(How) Should Risk Assessors Think with Models?

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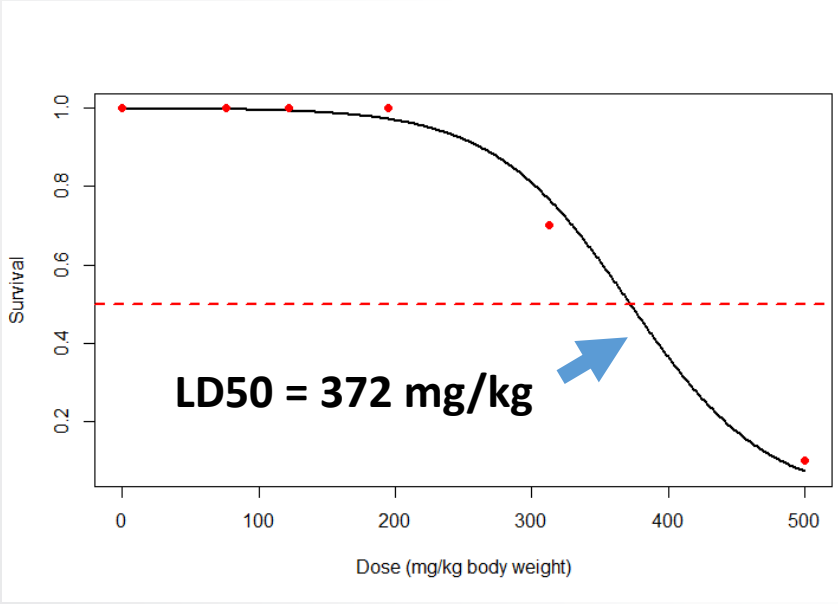


?

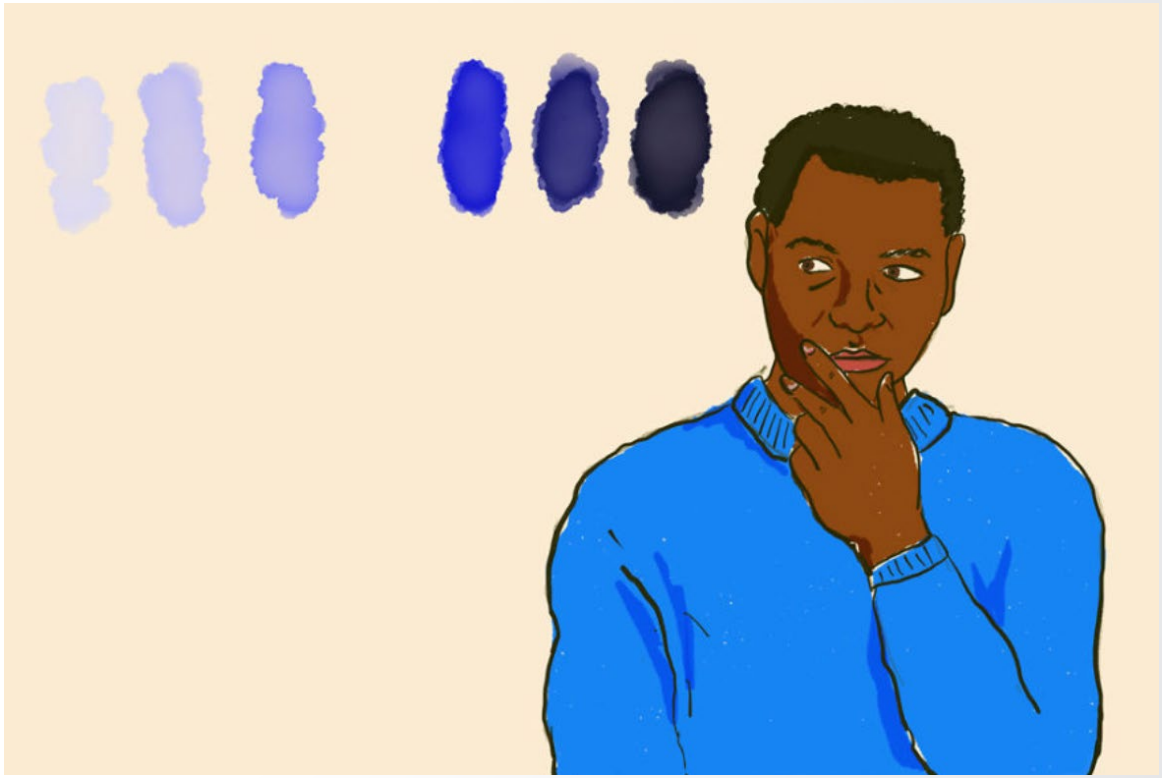
$\lambda,$

$Pr(\text{extinction})$

The views expressed in this presentation are those of the authors and do not necessarily reflect the views or policies of the US EPA

Presentation in 3 parts

- Part I – Introduction to population modeling for risk assessment
- Part II – A couple of thought experiments
- Part III – (How) Should risk assessors think with models?



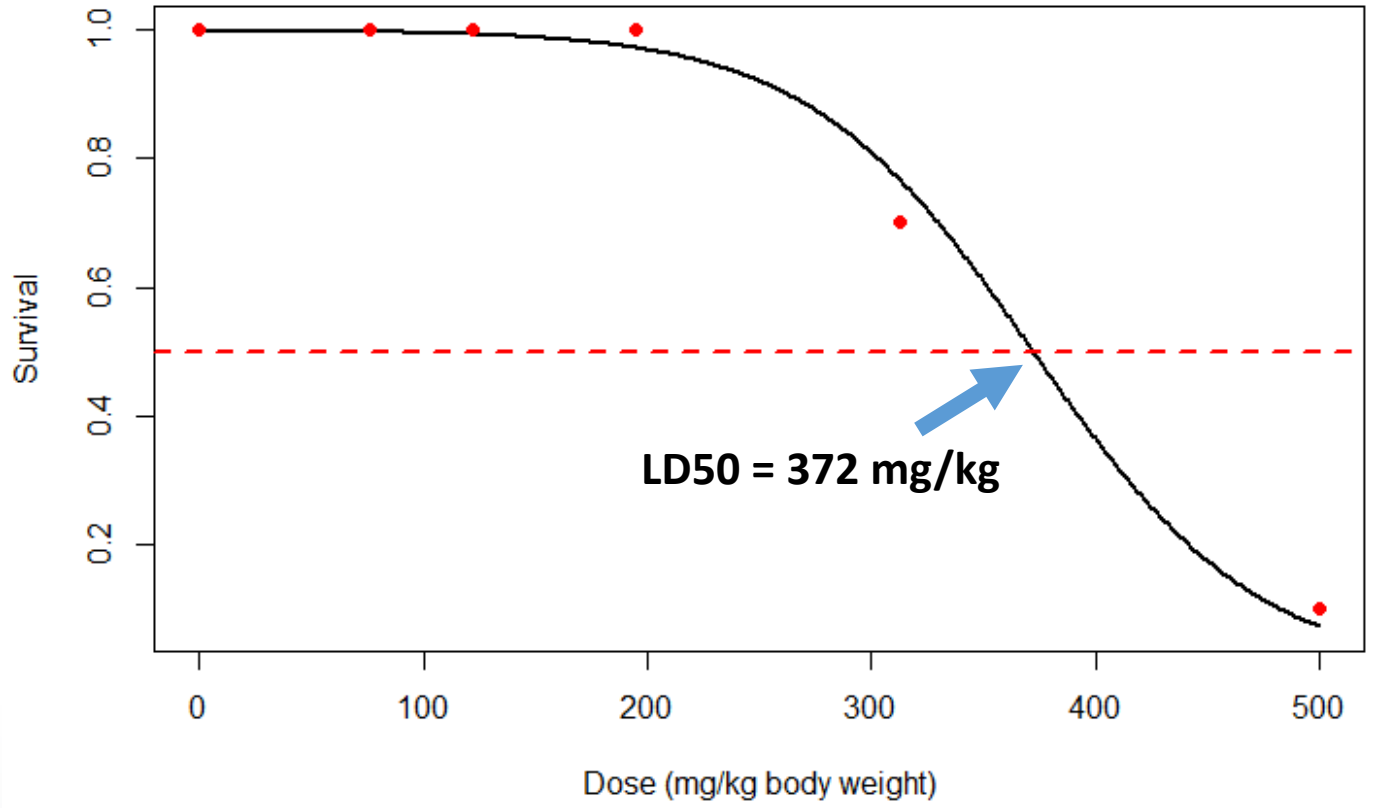
Part 1: (How) Introduction to population models

- EPA uses Risk Assessment to determine whether use is safe or not
  - For people, risk endpoints are individual measures of health/biological impairment
  - For other species, legislation targets protection of ***populations and/or communities***

- Mathematical models play a large role in Ecological Risk Assessment
  - Data analysis & inferential statistics
  - Extrapolation & forecasting

The dose-response experiment

- LD50 = the dose of a toxicant predicted to kill 50% of test subjects
  - Fixed duration of observation (96-hours)
  - 4-5 dose levels + control
  - LD50 interpolated using regression techniques



Let's limber up our thought-experiment muscles

- 8,000 regulated pesticides (Federal Insecticide, Fungicide and Rodenticide Act)
- 80,000 non-pesticide chemicals (Toxic Substances Control Act)
- 700 bird species

Test	LD50
Duration	4 days
Total Time	675,000 years

Conclusion – we cannot test all species for all chemicals!

Let's test all the species!
(Nate Pollesch)

Toxicity Translation

We must extrapolate:

- From chemical A to chemical B
- From species A to species B
- From laboratory to field
- From individual to population

“We need models, lots of models”

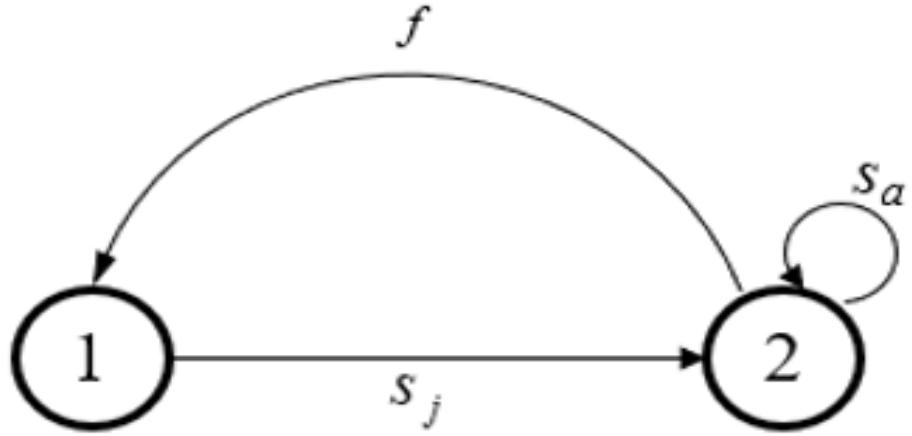
So, what is a population model?

- Dynamic model of the number of individuals in a population over time
- Typically incorporates vital rates (survival, growth, reproduction)
- Predictions include population growth rate, extinction probability, recovery time, equilibrium states

Parameters:

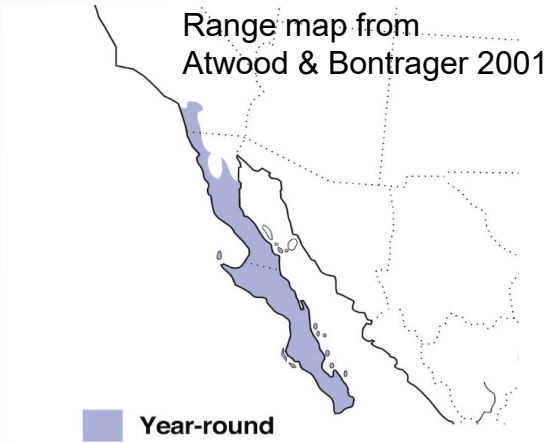
- S_a = annual adult survival
- S_j = annual juvenile survival
- β = annual reproductive success
- λ = annual rate of population change

$$\lambda = \frac{N_{t+1}}{N_t} = s_a + s_j\beta$$

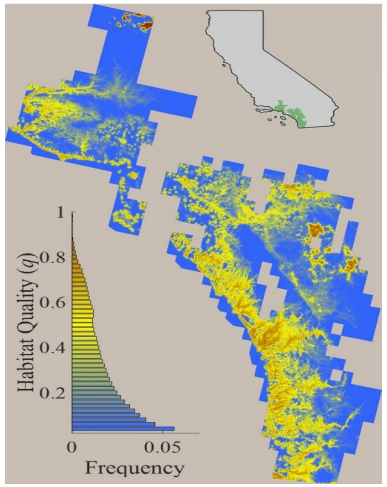


How about an example?

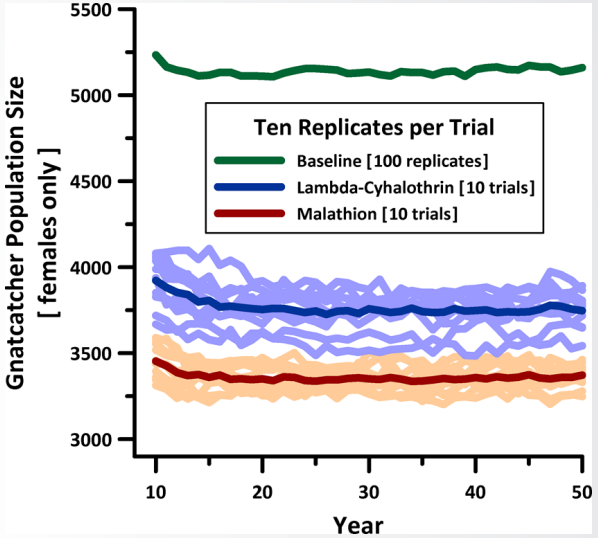
- California Gnatcatcher
- Federally Threatened Habitat loss & nest parasitism
- Effect of pesticides unknown



- Mostly in Baja



- Pre-existing habitat map
- Spatially explicit simulation
- Spatially referenced pesticide use



- Pre-existing habitat map
- Spatially explicit simulation
- 50 year projections

Etterson et al. 2021. PLoS One

Easy, right? So why are risk assessors skeptical?

Part II: A thought experiment to introduce thought experiments

- Suppose we build a population model that incorporates chemical effects (never mind the details)
- Further, suppose our model predicts $\lambda = N_{t+1}/N_t$ = 1.01 +/- 0.05 (SE)
- What would happen to a population of 10,000 birds in 50 years?
- Answer 1: expected population size is 16,446 birds
- Answer 2: With 95% confidence, there will be between 100 birds and 1.7 million birds!
- Even with SE = 0.02, the 95% CI is 2,272 to 110,386 birds

1. Do birds live forever? (Miller & Botkin)

Assumption:

Adult birds do not senesce

- Let A = age
- N = population size
- Then: $Pr(A) = S^A$
- Solve for the expected age of the oldest bird ($Pr(A) = 1/N$): $A = -\frac{\ln(N)}{\ln(S)}$
- Royal Albatross suffer 3% mortality per year

Population Size	Expected age of oldest bird
N= 1,000	$A = 226$ yr
N = 10,000	$A = 302$ yr
N = 100,000	$A = 378$ yr

Conclusion: assumption that royal albatross do not senesce is false!

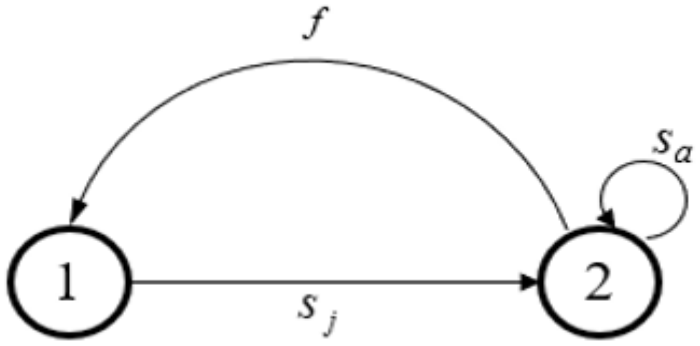
2. Is space just noise? (Pulliam)

Assumption:

Birds compete for limited high-quality breeding sites

Parameters:

- s_a = annual adult survival
- s_j = annual juvenile survival
- f = annual reproductive success
- λ = annual rate of population change



$$\lambda = \frac{N_{t+1}}{N_t} = s_a + s_j f$$

$$M = \begin{bmatrix} f s_j & f s_j \\ s_a & s_a \end{bmatrix}$$

2. Is space just noise? (Pulliam)

- Definition of source: $\lambda > 1$: ($N_{t+1} > N_t$).
- Assume $\hat{n}$ available breeding sites in source
- What happens when all $\hat{n}$ sites are occupied?
- Reproductive success for the population will be:

$$f(N) = \begin{cases} f & \text{if } N \leq \hat{n} \\ \frac{\hat{n}}{N} f & \text{if } N > \hat{n} \end{cases}$$

- Therefore, when all sites are occupied population growth rate is given by:

$$\lambda(N) = s_a + \frac{\hat{n}}{N} s_j f$$

2. Is space just noise? (Pulliam)

At equilibrium (N^*: $N_{t+1} == N_t$), $\lambda(N) = 1$

$$1 = s_a + \frac{\hat{n}}{N^*} s_j f$$

Subtract s_a:

$$1 - s_a = + \frac{\hat{n}}{N^*} s_j f$$

Multiply by N^*:

$$N^*(1 - s_a) = \hat{n} s_j f$$

Divide by $(1 - s_a)$:

$$N^* = \hat{n} \frac{s_j f}{(1 - s_a)}$$

But!:

$$s_a + s_j f > 1$$

$$s_j f > 1 - s_a$$

$$\frac{s_j f}{1 - s_a} > 1$$

Therefore:

$$N^* > \hat{n}$$

2. Is space just noise? (Pulliam)

- Definition of sink: $\lambda < 1$
- Assume only difference between source (habitat 1) and sink (habitat 2) is reproductive success ($f_1 >> f_2$)
- Therefore:
  - Source: $\lambda_1 = s_a + s_j f_1 > 1$
  - Sink: $\lambda_2 = s_a + s_j f_2 < 1$

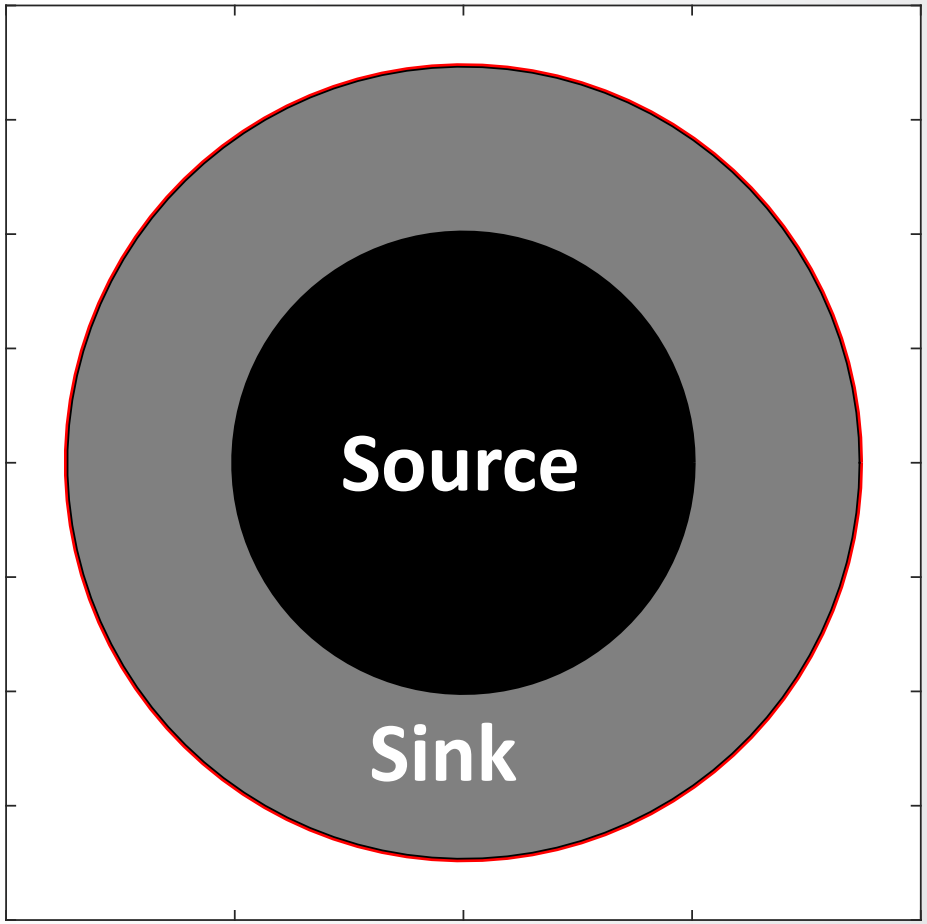
Pulliam showed that equilibrium ratio of source to sink (n_2/n_1) is estimated as:

$$\frac{n_2}{n_1} = \frac{(\lambda_1 - 1)}{(1 - \lambda_2)}$$

2. Is space just noise? (Pulliam)

- $\lambda_1 = 1.1, \lambda_2 = 0.95$

- Sink population is 3 times the source population!



Conclusion(s):

- **occupancy may be a misleading indicator of habitat quality**
- **Spatial habitat configuration may determine population growth rates**
- **Anthropogenic activities may create sinks**

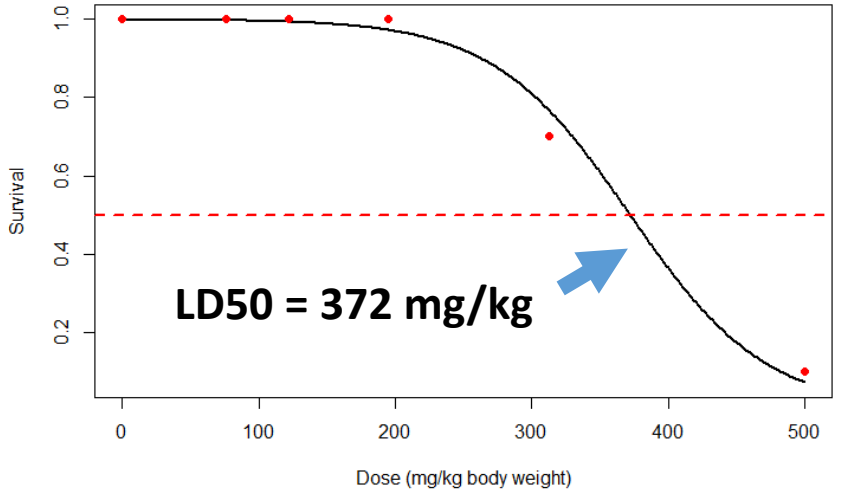
How did we learn from the examples?

1. Do birds live forever?	2. Is space just noise?
Used a *reductio* argument to reject an ***assumption***	Used a model to explore the emergent consequences of an ***assumption***

Thought experiments explore the consequences of assumptions

Part III. (How) Should risk assessors think with models?

- Too many chemicals
- Too many species
- Not enough toxicity data
- Not enough time
- Models are too uncertain for forecasting



$$\lambda, \xrightarrow{?} Pr(\text{extinction})$$

What do Risk Assessors want from pop models?

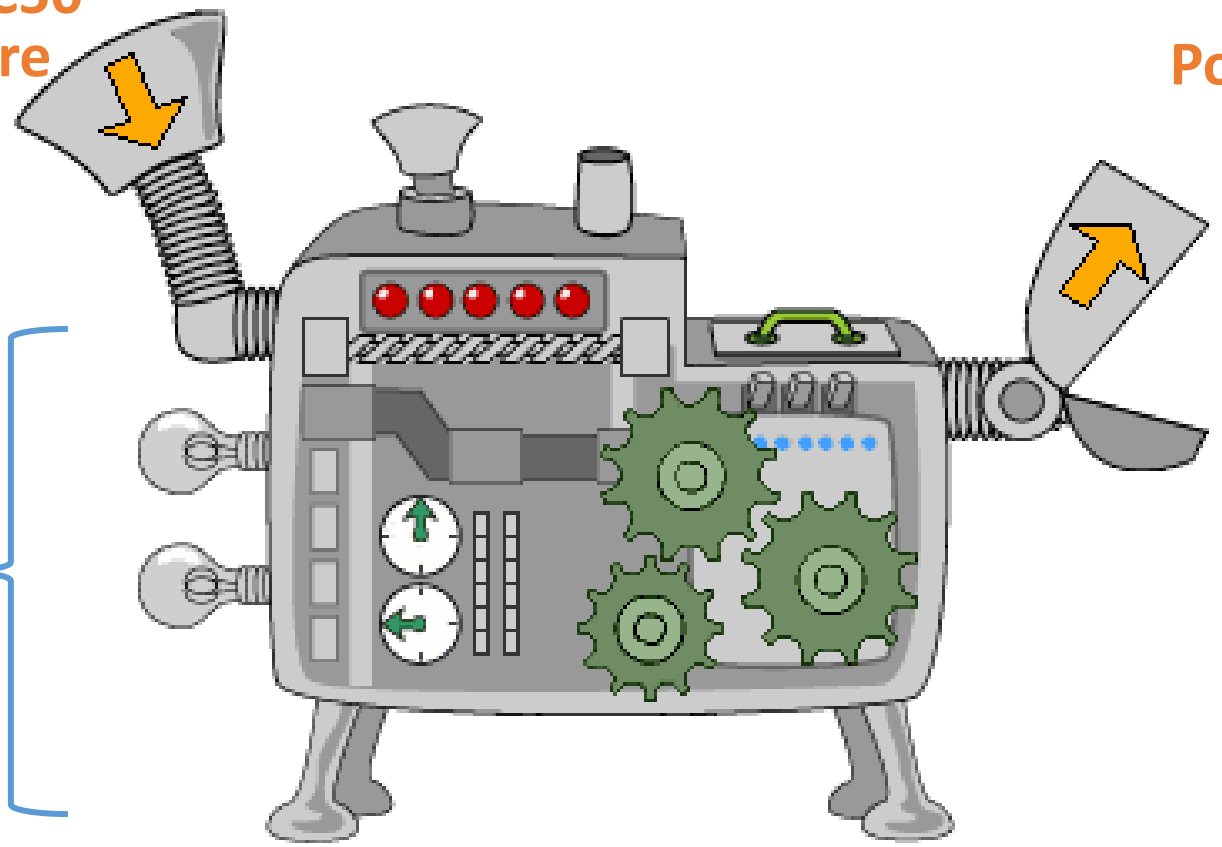
- To integrate separate toxicological effects on survival, growth, and reproduction into a single metric of effect (λ)
- To identify sensitive life-history stages
- To incorporate adverse outcome pathways
- To study the interaction between environment and chemical stressors

Toward a foundation for ecotoxicological thought experiments

LD50 NOEC

LC50

Exposure



Population Response (Δλ)

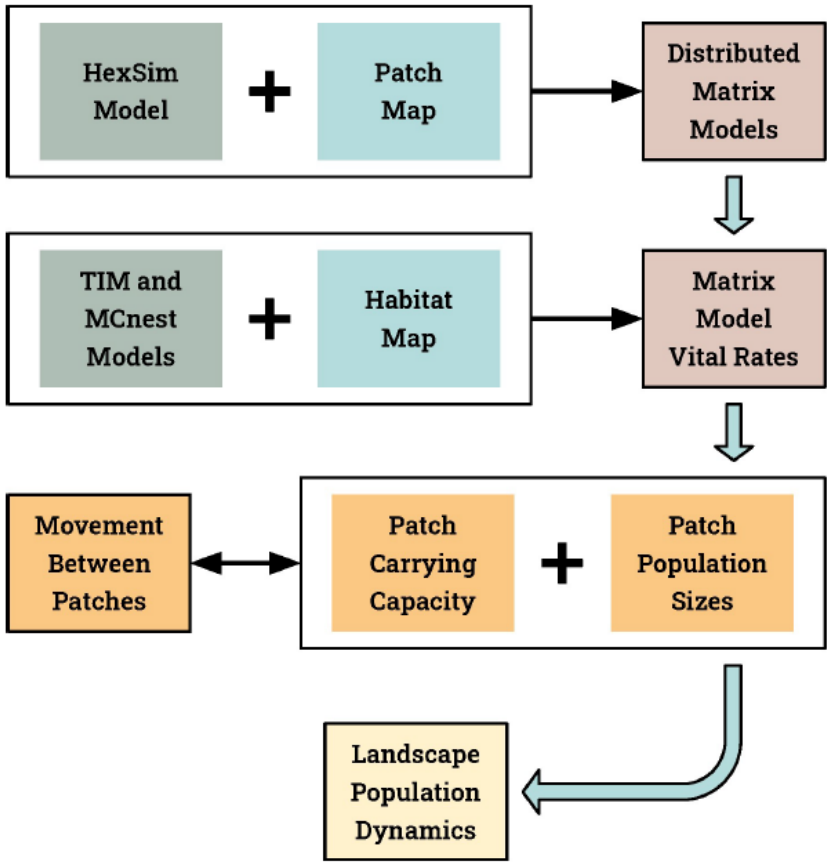
Endogenous systems

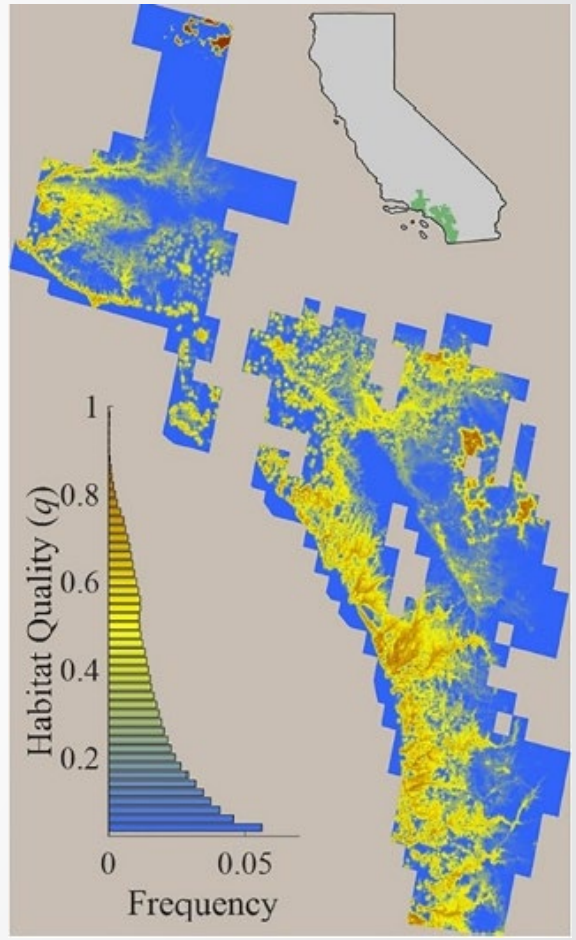
Lifecycle
Reproductive cycle
Hormone signaling
Immune systems
Organ function
Metabolism & other cellular processes
Gene regulation
Homeostatic mechanisms

Exogenous factors

Population size
Population structure
Habitat quality
Density dependence
Environ. stochasticity
Behavioral interactions
Competition
Predation
Resource limitation
Landscape structure

Exogenous factors are difficult to parameterize and often poorly understood





Etterson et al. 2021. A spatially explicit model for estimating risks of pesticide exposure to bird populations. PLOS One

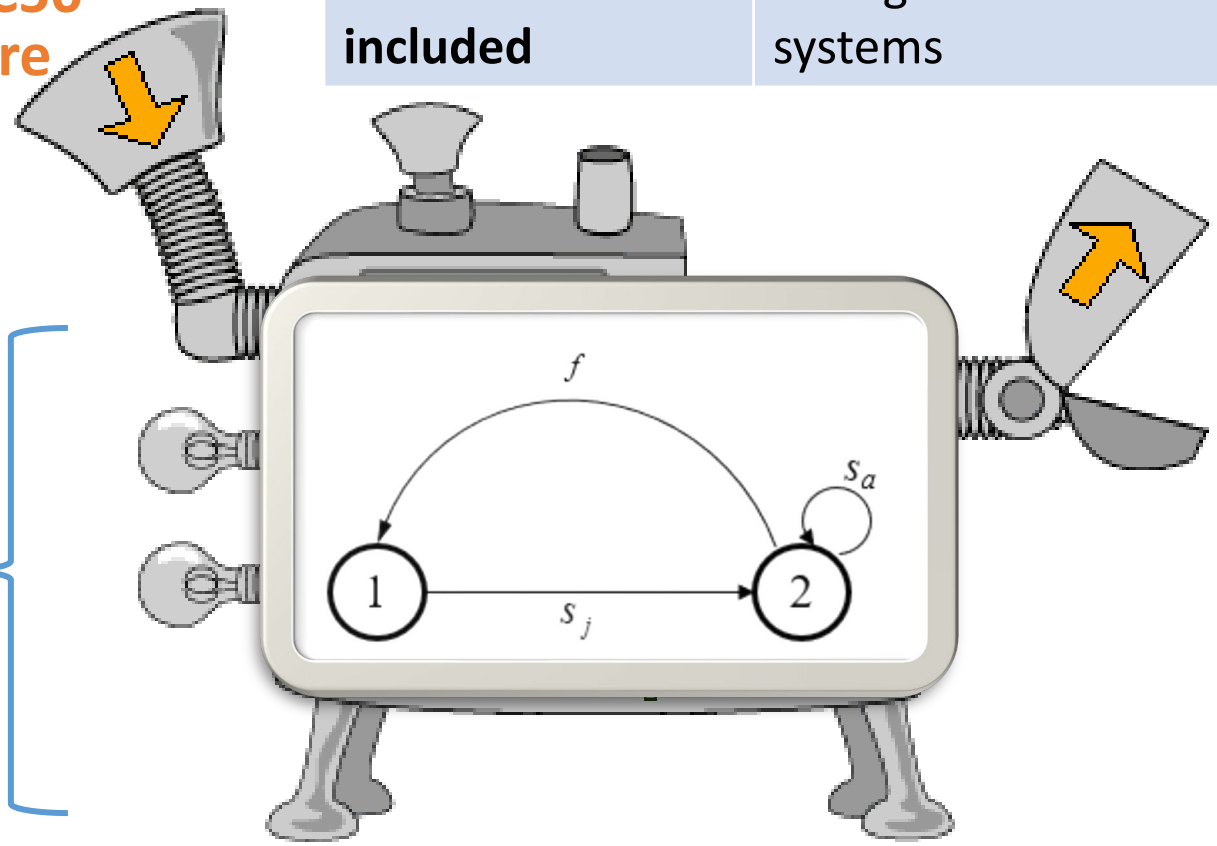
Endogenous Lifecycle Models (ELMs)

	ELM	Population model
Subject	Lifecycle	Collection of individuals
Predictions	Fitness	ΔN, Extinction Probability
Processes included	Endogenous systems	Endogenous systems & Exogenous factors

LD50 NOEC

LC50

Exposure



Endogenous systems

Lifecycle
Reproductive cycle
Hormone signaling
Immune systems
Organ function
Metabolism & other cellular processes
Gene regulation
Homeostatic mechanisms

Fitness

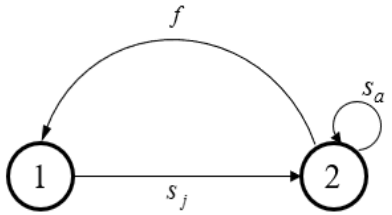
~~**Exogenous factors**~~
~~Population size~~
~~Population structure~~
~~Habitat quality~~
~~Density dependence~~
~~Environ. stochasticity~~
~~Behavioral interactions~~
~~Competition~~
~~Predation~~
~~Resource limitation~~
~~Landscape maps~~

OK, maybe…let's see some examples

Parameter definitions:

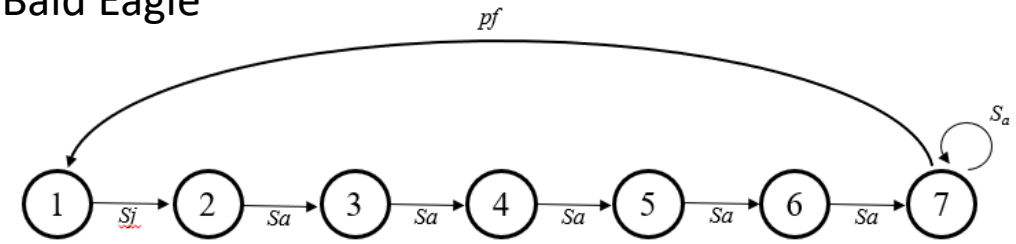
- s_j = survival from fledging to 1st year
- s_a = survival after 1st year
- f = annual fecundity (offspring/year)
- p = breeding propensity

Tree Swallow



Lifecycle adapted from Pulliam 1988. American Naturalist

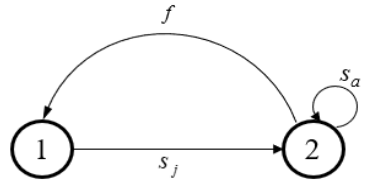
Bald Eagle



Lifecycle from Young 1968. Ecology

The lifecycle graph and model are isoinformatic

Tree Swallow



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$$M = \begin{bmatrix} f\,s_j & f\,s_j \\ s_a & s_a \end{bmatrix}$$

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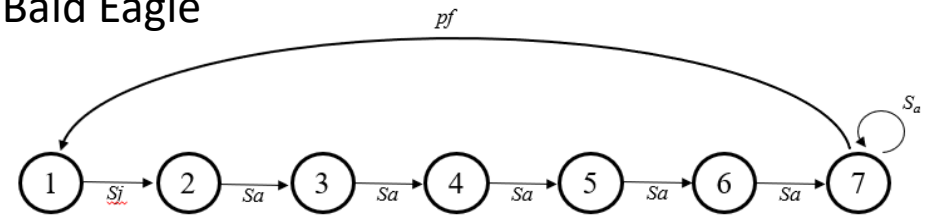
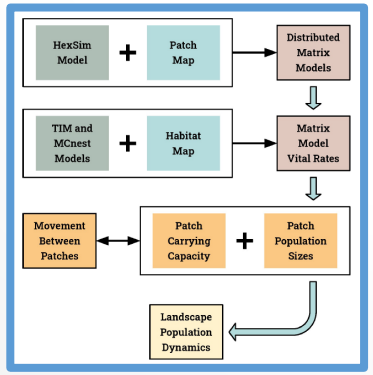


Lifecycle from Young 1968. Ecology

$$M = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & pf \\ s_j & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & s_a & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & s_a & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & s_a & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & s_a & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & s_a & s_a \end{bmatrix}$$



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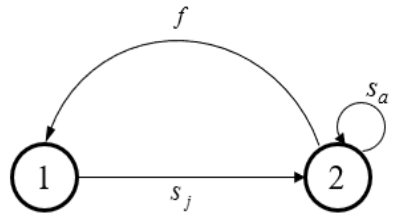
Stakeholders can reach consensus on the lifecycle graph without reference to the mathematics

Fitness predictions

Tree Swallow



$$M = \begin{bmatrix} f s_j & f s_j \\ s_a & s_a \end{bmatrix}$$

Fitness predictions:

- Intrinsic fitness (λ_f) = expected annual production of genetic descendants (including self)

$$\lambda_f = s_a + f s_j$$

- Lifetime reproductive success (LRS) = expected lifetime production of offspring

$$LRS = f \frac{s_j}{1 - s_a}$$

What do Risk Assessors want from pop models?

- ✓To integrate separate toxicological effects on survival, growth, and reproduction into a single metric of effect (λ)
- To identify sensitive life-history stages
- To incorporate adverse outcome pathways
- To study the interaction between environment and chemical stressors

Identification of sensitive life stages

		$\lambda_f = s_a + f s_j$	$LRS = f \frac{s_j}{1 - s_a}$
Process	Parameter	λ_f Sensitivity	LRS Sensitivity
Juvenile Survival	s_j	$\frac{\partial \lambda_f}{\partial s_j} = f$	$\frac{\partial LRS}{\partial s_j} = \frac{f}{1 - s_a}$
Adult Survival	s_a	$\frac{\partial \lambda_f}{\partial s_a} = 1$	$\frac{\partial LRS}{\partial s_a} = \frac{s_j f}{(1 - s_a)^2}$
Fecundity	f	$\frac{\partial \lambda_f}{\partial f} = s_j$	$\frac{\partial LRS}{\partial f} = \frac{s_j}{(1 - s_a)}$

***A priori* ordering of sensitivities:**

- Juvenile survival (s_j) is the most sensitive process $f > 1 > s_j$
- Practical utility – a formal way of weighting the results of toxicity tests

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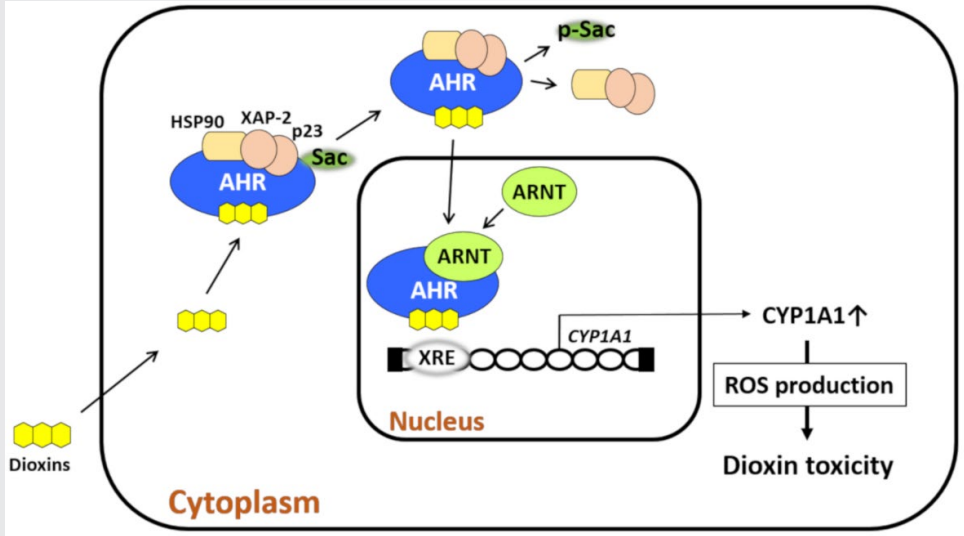
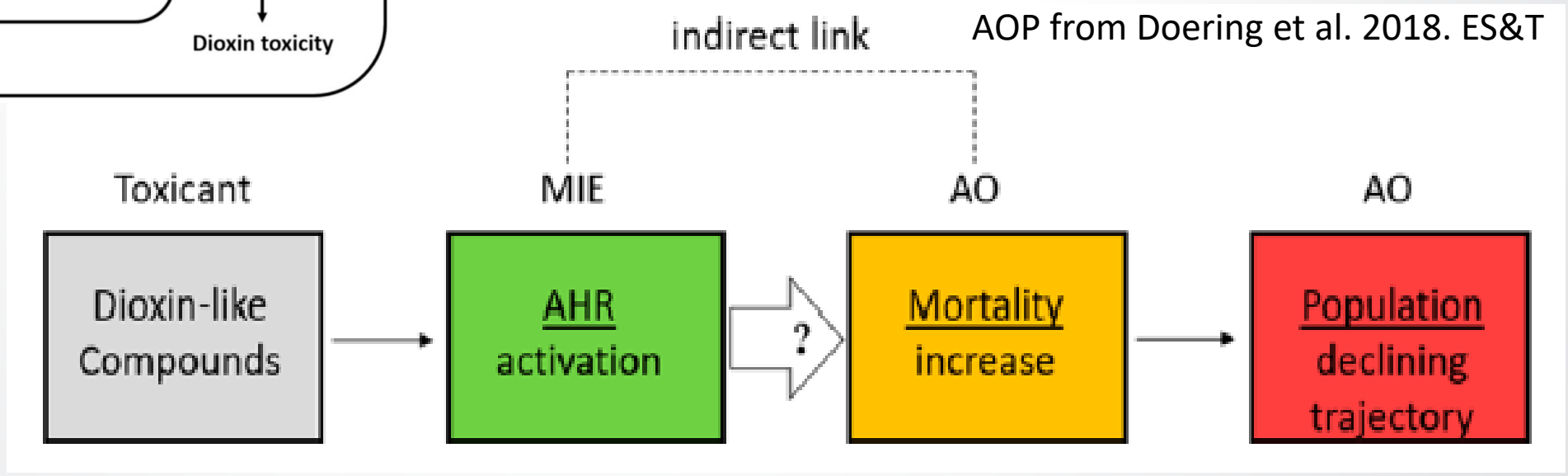
Integration with adverse outcome pathways

- AOPs describe perturbations to endogenous biological systems



Furue et al. 2021. IJMS

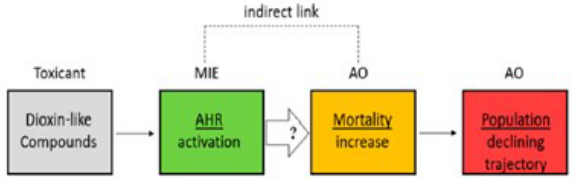
AOP from Doering et al. 2018. ES&T



ELM = a series of directed graphs

AOP

Conceptual Model



AOP from Doering et al. 2018. ES&T

Model & Parameters

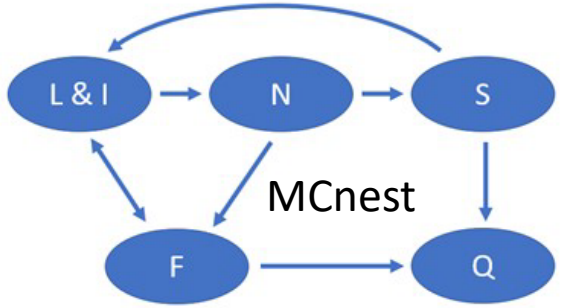
LDx	m_x	b_x
0	0.6764	3.33
10	0.7471	3.063
50	0.7123	2.775
100	0.7599	2.365

$$log_{10}(LDx) = log_{10}(DLC) - b_x + m_x log_{10}(EC50)$$

Predictions

Embryo survival(DLC) = 1-x/100

Endogenous System



Model & Parameters

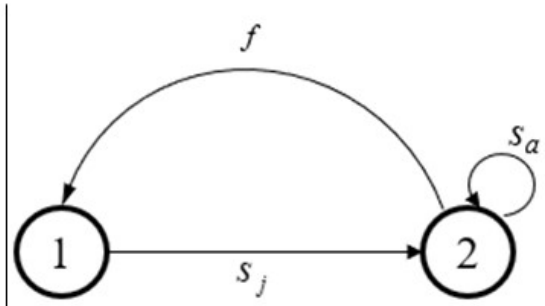
$$\begin{array}{c} \text{L\&I} \quad \text{N} \quad \text{S} \quad \text{F} \quad \text{Q} \\ \begin{bmatrix} 0 & s_i^{d_i} & 0 & 1-s_i^{d_i} & 0 \\ 0 & 0 & s_n^{d_n} & 1-s_n^{d_n} & 0 \\ 1-q_s & 0 & 0 & 0 & q_s \\ 1-q_f & 0 & 0 & 0 & q_f \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix} \begin{array}{c} \text{L\&I} \\ \text{N} \\ \text{S} \\ \text{F} \\ \text{Q} \end{array} \end{array}$$

Adapted from Etterson et al. 2009. Ecological Applications

Predictions

$$f = \left(1 - \frac{x}{100}\right) c \frac{s_i^{d_i} s_n^{d_n}}{q_f + s_i^{d_i} s_n^{d_n} (q_s - q_f)}$$

ELM



Model & Parameters

$$\begin{bmatrix} f s_j & f s_j \\ s_a & s_a \end{bmatrix}$$

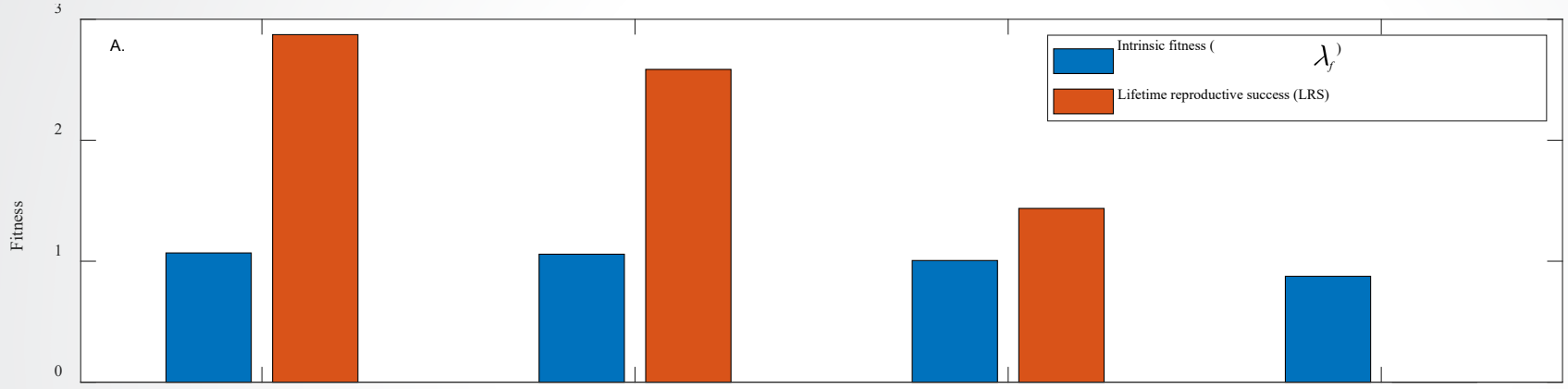
Predictions

$$LRS = f \frac{s_j}{1 - s_a}$$

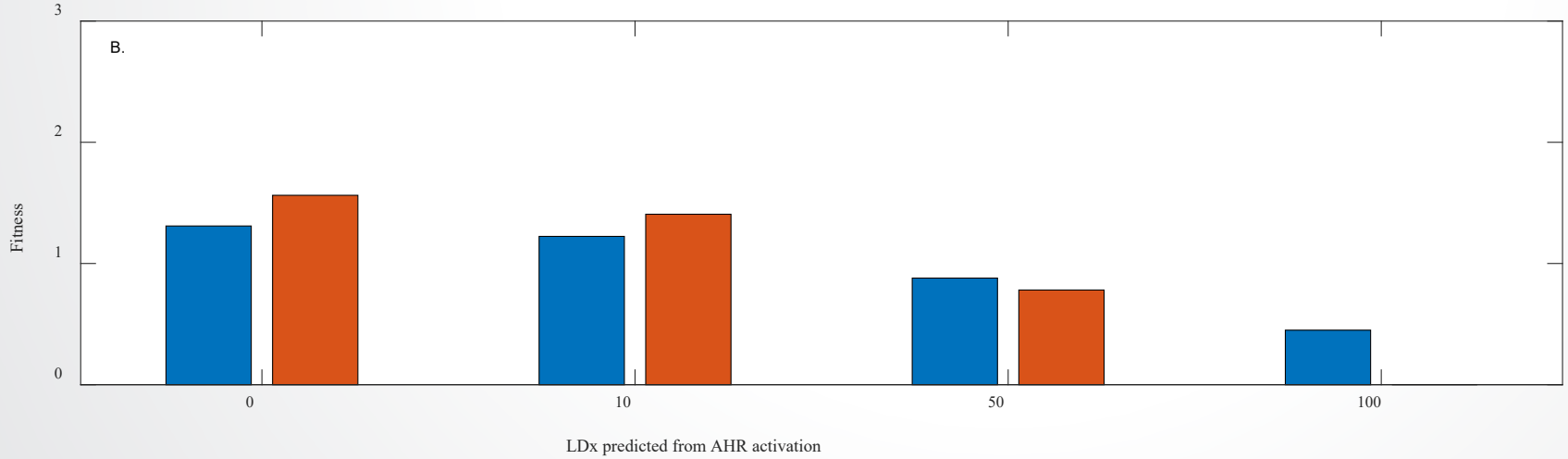
$$\lambda_f = s_a + f s_j$$

Response depends on lifecycle

Bald Eagle



Tree Swallow



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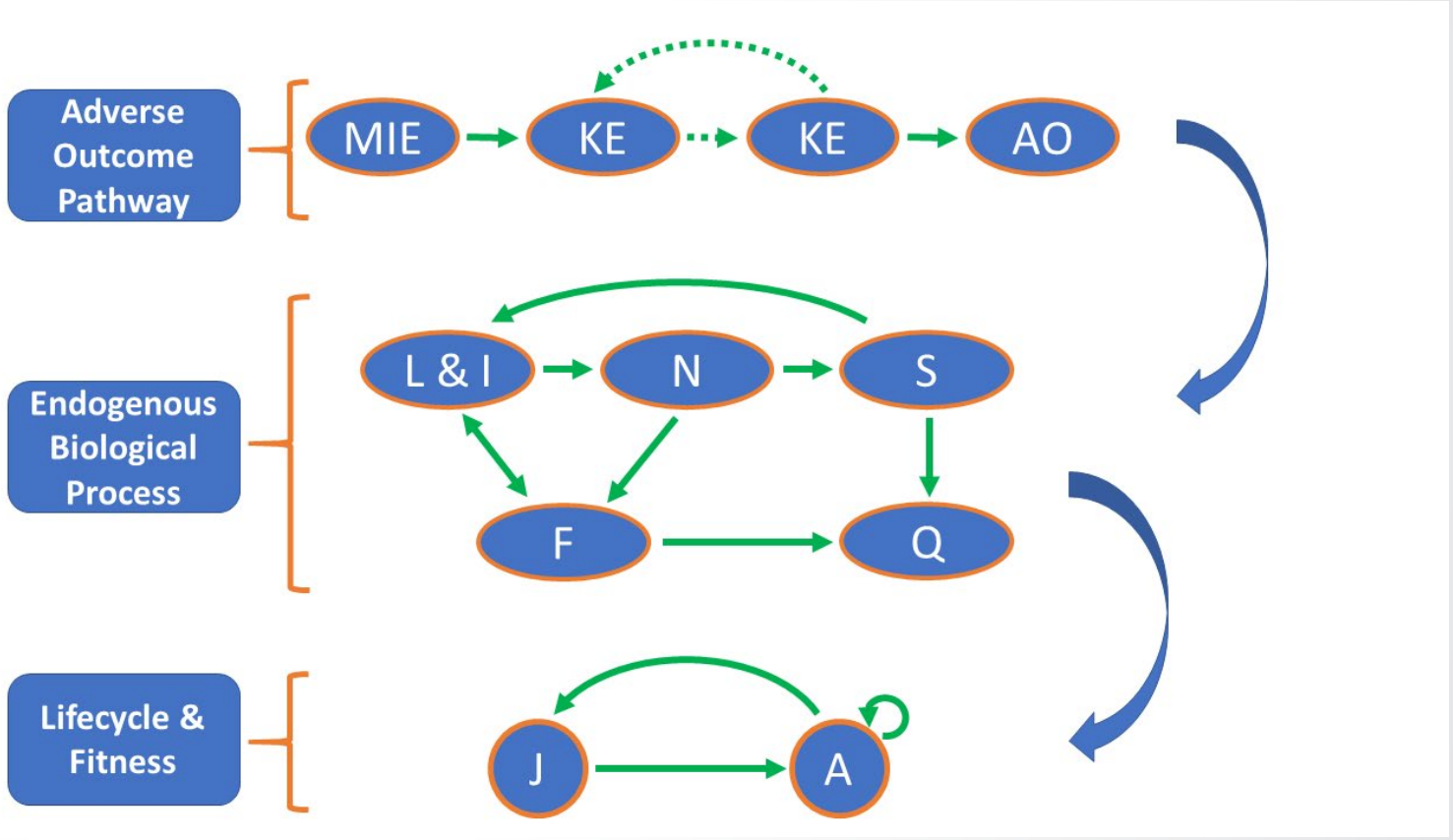
- Ø To study the interaction between environment and chemical stressors

ELMs are a great foundation for exploring the consequences of assumptions about toxicity

The ELM Advantage:

- (relatively) easy to formulate
- Rapid analysis
- Ideal for questions about the consequences of upstream events



Etterson & Ankley 2021. ES&T