Importance of Basic and Translational Approaches in Bed Bug Research

Coby Schal <coby_schal@ncsu.edu>

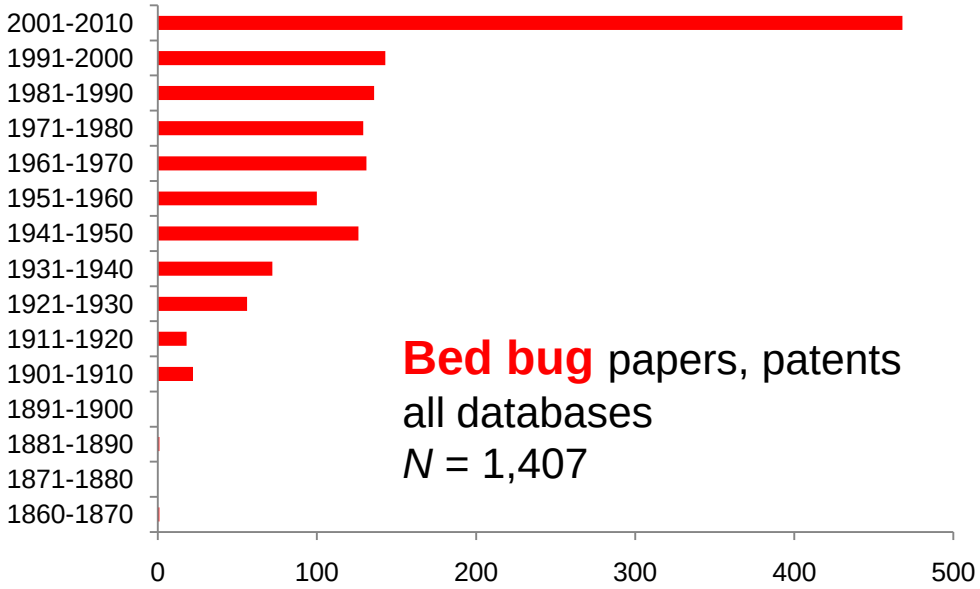
Department of Entomology
W. M. Keck Center for Behavioral Biology
North Carolina State University

BB Summit, DC 2011

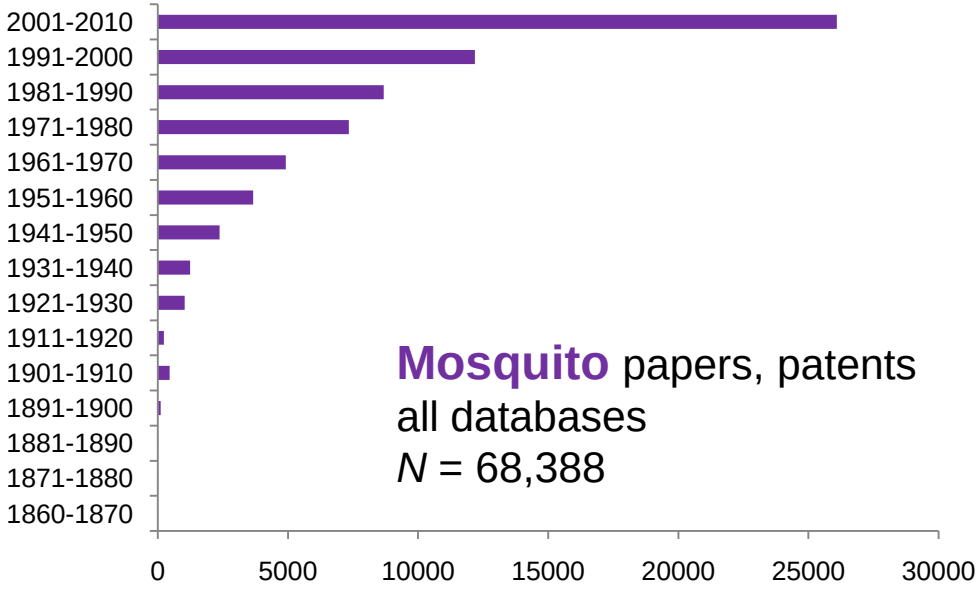
Presentation Outline

- **Trends of scientific publishing on BB**
- **Research approaches**
- **3 Examples of translational research**
  1. Chemical ecology: Pheromones, other semiochemicals
  2. Population genetics
  3. Gene expression & transcriptomes
- **Perspective:** Fundamental & translational research

Literature trends



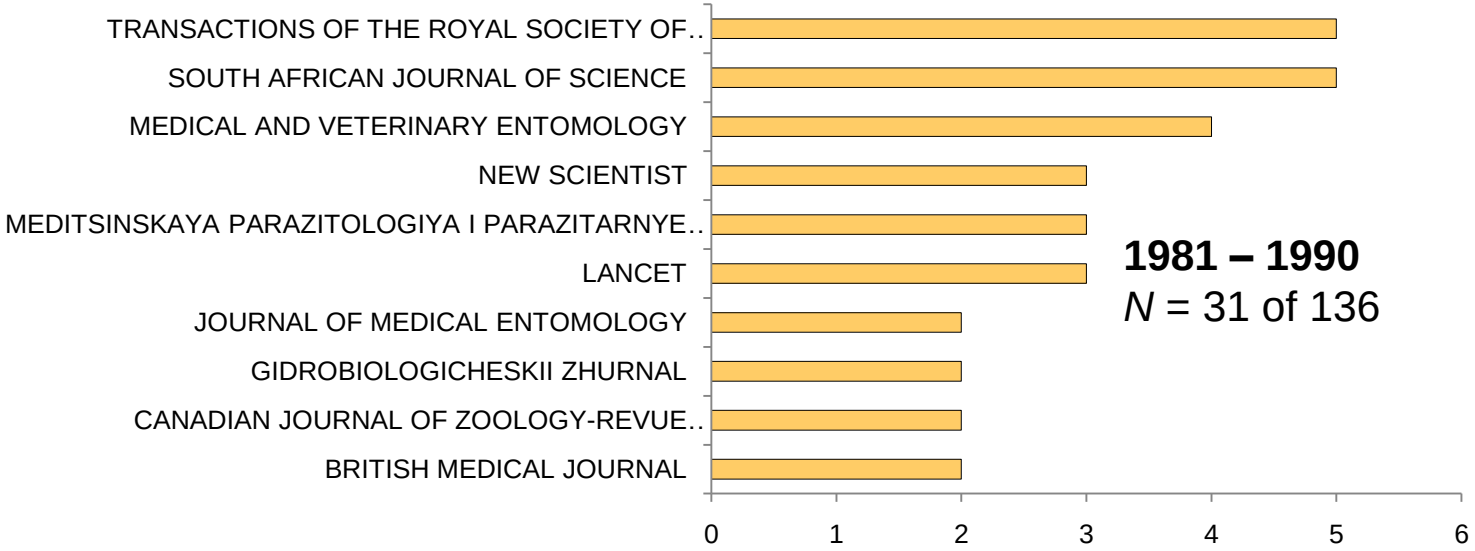
- "flat" productivity for 60 yrs – 1940 – 2000
- upsurge in information in the last decade

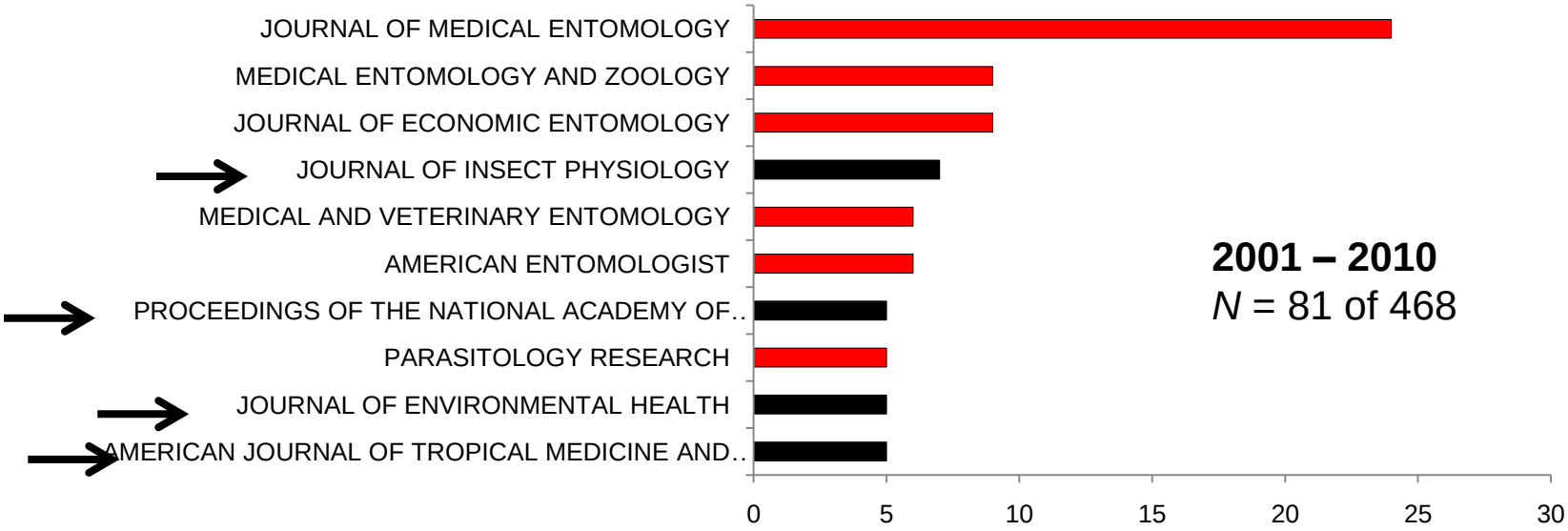


- mosquito : BB = 50 :1

Literature trends

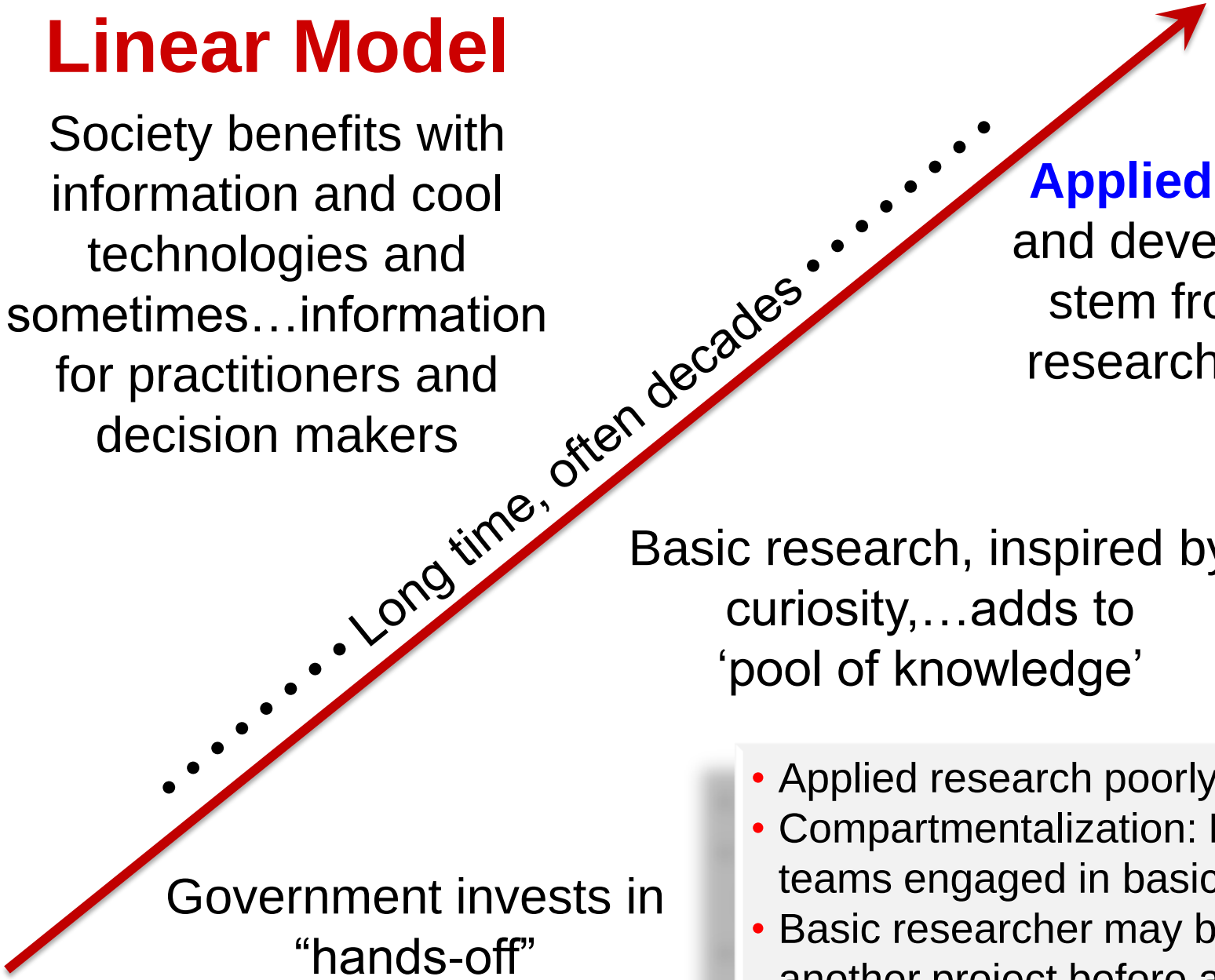
Bed bugs: all databases, top 10 journals





Linear Model

Society benefits with information and cool technologies and sometimes…information for practitioners and decision makers



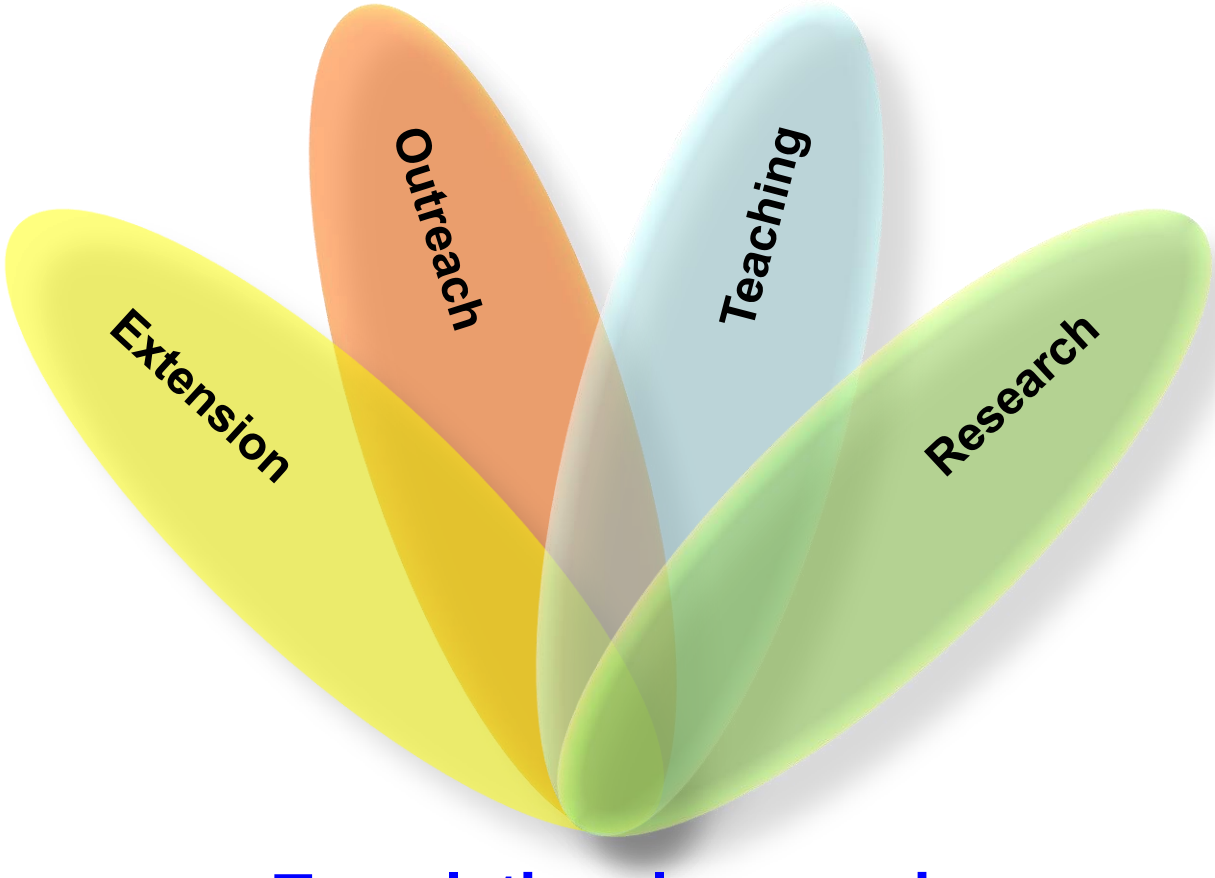
Applied research and development... stem from basic research spin-offs

Basic research, inspired by curiosity,…adds to 'pool of knowledge'

- Applied research poorly funded
- Compartmentalization: Different teams engaged in basic & applied
- Basic researcher may be off on another project before application

Government invests in "hands-off" **Basic** research

21st Century Approach:
Integrating Research, Extension, Outreach and Teaching



Translational research

mission-oriented, multidisciplinary, incentivized

shorter time-frame to practical applications

A (partial) 'Laundry' List of Needs

- Disease vectors, bite allergies, asthma
- Abiotic interactions: temp, humidity
- Biological control agents: viruses, fungi, bacteria
- New pesticides, modes of action, resistance
- Novel non-chemical targets: cuticle, midgut, ovaries

1. BB behavior, communication, aggregation
2. Population biology
3. Unique genes and interactions of gene products, BB genome

- More topics later…… Dr. Kells

Example 1: Host finding, chemicals

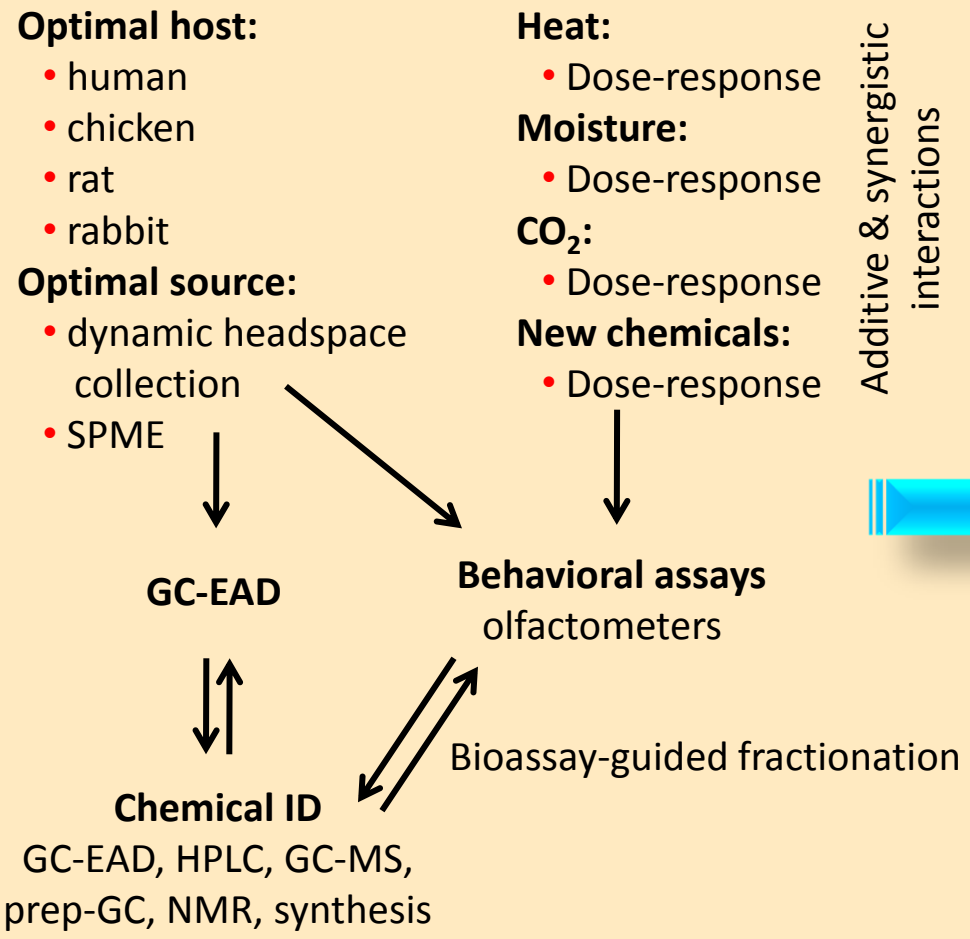
Host seeking

Host location

Host cues
CO_2
Host odors
Temperature

Host rejection/acceptance; engorgement

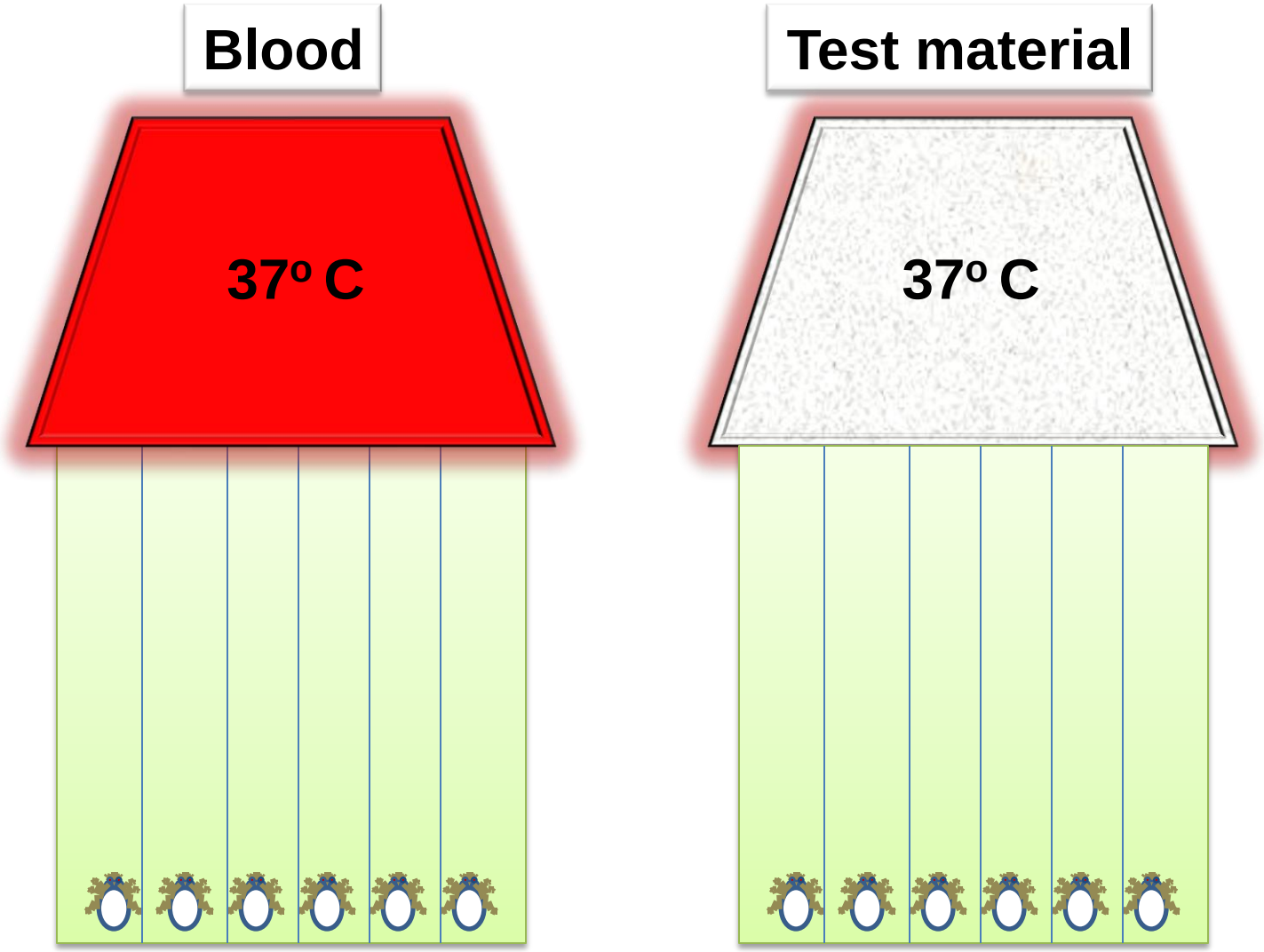
Sensory ecology associated with host-seeking behavior



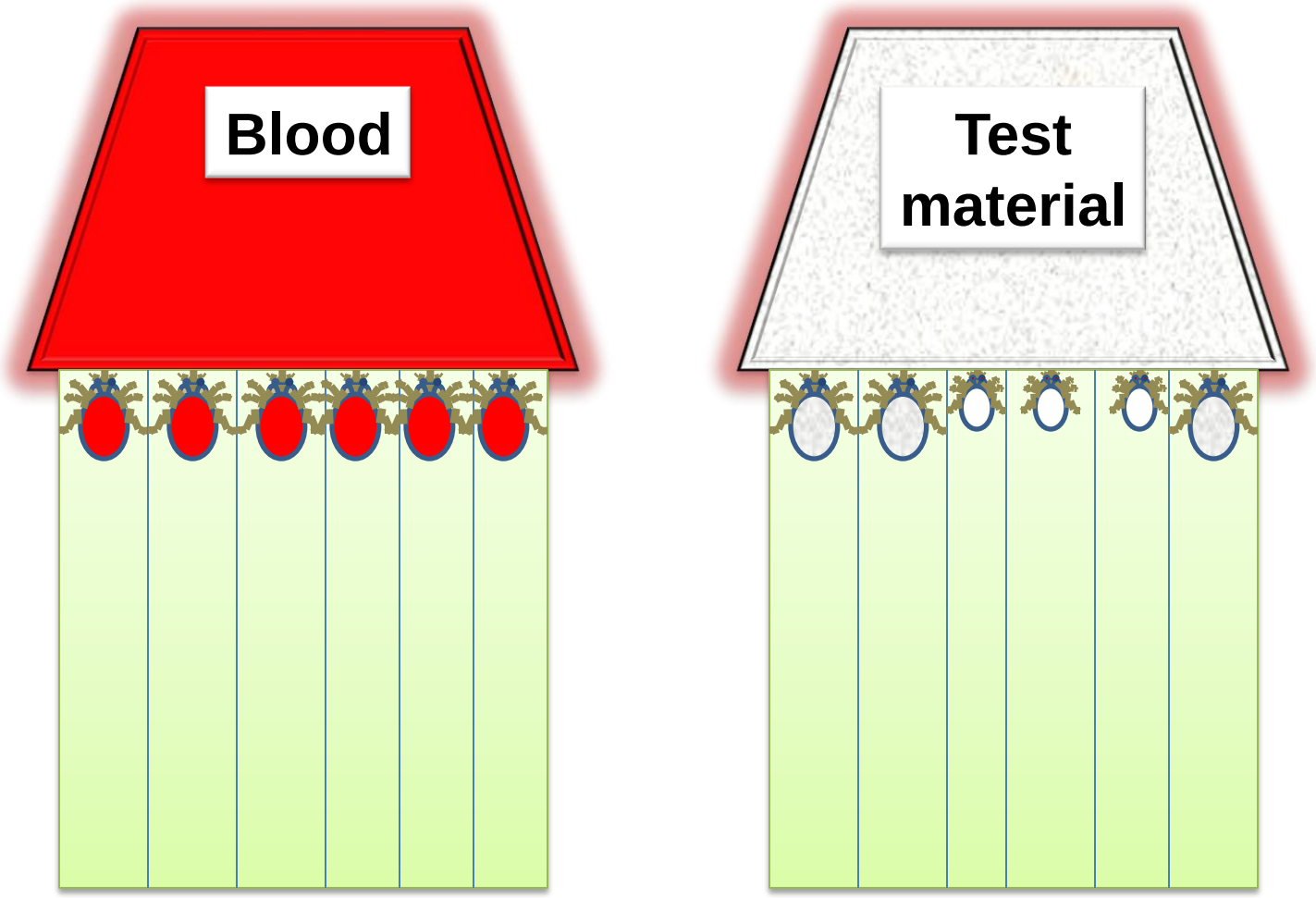
Alvaro Romero: NSF Post-Doctoral Fellow

- Host-attractants for traps
- Sex pheromones
- Aggregation pheromones
  - ✓ Detection
  - ✓ Monitoring
  - ✓ Dissemination of biological control agents
  - ✓ Attract-and-Kill
- Repellents
- Attractants for baits?
- Phagostimulants
- **More…… Dr. Feldlaufer**

What's in blood that bed bugs like?

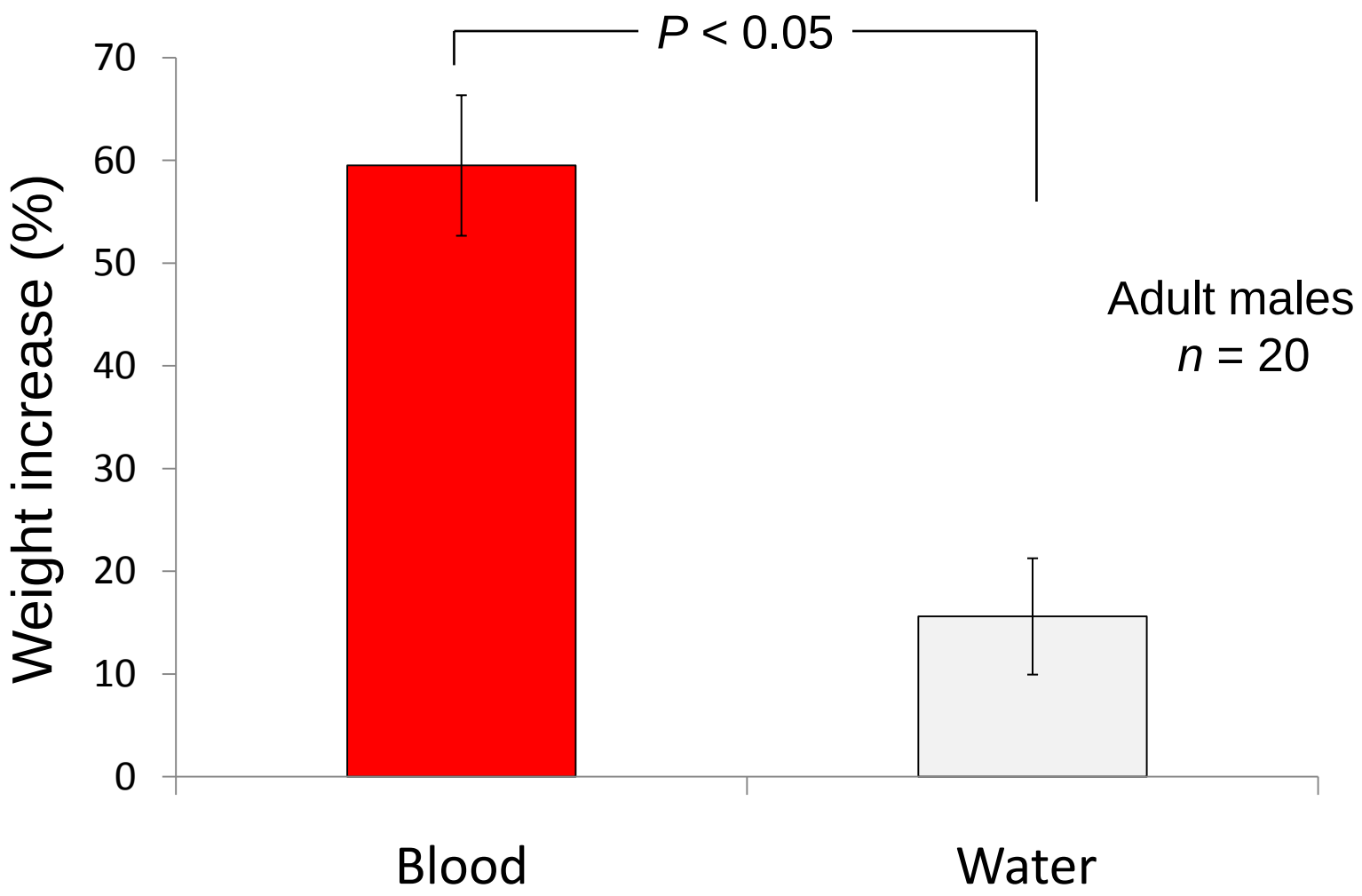


15 min feeding period

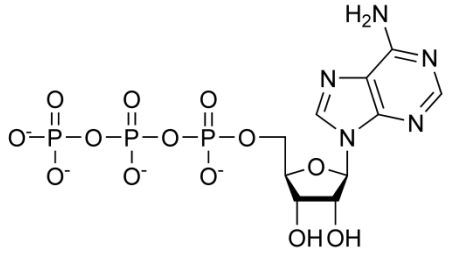


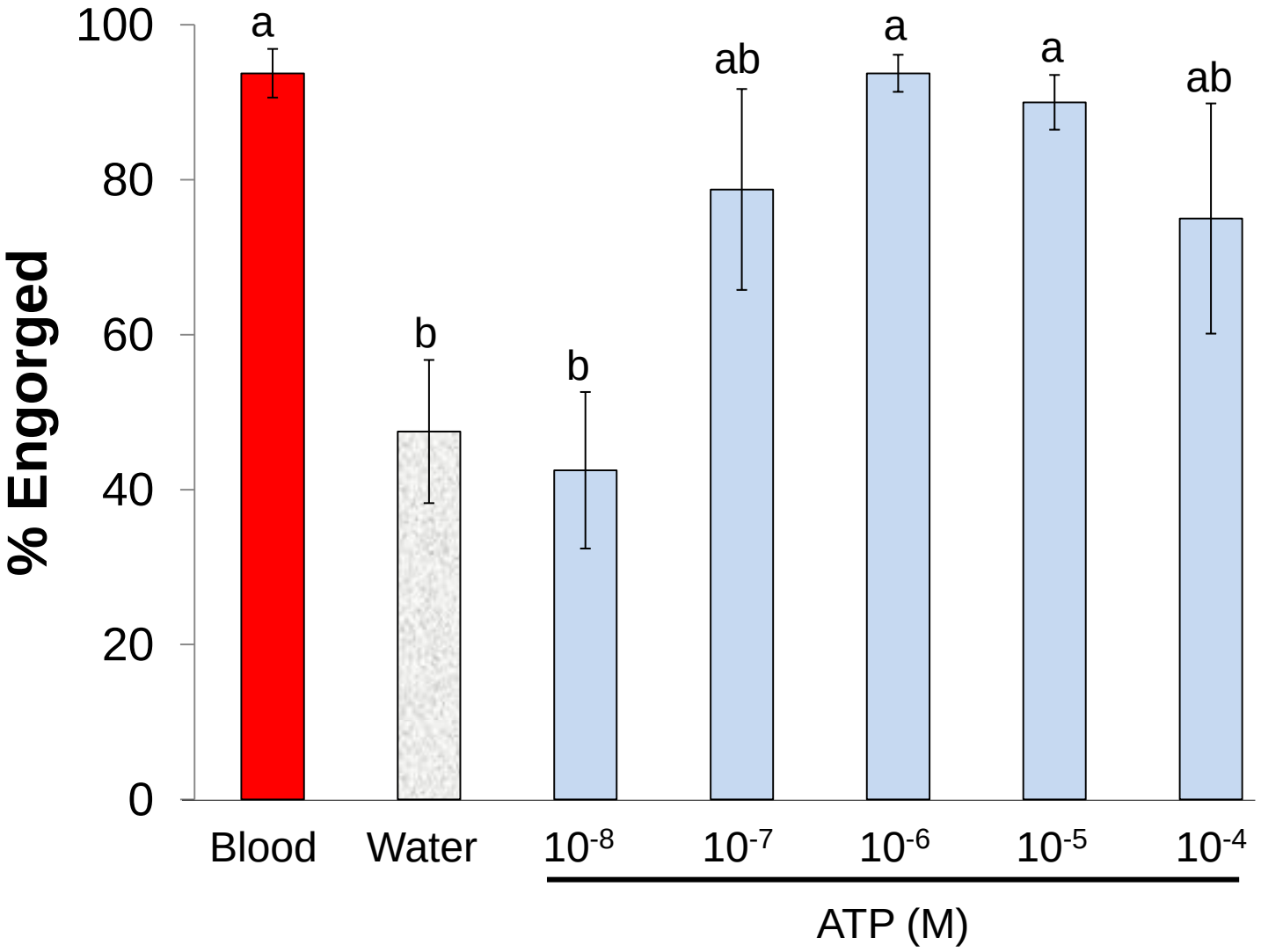
Individual bugs weighed before and after feeding

Blood contains phagostimulants



Water + ATP = Blood!





- Blood contains phagostimulants


Richard Naylor

- ATP is a highly effective phagostimulant
- All life stages displayed similar gorging responses to ATP
- ATP is a more effective phagostimulant than other adenosine nucleotides

  ATP > ADP > AMP

- Other phagostimulants?

Alvaro Romero

Example 2: Population genetics

Where have bed bugs resurged from?

3 Major hypotheses:

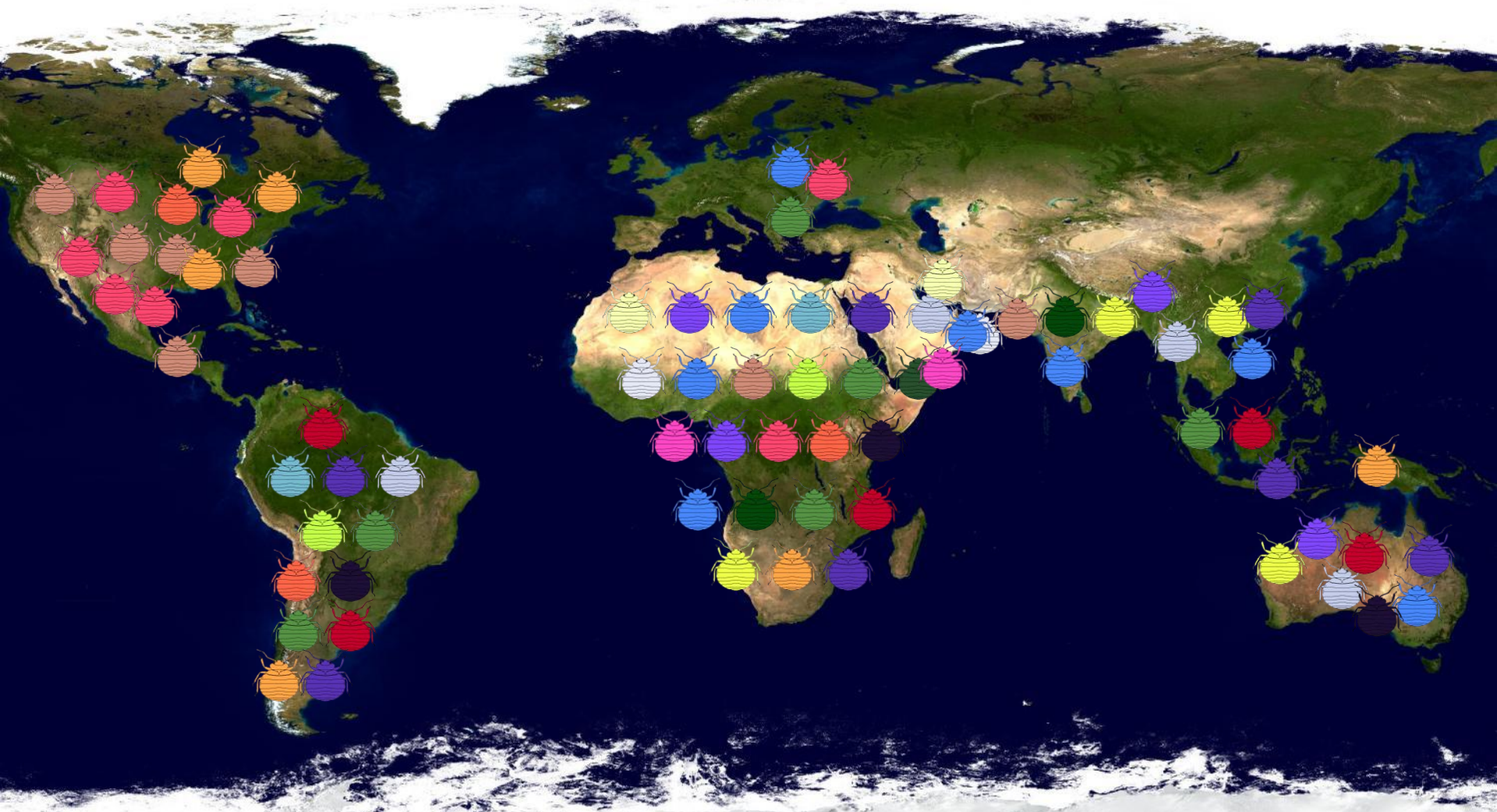
Local "home grown" bed bug populations

1. Residential, urban reservoirs
2. Agricultural (e.g., poultry farms) reservoirs

Global "immigrant" bed bugs

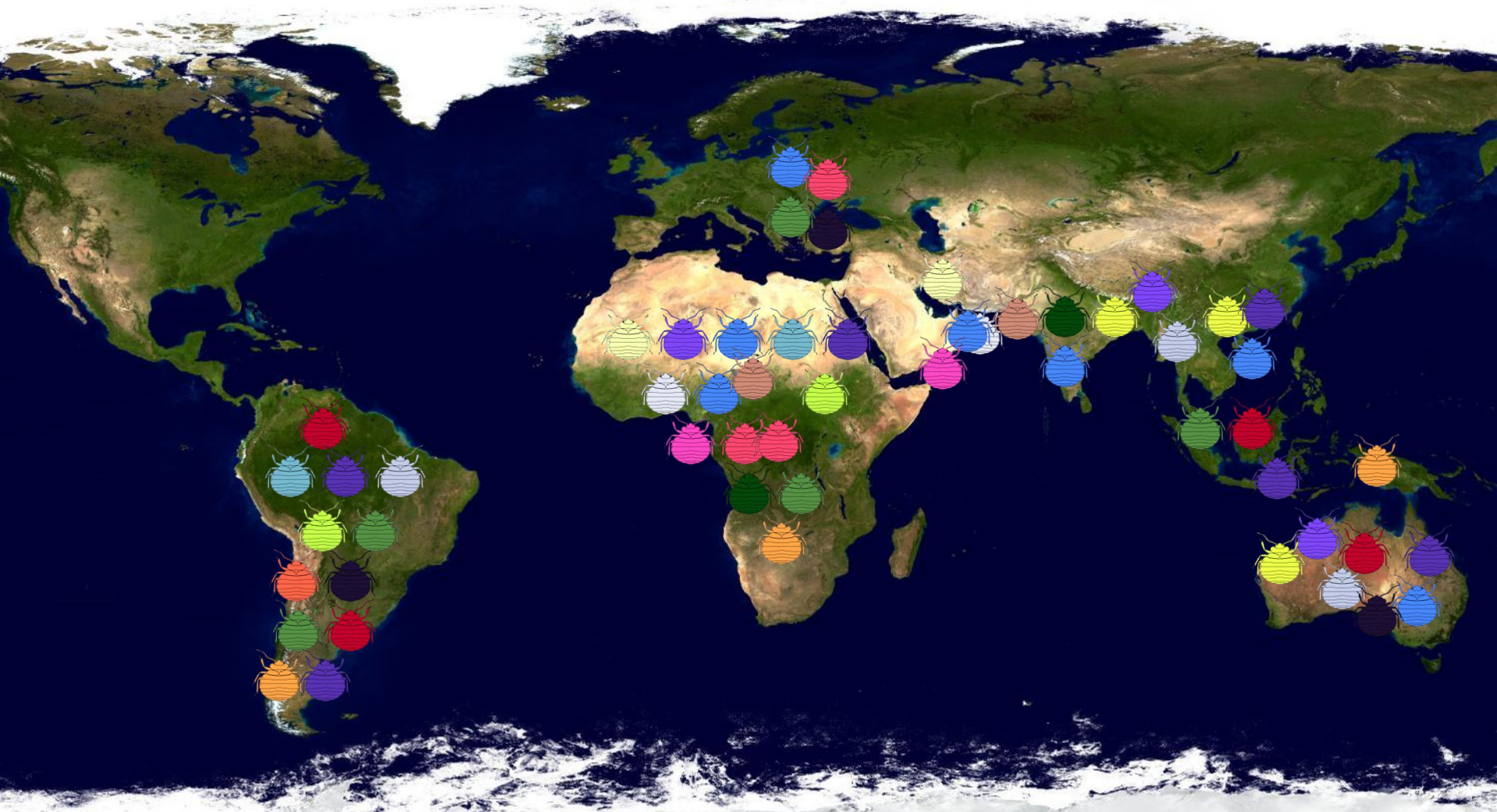
3. Outside USA: travel, globalization

A single, or few, invasion(s): Low diversity



Allele Diversity: immigrant population(s) << global populations

Multiple, independent invasions: High diversity



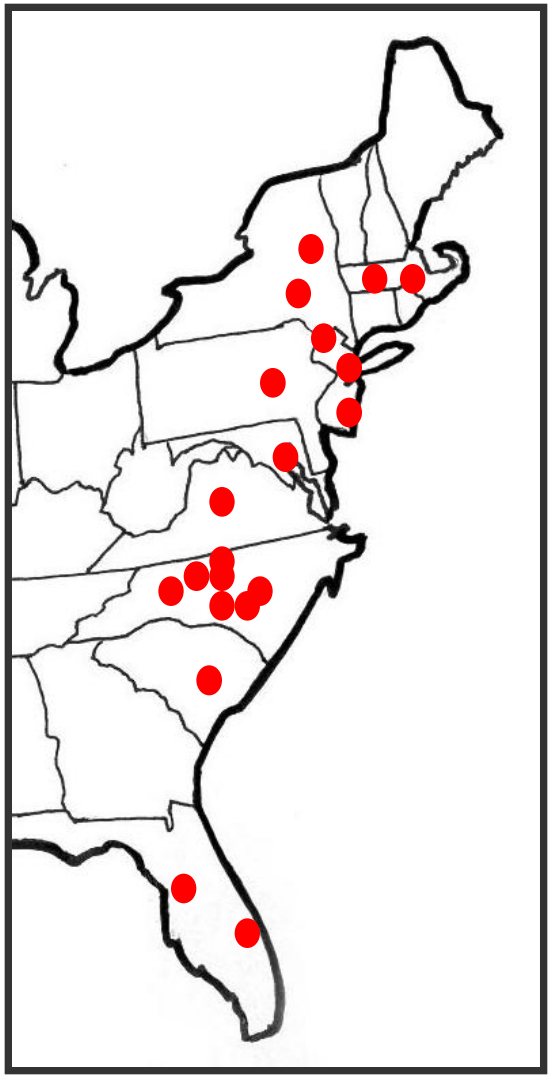
Allele Diversity: immigrant population**S** ~ source population**S**

Broad-scale BB population genetics

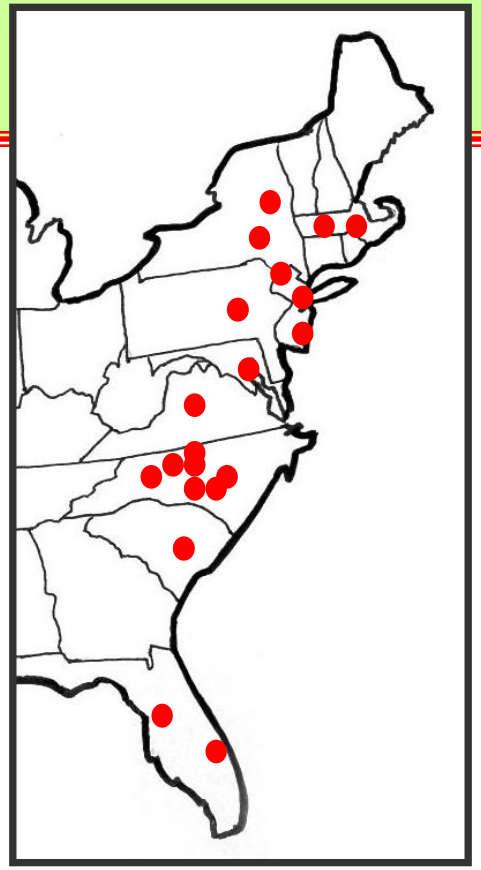
(Vargo, Booth, Saenz, Schal)

- Microsatellite markers:
  - ✓ Genetic diversity
  - ✓ Genetic differentiation
- 21 populations from 9 states

Virna Saenz



Genetic diversity



Across populations

- **Very high genetic diversity**
  - 3 to 17 alleles/locus (mean = 8.4)
  - But, need comparisons to “candidate” source populations
  - Suggests multiple sources

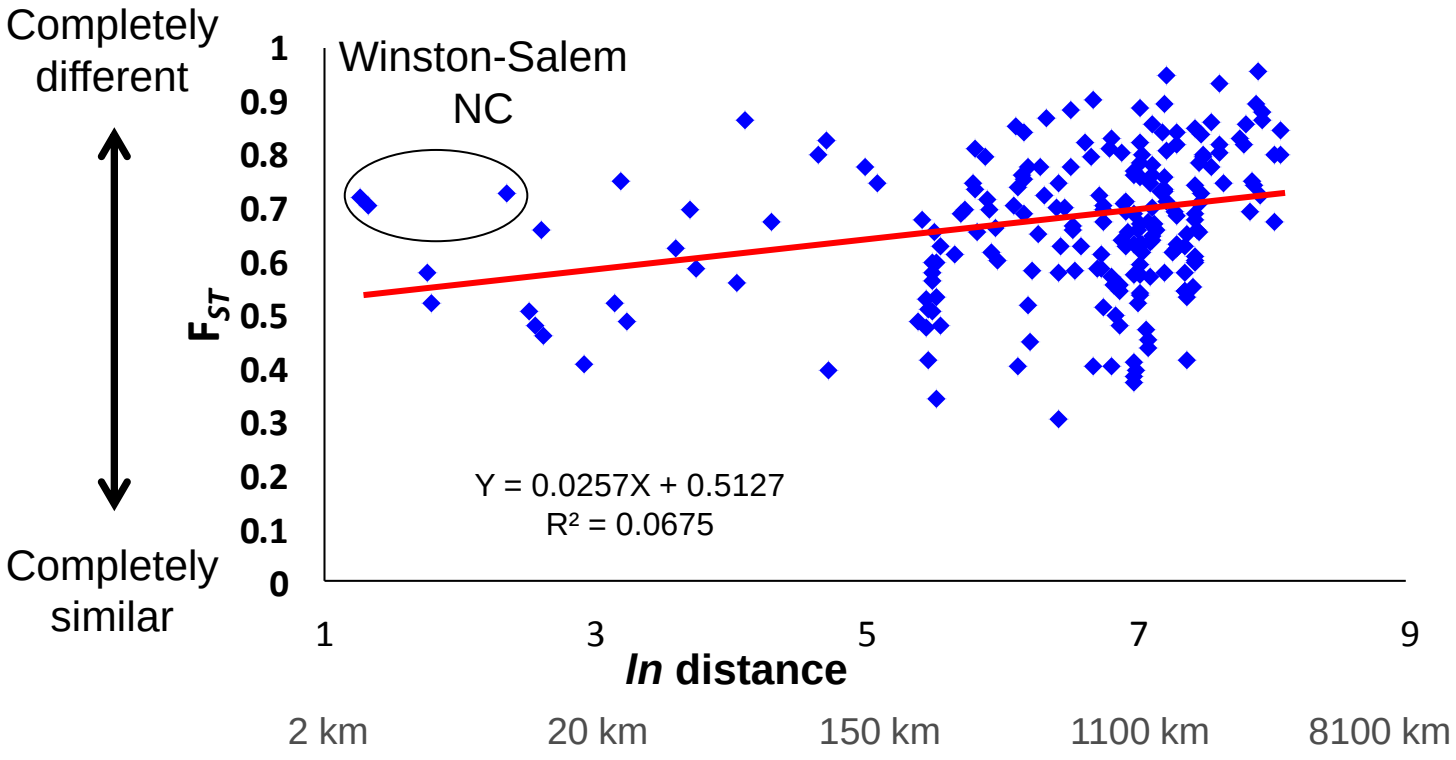
Within populations

- **Very low genetic diversity**
  - 1 to 4 alleles/locus
  - Mean relatedness of individuals
    - r = 0.75 (0.5 = sibs)
  - Very high levels of inbreeding
  - Suggests single/few sources per infestation

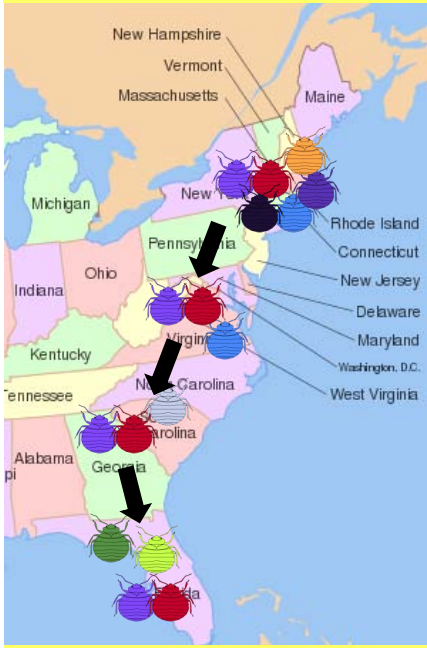
Genetic differentiation of populations

strong genetic differentiation!

but, no “Isolation-by-Distance”



invasion & spread



local spread

Broad-scale BB population genetics

(Vargo, Booth, Saenz, Schal)

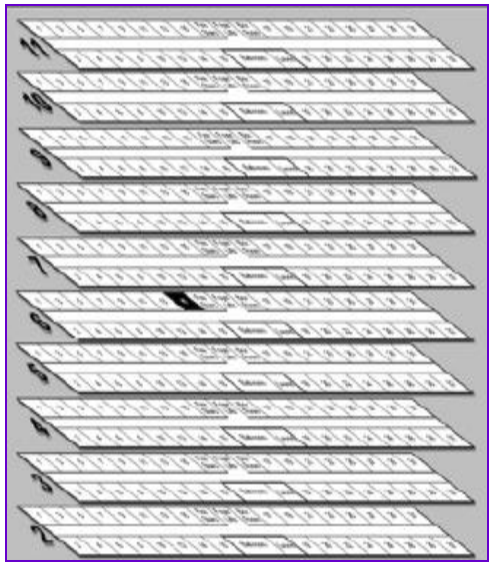
- **Within** populations: Very low genetic diversity & high inbreeding
  - Populations appear to be founded by a singly mated female

yet,

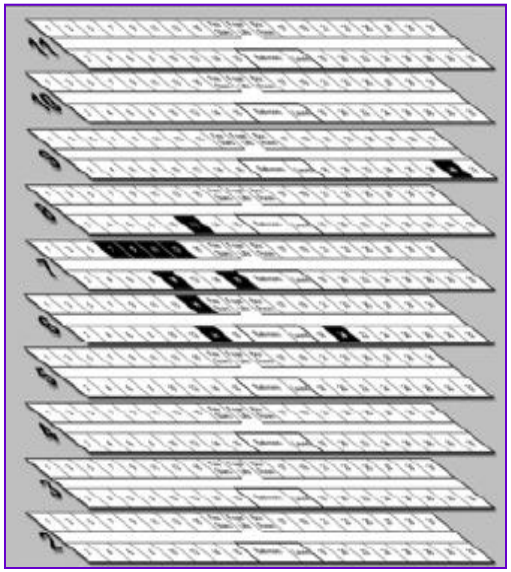
- **Across** populations: Very high genetic diversity & high genetic differentiation
  - Multiple introductions
  - “Jump”, human-mediated transport

How do bed bugs spread within a building?

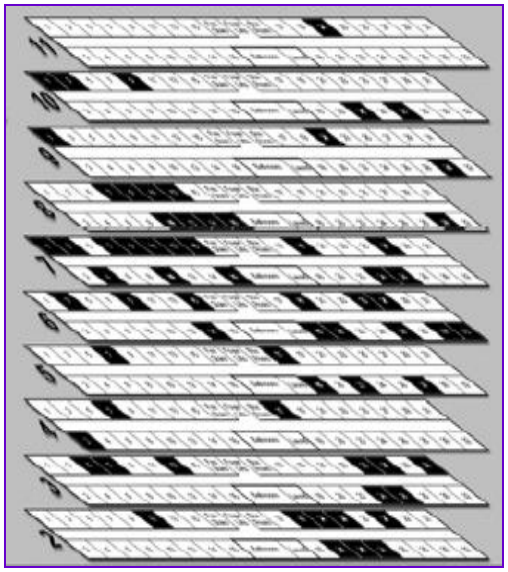
May 2003



May 2004



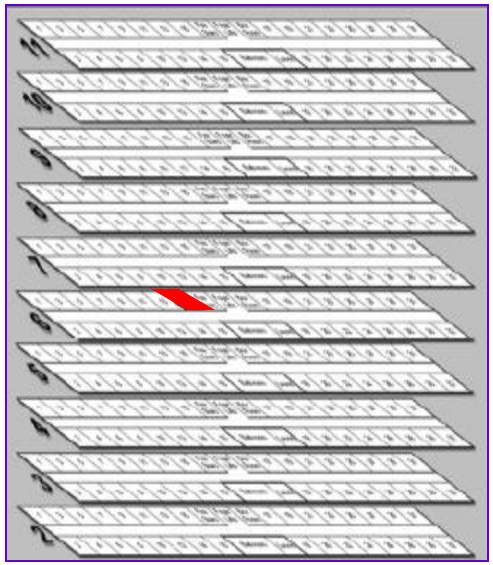
June 2005



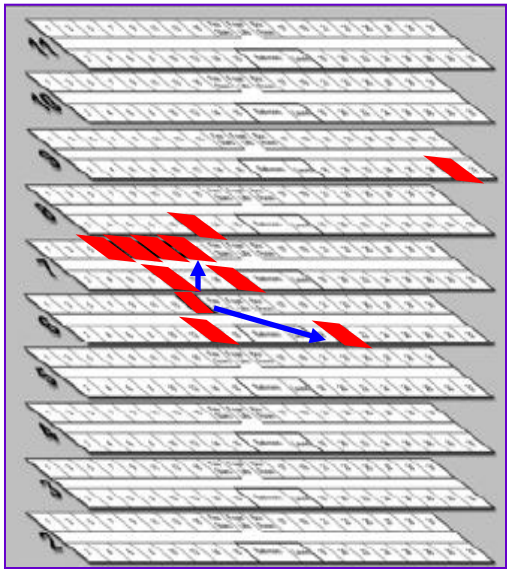
Doggett and Russell. 2008.

How do bed bugs spread within a building?

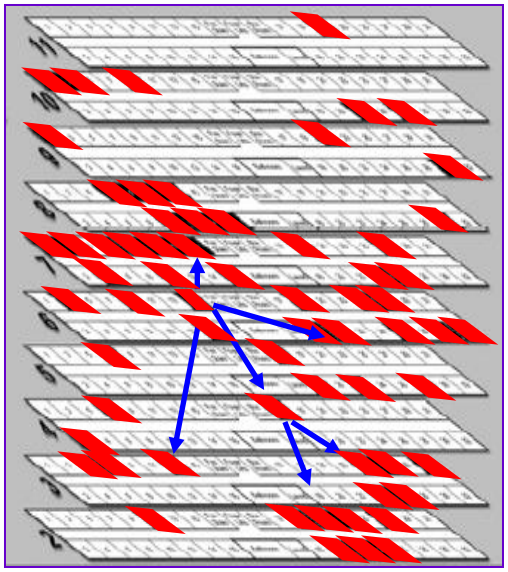
May 2003



May 2004



June 2005

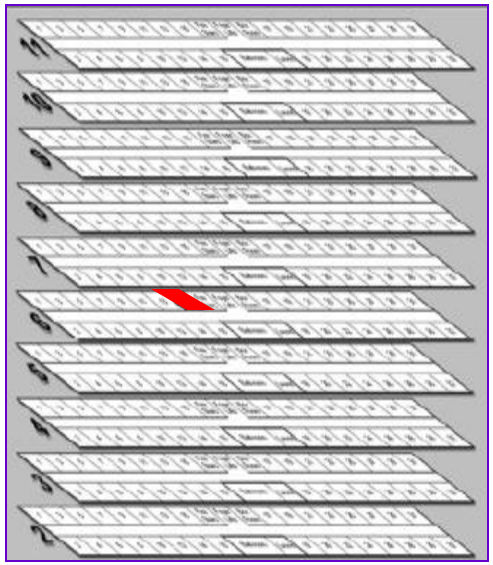


Single introduction?

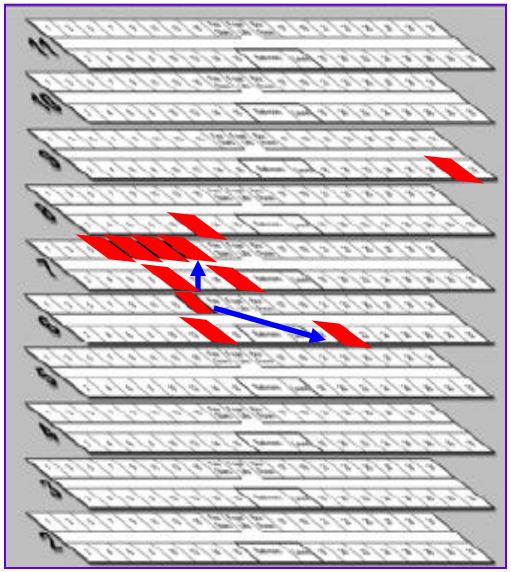
Doggett and Russell. 2008.

How do bed bugs spread within a building?

May 2003

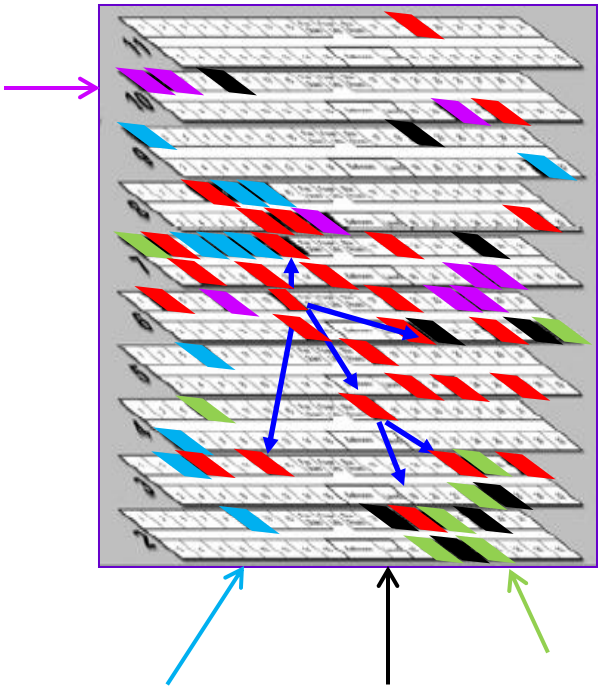


May 2004



Single introduction

June 2005



Multiple introductions?

Doggett and Russell. 2008.

Empirical test: BB spread within a building

How many individuals start an infestation?

Within apartments

- Low genetic diversity
  - ✓ 1 to 4 alleles/locus → Few!
- High relatedness
  - ✓ *r* = 0.54

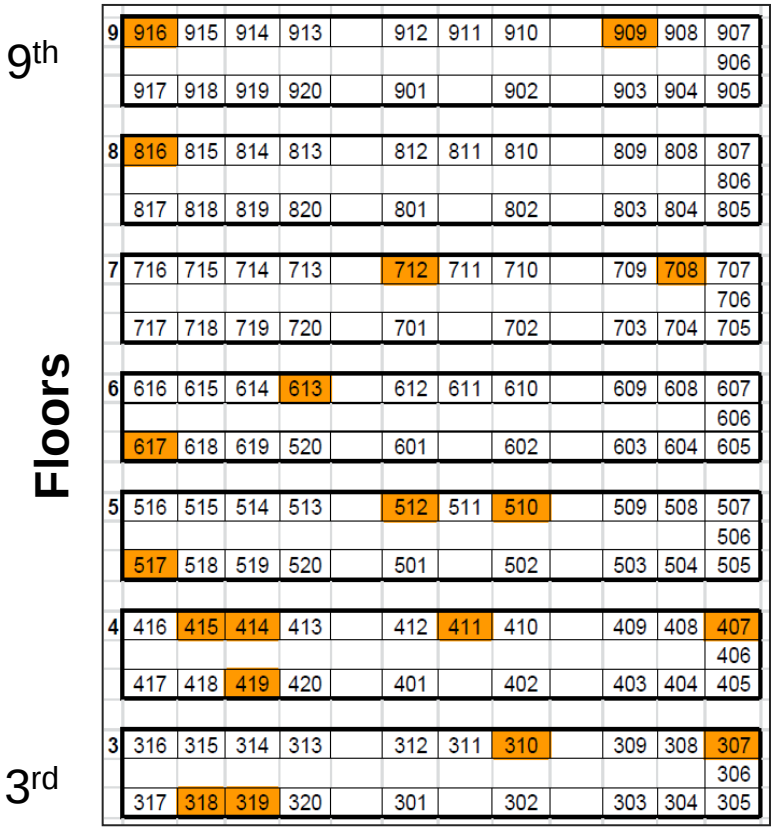
How many introductions?

Among apartments

- Low genetic diversity
  - ✓ 2 to 5 alleles/locus → Single!

Raleigh, NC

Isolated building, recent infestation



Empirical test: BB spread within a building

How many individuals start an infestation?

Within apartments

- Low genetic diversity
  - ✓ 1 to 4 alleles/locus → Few!
- High relatedness
  - ✓ *r* = 0.65

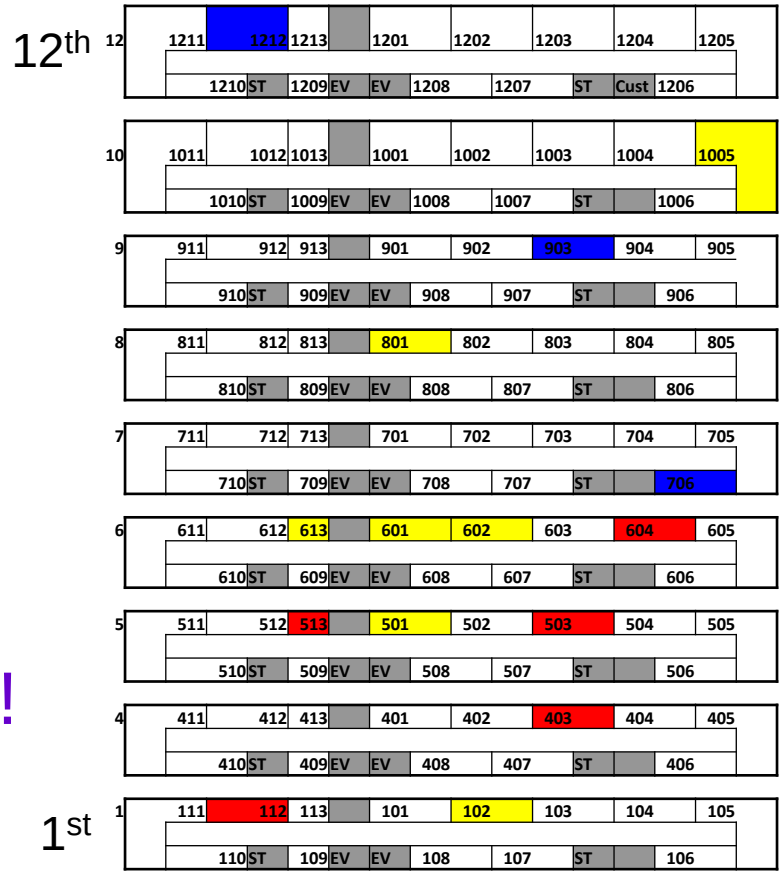
How many introductions?

Among apartments

- High genetic diversity
  - ✓ 2 to 11 alleles/locus → Multiple!

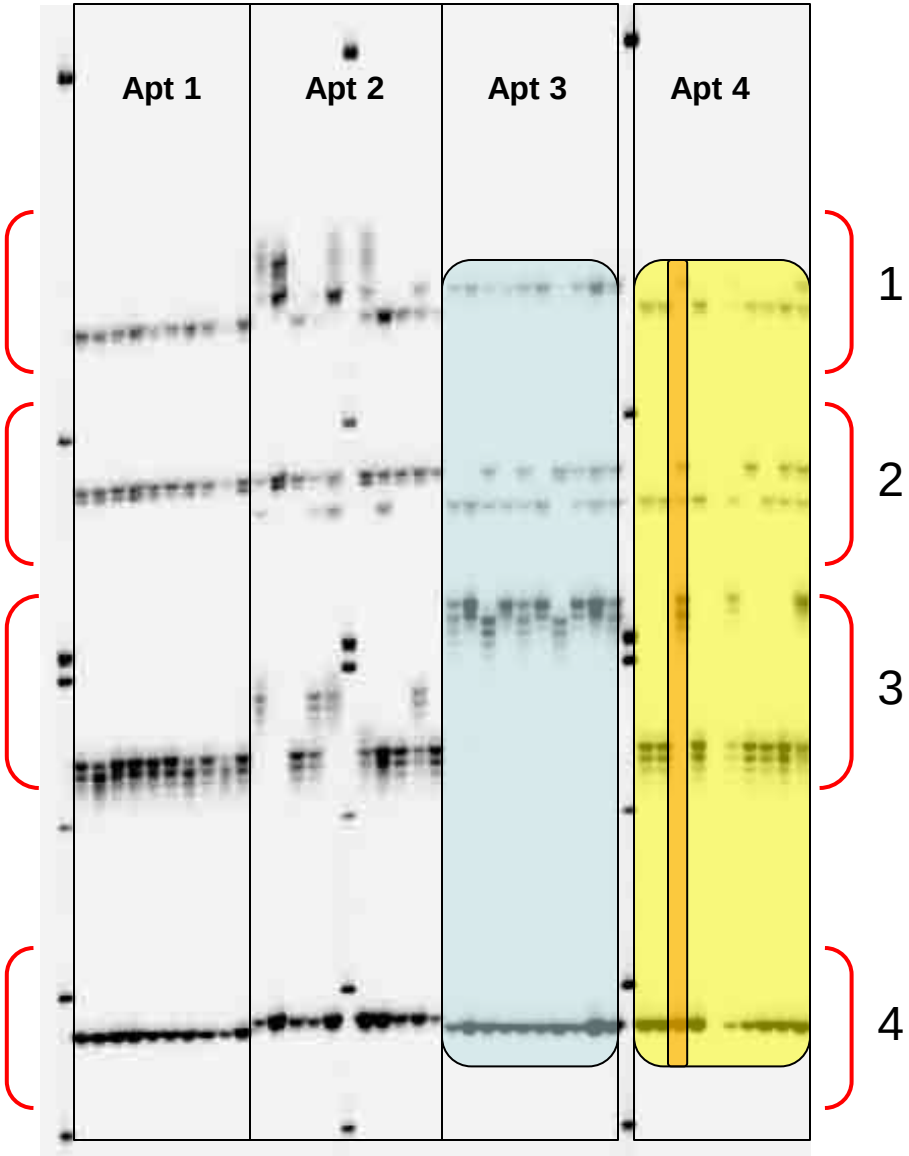
Jersey City, NJ

Building complex, old infestation



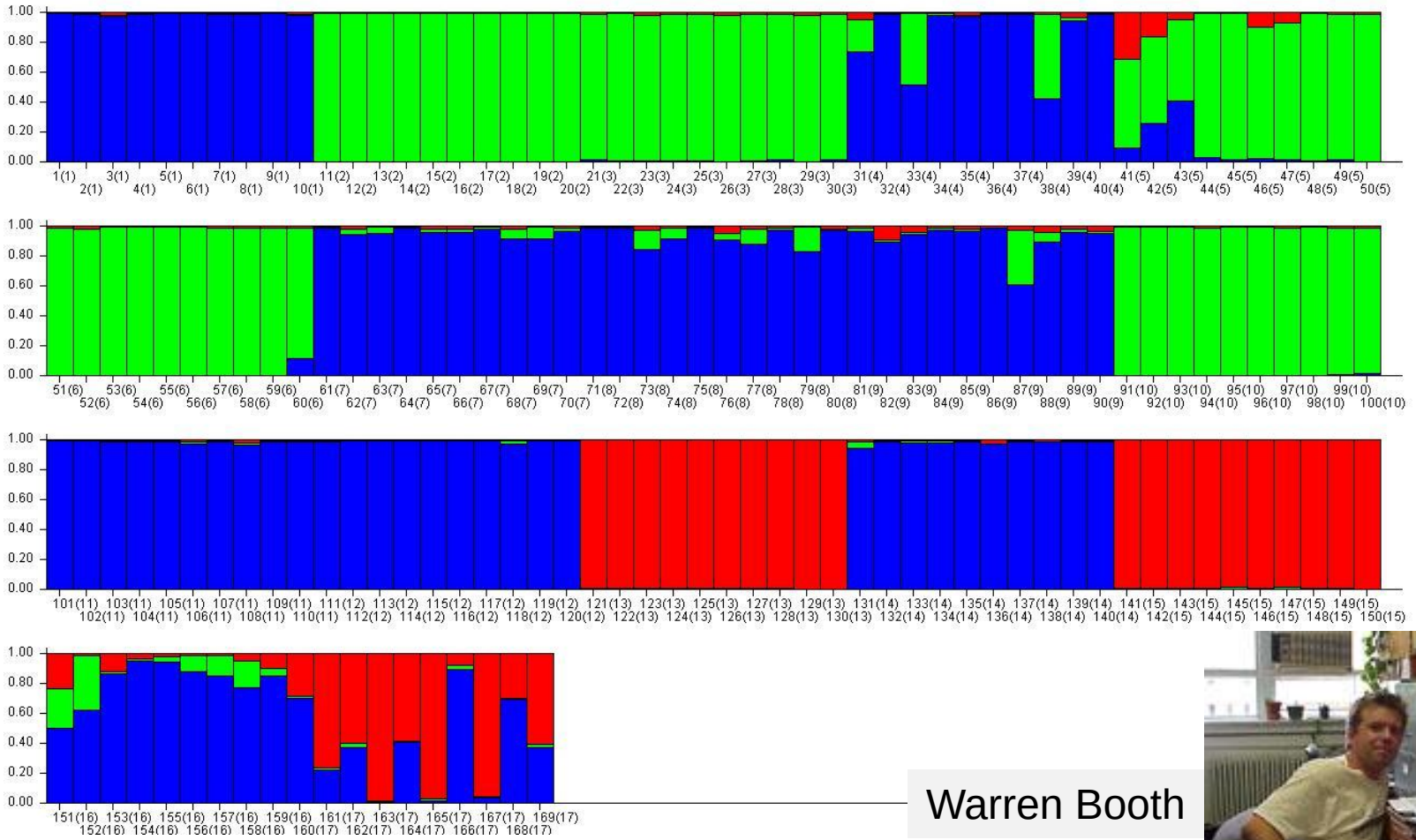
collections by Changlu Wang

Empirical test: BB spread within a building



Empirical test: BB spread within a building

Jersey City, NJ: 17 populations
3 genetic clusters



Warren Booth

software: STRUCTURE

Implications of Population Genetics

Large scale (continental, East Coast)

- Bed bug populations come from multiple geographic sources
- Extensive human-mediated movement of bed bugs across large geographic areas

  Interception important at transportation hubs

Fine scale (within buildings)

- Infestations often start with a single introduction, and then spread; but also multiple introductions

  Early detection critical

Forensic applications: sources of bed bug infestations

Example 3: Genome, Transcriptome

- Genes common to BB and other insects?
- Genes common to hematophagous arthropods
- Genes and gene products unique to BB
- Why do BB not vector diseases?
- When and where genes are turned on or off

  (transcripts specific to tissue-, time-, instar-, feeding-, resistance-, etc.)
- Gene networks:

  immunity, heat/cold response, feeding behavior, sexual behavior, host-finding……

Example 3: Genome, Transcriptome

OPEN ACCESS Freely available online

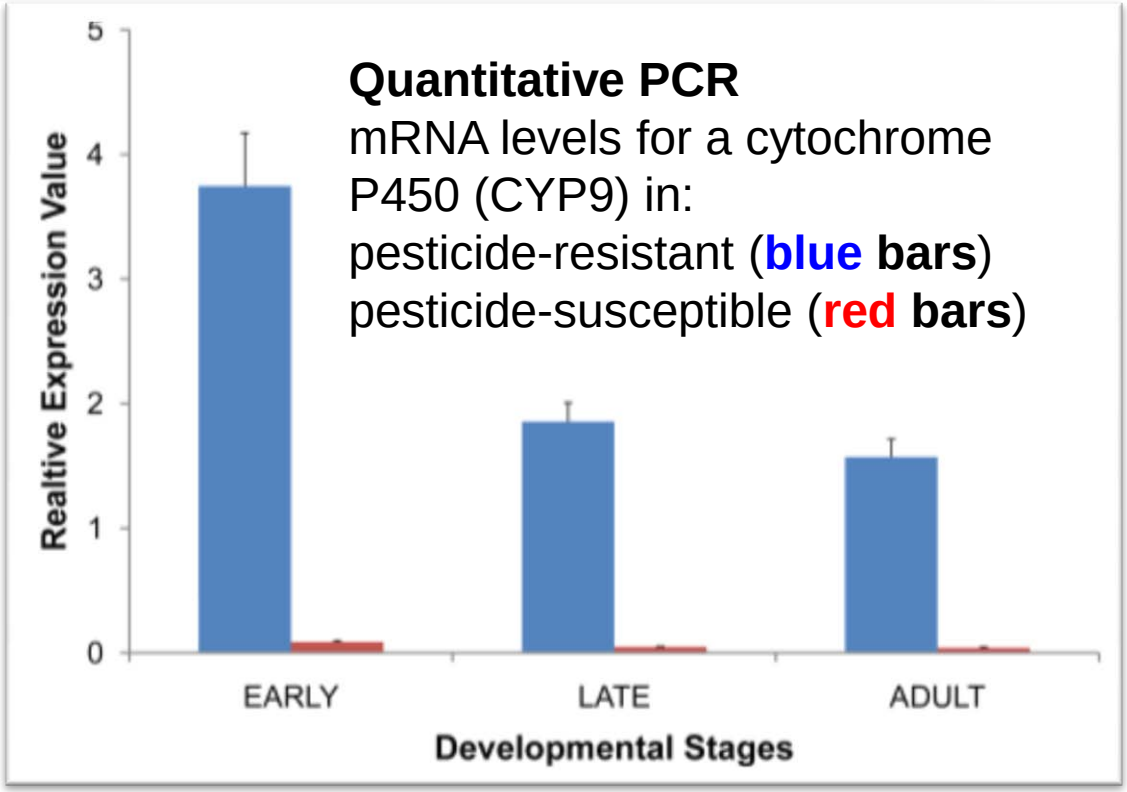
PLoS one

Transcriptomics of the Bed Bug (*Cimex lectularius*)

Xiaodong Bai[1☯], Praveen Mamidala[1☯], Swapna P. Rajarapu[1], Susan C. Jones[2], Omprakash Mittapalli[1*]

1 Department of Entomology, Ohio Agricultural and Research Development Center, The Ohio State University, Wooster, Ohio, United States of America, 2 Department of Entomology, The Ohio State University, Columbus, Ohio, United States of America

"*Nearly 85.9% of the C. lectularius sequences showed similarity to insect sequences, but* ***44.8%*** ***of the deduced proteins of C. lectularius did not show similarity with sequences in the GenBank***"



Quantitative PCR
mRNA levels for a cytochrome P450 (CYP9) in:
pesticide-resistant (**blue bars**)
pesticide-susceptible (**red bars**)

Perspective: Fundamental and Translational research

- **Government & private sector investments**
- **Innovative, medium- and long-term**
- **Accountable to stakeholder input**
- **Spawns ideas for novel tactics, products**
- **Research $\rightleftharpoons$ Pest control**
- **Apply discoveries from research in the lab to “clinical” studies**
- **Break down compartmentalization**

Collaborators & co-workers: Ed Vargo

Warren Booth, Alvaro Romero, Virna Saenz, Rick Santangelo

Changlu Wang

Blanton J. Whitmire Endowment **NC State University**

USDA-NIFA-AFRI

NSF Postdoctoral Research Fellowship in Biology

Pest management companies:

Orkin

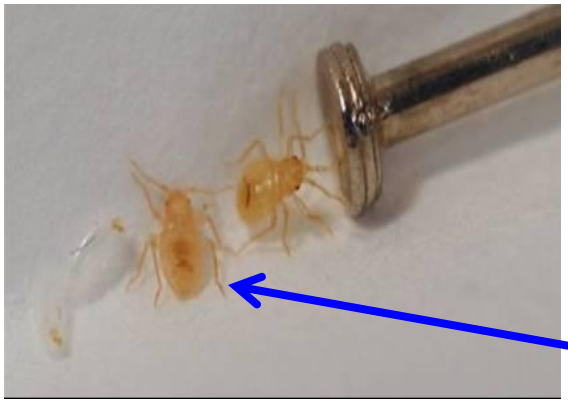
Cooper

Rentokil/JC Ehrlich

Terminix

Life cycle

Egg to Adult = 45 days at 26º C



bedbuginfo.dondodd.com/

sciencedude.ocregister.com