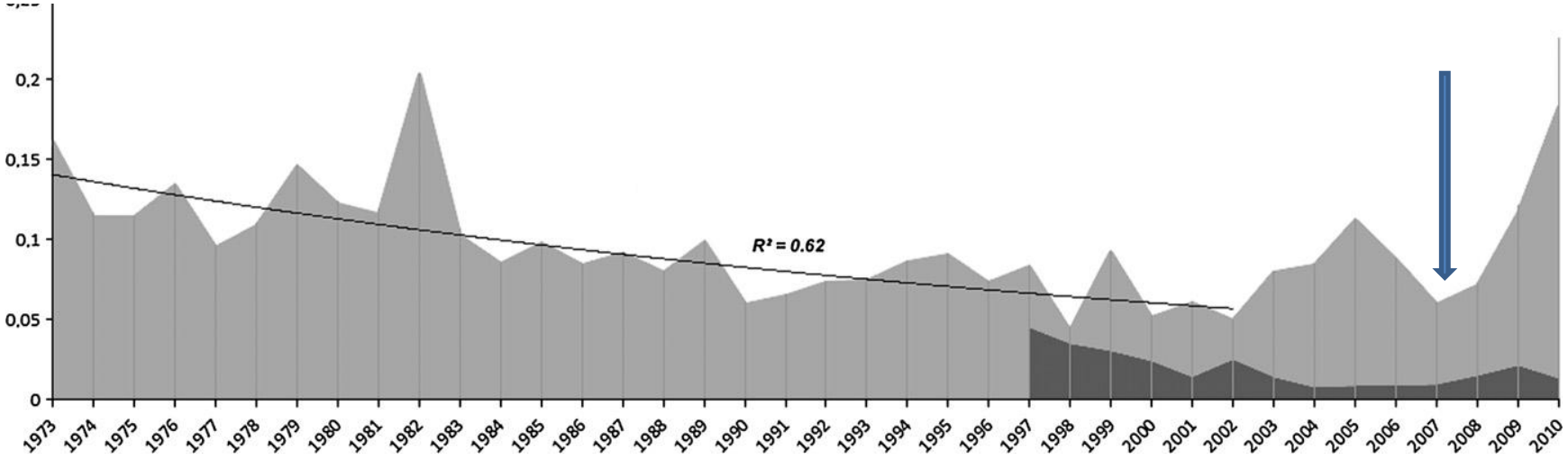
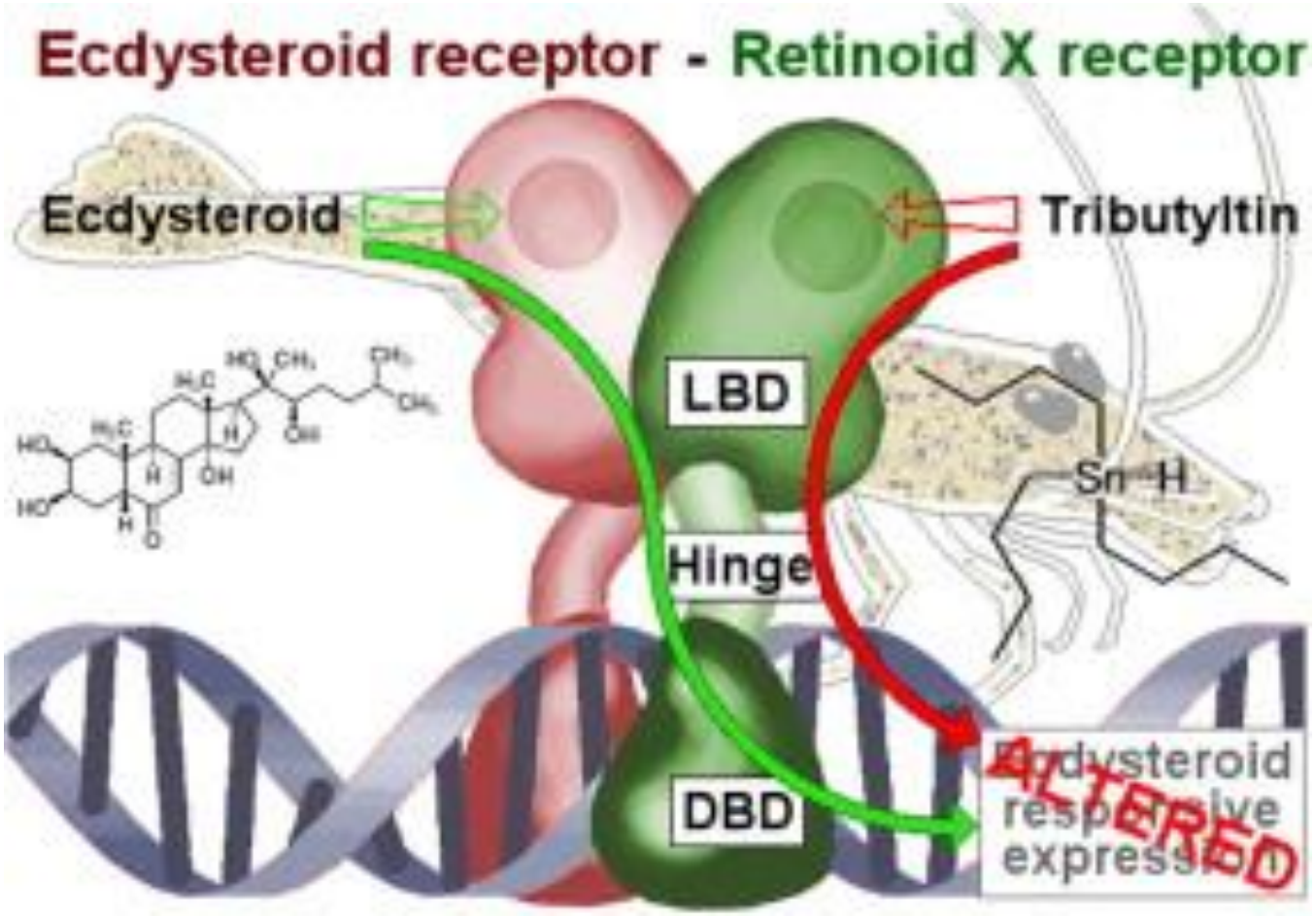


Fig. 4. Long-term annual time series of LPUEs for the Southern Bight (Y-axis, average monthly LPUEs in kg FW horsepower1 fishing hours1) for shrimp (light gray) and cod and whiting (dark gray) during 1973–2010 and 1997–2010, respectively (X-axis).

Mechanism is Not EAT.



Verhaegen et al., 2010, 2011

It is likely that EDCs in wildlife environments are contributing to current declines in wildlife populations and decreased biodiversity

Some population level effects evident

- Large proportions of male fish living downstream from wastewater treatment works are hermaphrodite and/or have reduced semen quality and reduced reproductive success (many papers)
- Recent results (not yet published from Exeter and Brunel) suggest effective population size is reduced

Evaluative framework for EDCs is needed

- Lack of consensus about weight of evidence
- Problems with applying weight of evidence criteria
  - Temporality (putative cause precedes harm)
  - Strength of association (linear dose response and threshold principles)
  - Endocrine principles violate the criteria
  - Consistency (needs rethinking…context matters)
  - Recovery (not if epigenetic mechanisms)

Gaps in our knowledge and needs

- Knowledge of endocrinology at the bottom of the food chain
- Other endpoints NOT just EAT
- Weight of evidence approaches
- Test methodologies