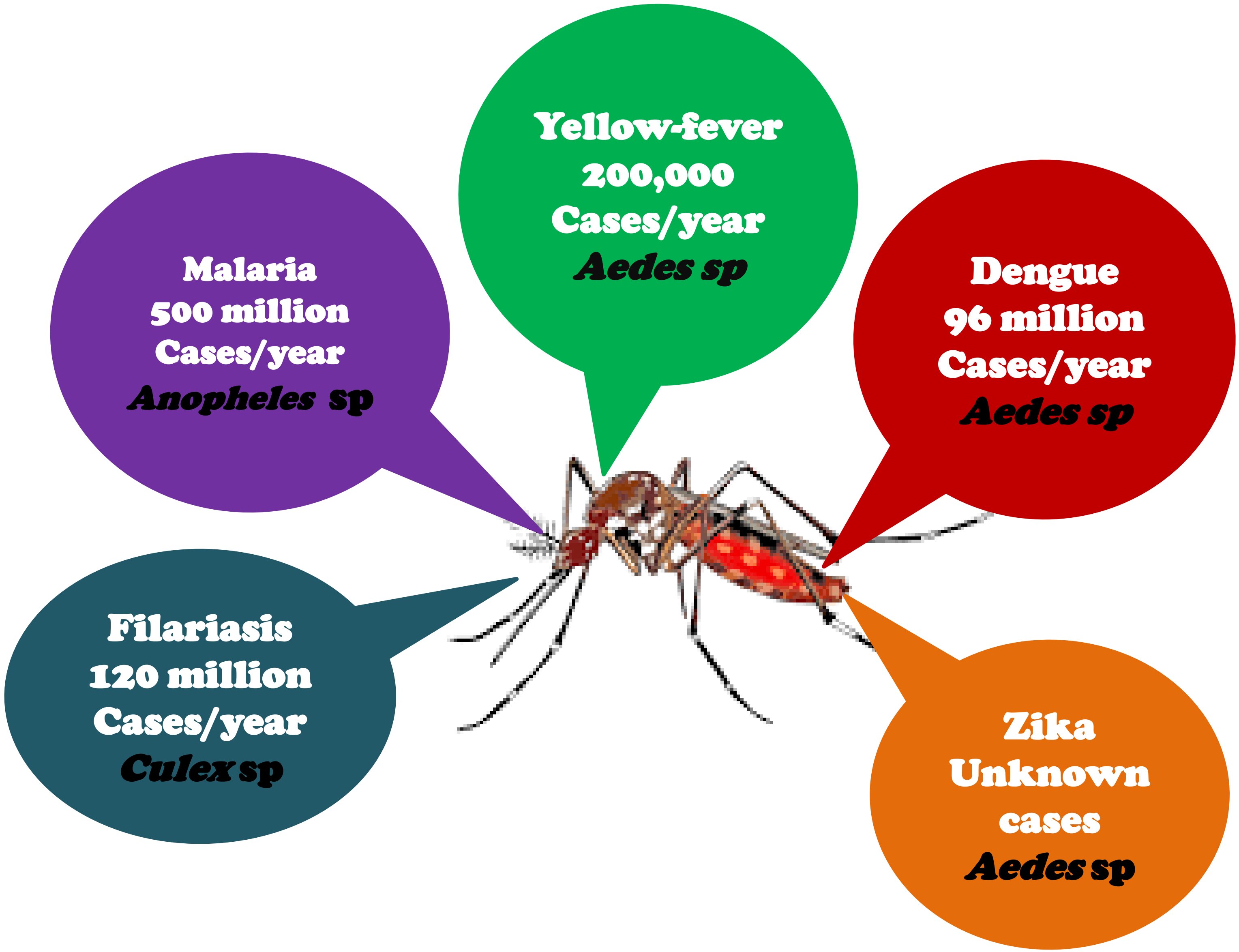
Controlling insect vectors in Sri Lanka: Is transgenesis a way forward?

S.N. Surendran

MOSQUITO-BORNE DISEASES

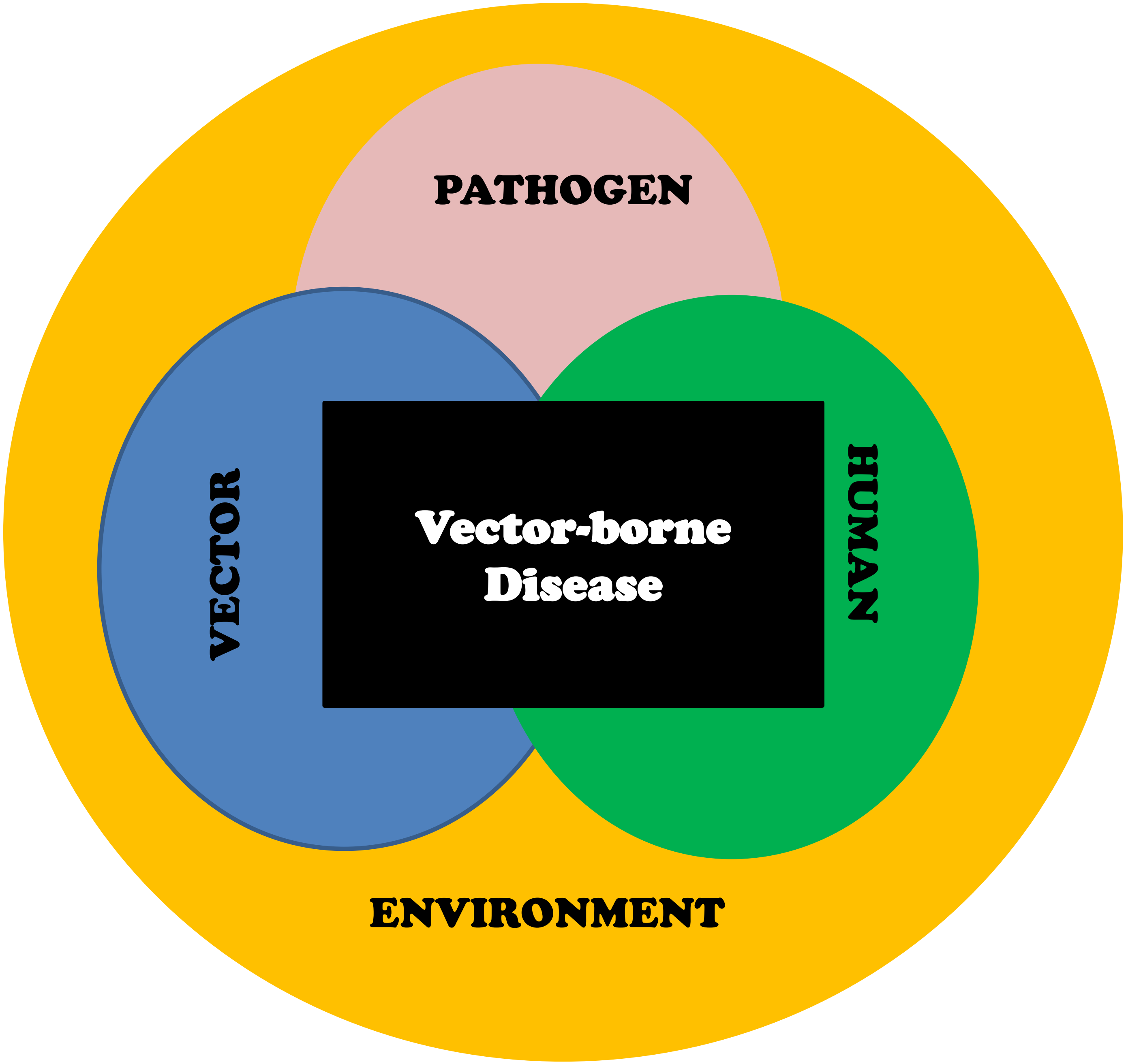


Mosquito-borne diseases (MBD) in Sri Lanka

- Malaria, dengue, chickungunya, JE and filariasis etc……
- Diseases prevalence
  - Malaria –prevention of reintroduction
  - Dengue – major public health problem with high morbidity and mortality

Transmission of Vector-borne diseases

- **Transmission of vector-borne diseases in tropical countries is strongly associated with factors**
  - parasite resistance to drugs and mosquitoes to insecticides
  - population movement and
  - environmental alterations due to changes in land-use pattern


PATHOGEN
VECTOR
Vector-borne
Disease
HUMAN
ENVIRONMENT

Importance of mosquito vector control for disease control

- Absence of a licensed vaccine against many mosquito-borne diseases.

- Drugs for specific treatment of arboviral diseases including dengue, chikungunya, yellow fever and Zika are not presently available.

- A vaccination trial has been planned to start in Sri Lanka later this year using a chimeric vaccine containing all 4 dengue viral types.

Importance of mosquito vector control for disease control

- **Control measures for arboviral diseases therefore rely heavily on measures such as**
  - minimizing human-mosquito contact,
  - reducing vector mosquito populations and
  - eliminating pre-imaginal development sites

Mosquito control measures

- Source reduction
- Spraying Insecticide
- Biological Control
- Personal Protection

Transmission of mosquito-borne diseases

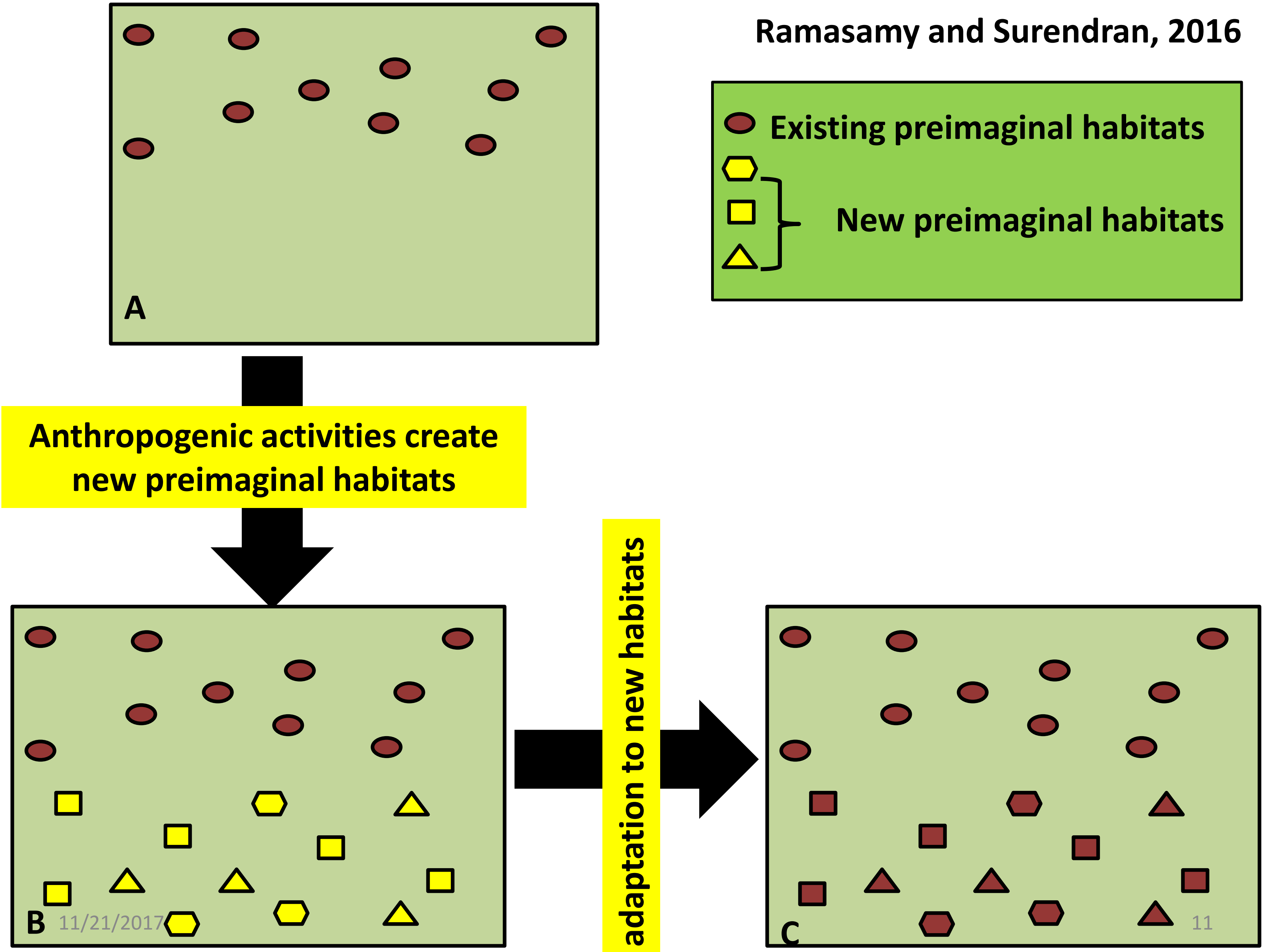
- **Mosquito vectors have evolved over a very long time (hundreds or thousands of years) to take advantage of increasing human populations, their geographical expansion, and societal features such as agriculture and urbanisation.**

Adaptation to new anthropogenic habitats - driving forces: Scenario I

- Anthropogenic activities can create suitable new habitats within the natural range of the vectors.

- The new and pre-existing habitats can then lead to an increase in vector population and therefore disease transmission.

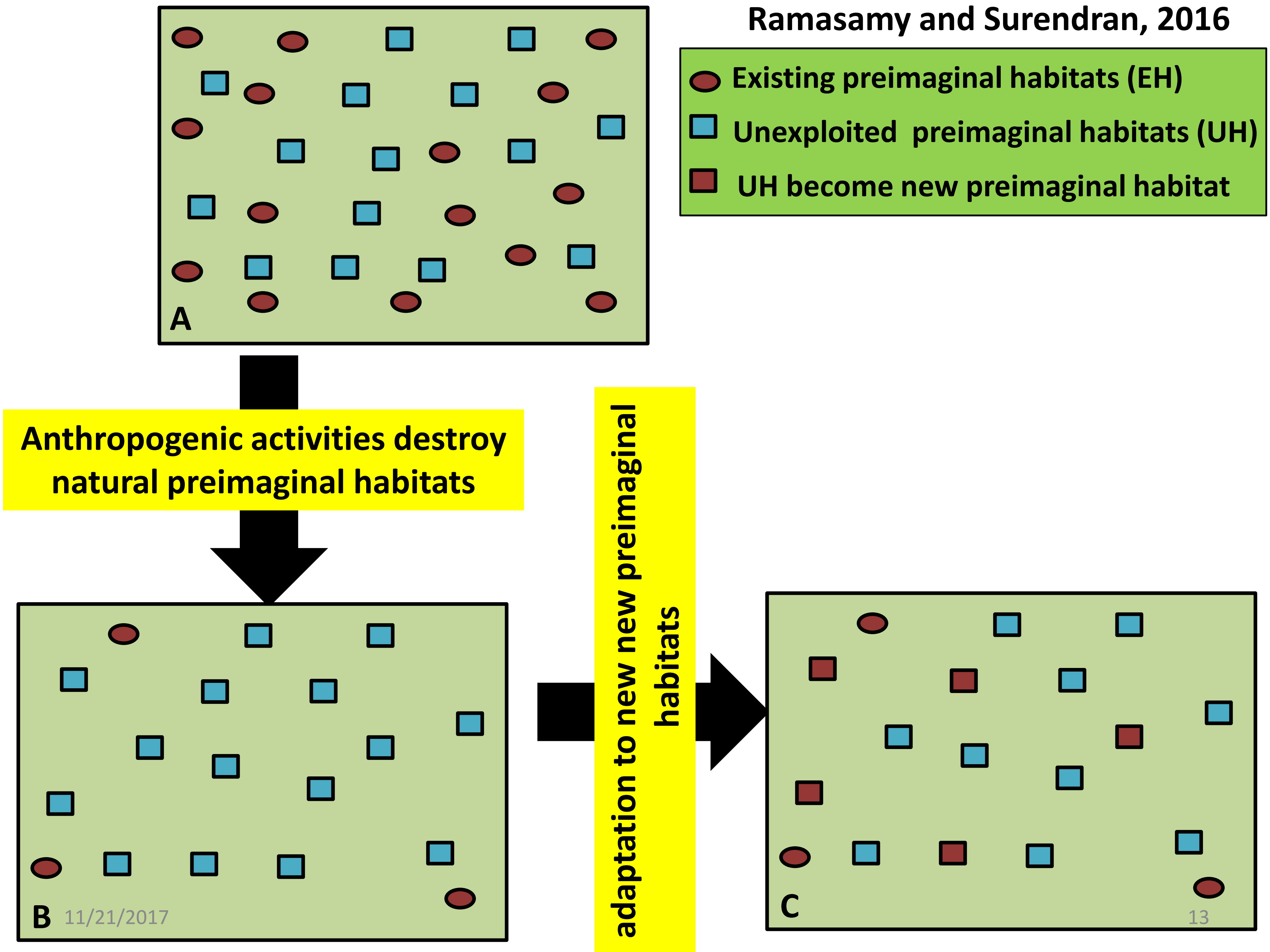
Ramasamy and Surendran, 2016


Ramasamy and Surendran, 2016
Existing preimaginal habitats
New preimaginal habitats
A
Anthropogenic activities create new preimaginal habitats
B
adaptation to new habitats
C

Adaptation to new anthropogenic habitats - driving forces: Scenario II

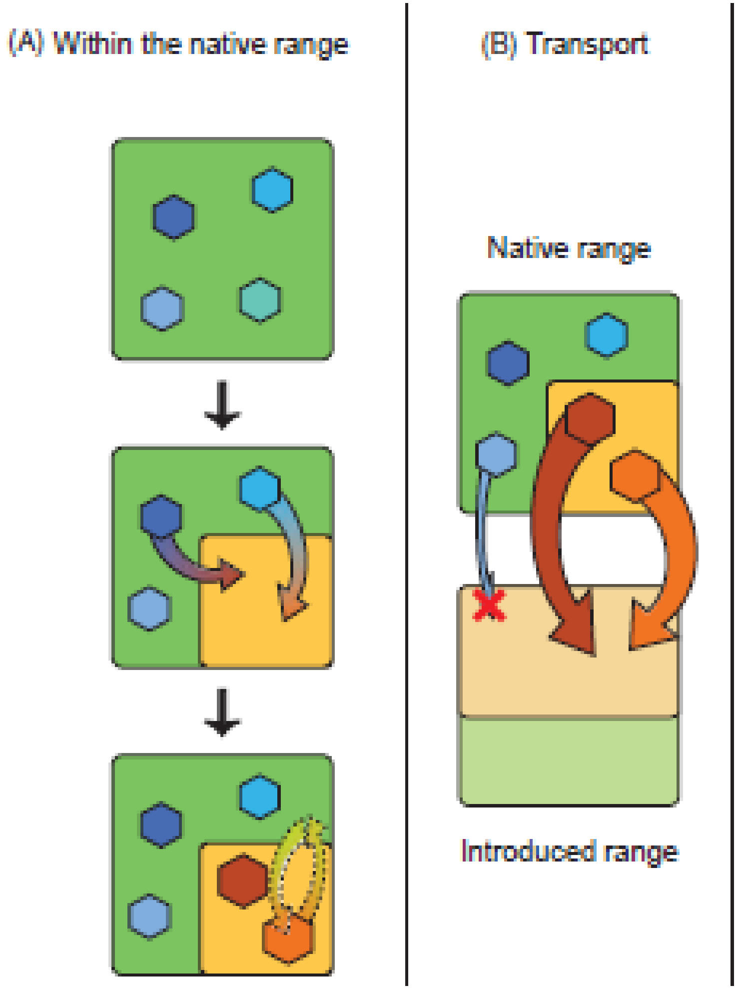
- Anthropogenic activities that eliminate or greatly minimise the preimaginal habitats preferred by vector mosquitoes can be the driving force for their adaptation to less optimal and under-utilised habitats within their normal range close to human populations

Ramasamy and Surendran, 2016


Ramasamy and Surendran, 2016
Existing preimaginal habitats (EH)
Unexploited preimaginal habitats (UH)
UH become new preimaginal habitat
A
Anthropogenic activities destroy natural preimaginal habitats
B
adaptation to new new preimaginal habitats
C

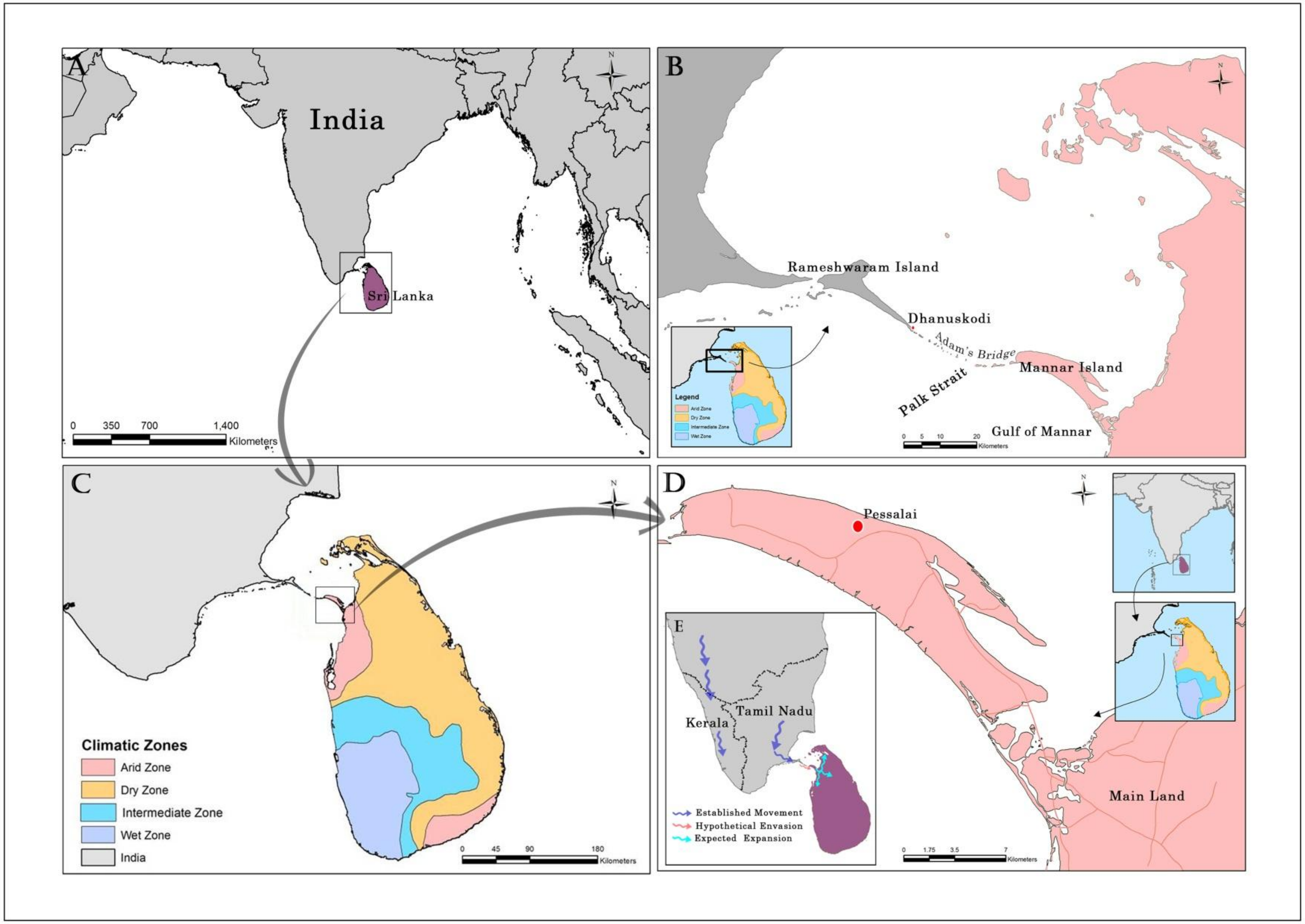
Adaptation to new anthropogenic habitats - driving forces……

- **This ability has been termed anthropogenically induced adaptation to invade (AIAI)** [Hufbauer et al. 2011] **and supportive evidence for its occurrence has been reported in agricultural insect pests**



[Hufbauer et al. 2011]

Invasive *An. stephenssi* in Sri Lanka



Challengers

Challengers

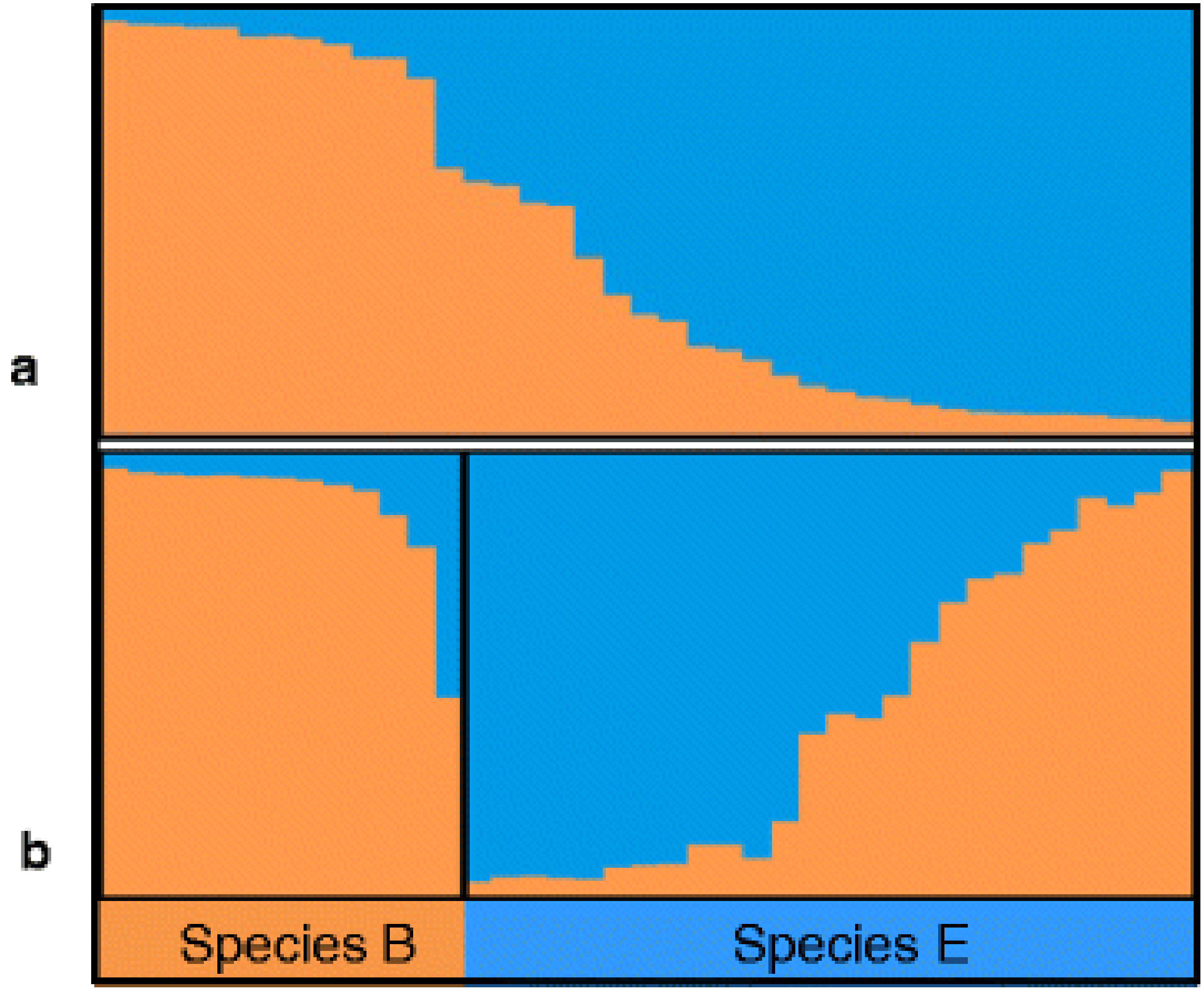
- Insecticide Resistance
- Atypical Adaptation
- More than one vector species

	Biochemical Mechanisms				
	Metabolic			Target-site	
	Esterases	Monoxegenases	GST	*kdr*	Altered AChE
Pyrethroids	•	●		●	
DDT		•	●	●	
Carbamates	•				●
OPs	●	•			●

Challengers....

- **Differential prevalence and adaptations**
  - ***Ae. albopictus*** **predominate in pre monsoon season and** ***Ae. aegypti*** **during monsoon season**
  - **Both species prevalent in urban and suburban areas**
  - **Both species breeding in brackish waters**

Ramasamy et al. 2011; Surendran et al. 2012

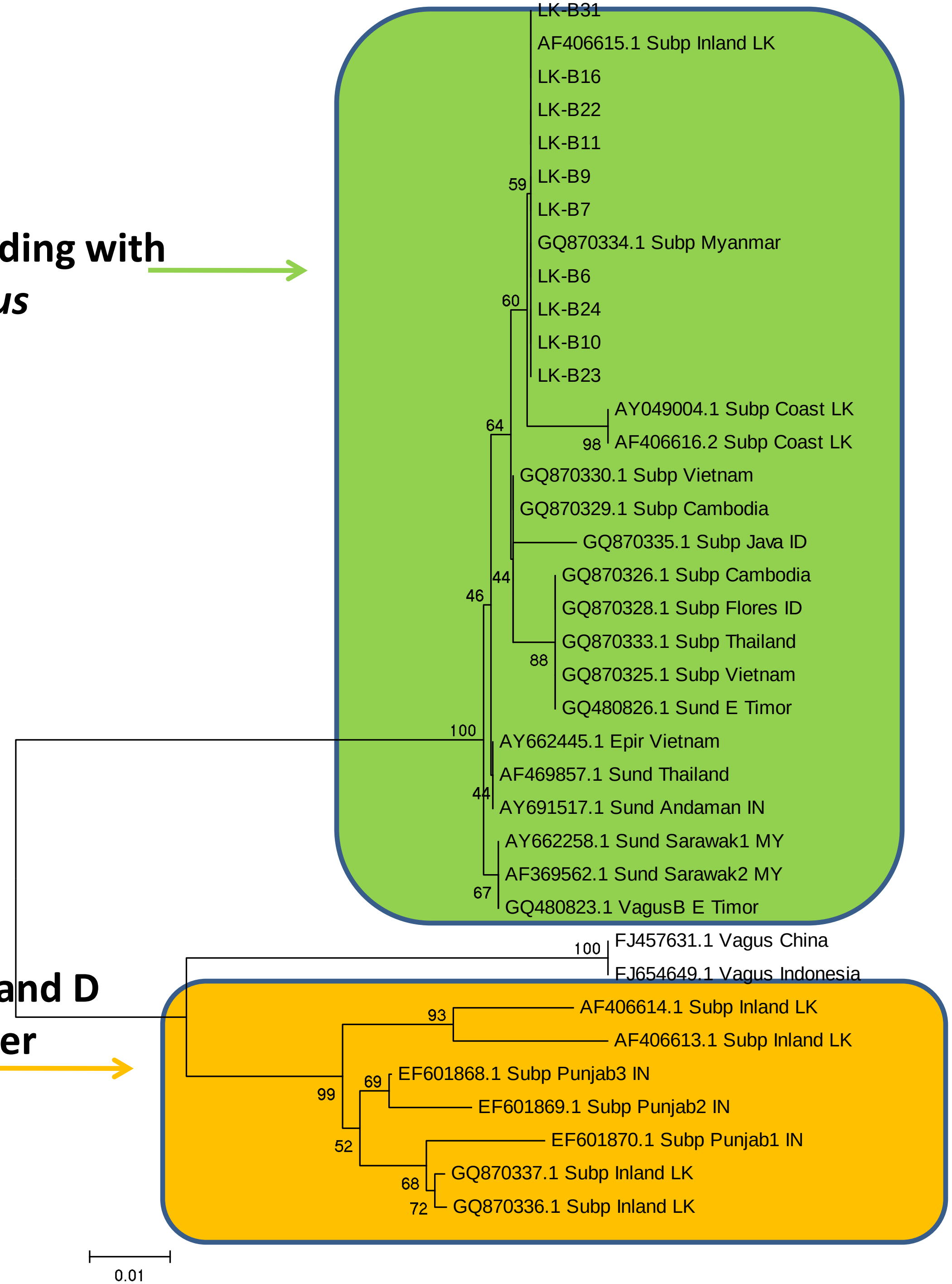


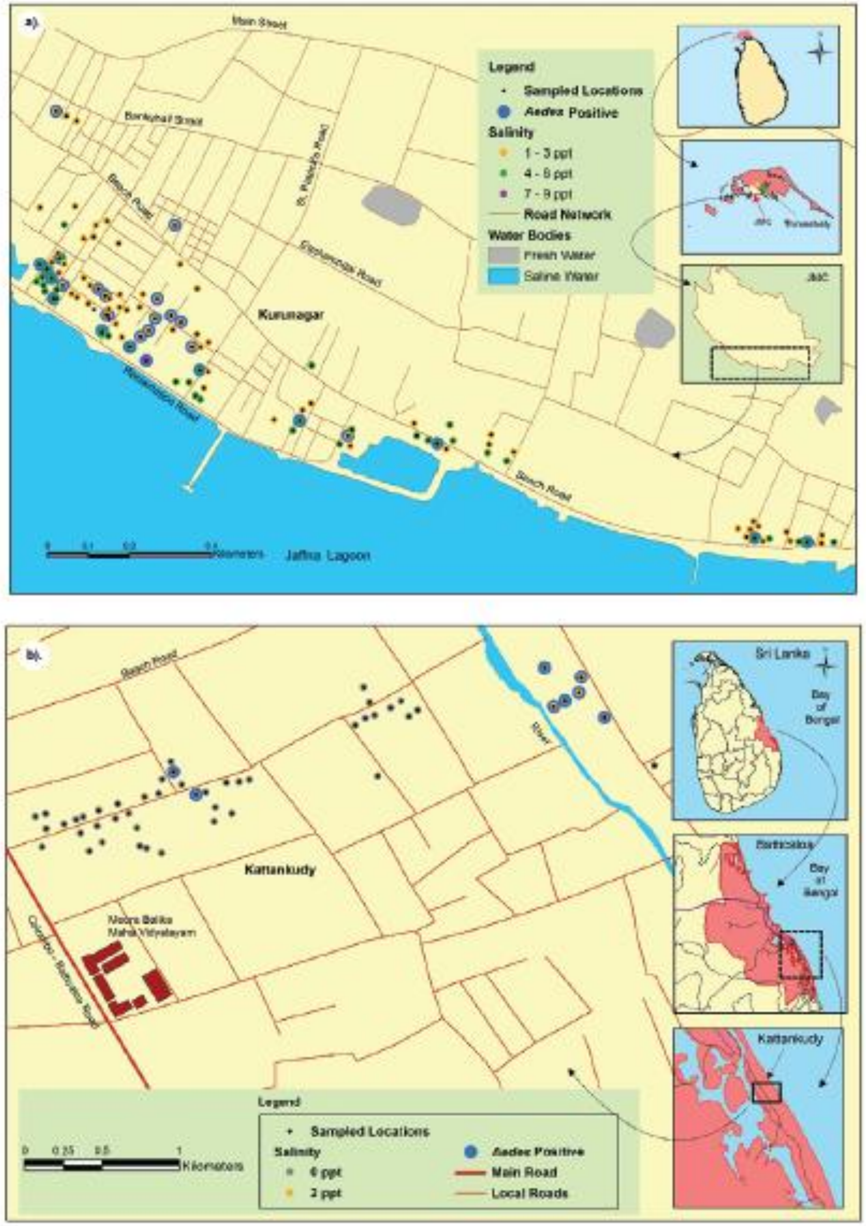
Surendran et al. 2015

Surendran et al. 2013

Sibling species B clading with *An. sundaicus*

Sibling species A, C and D clading with other *An. subpictus* populations





Surendran et al. 2012

Alternative strategies

Vector Control

- Releasing Genetically Modified Mosquitoes (GMM)
- Many shortfalls in vector control justify the need genetic manipulation of mosquitoes to control mosquito-borne diseases

Genetic Manipulation of Vectors

- **Transgenesis** - is the process of introducing an exogenous gene — called a transgene — into a vector

- **Paratransgenesis** - utilizing genetically modified insect symbionts to express transgene within the vector

Two Strategies

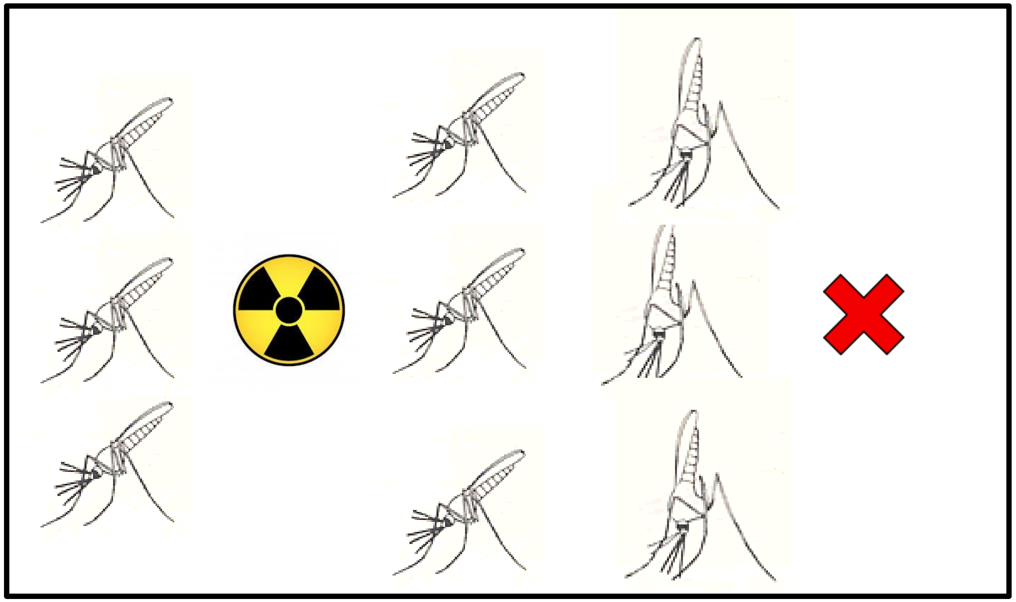
- Population replacement
- Population reduction

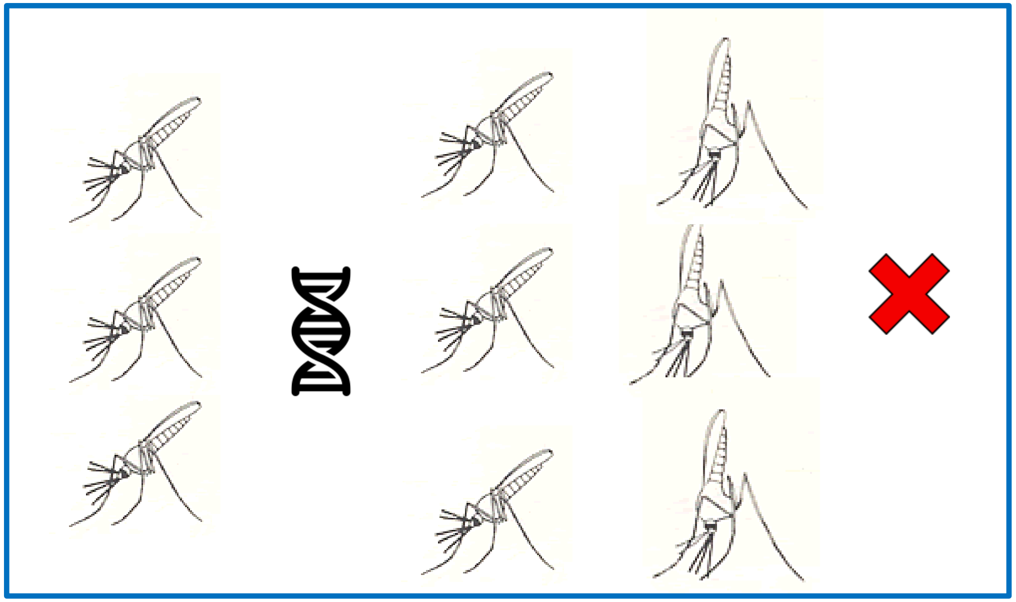
Population Reduction

- Insecticide application
- Sterile Insect Technique (SIT)
- Cytoplasmic incompatibility
- Transgenic sterilization

Genetic Sterilization

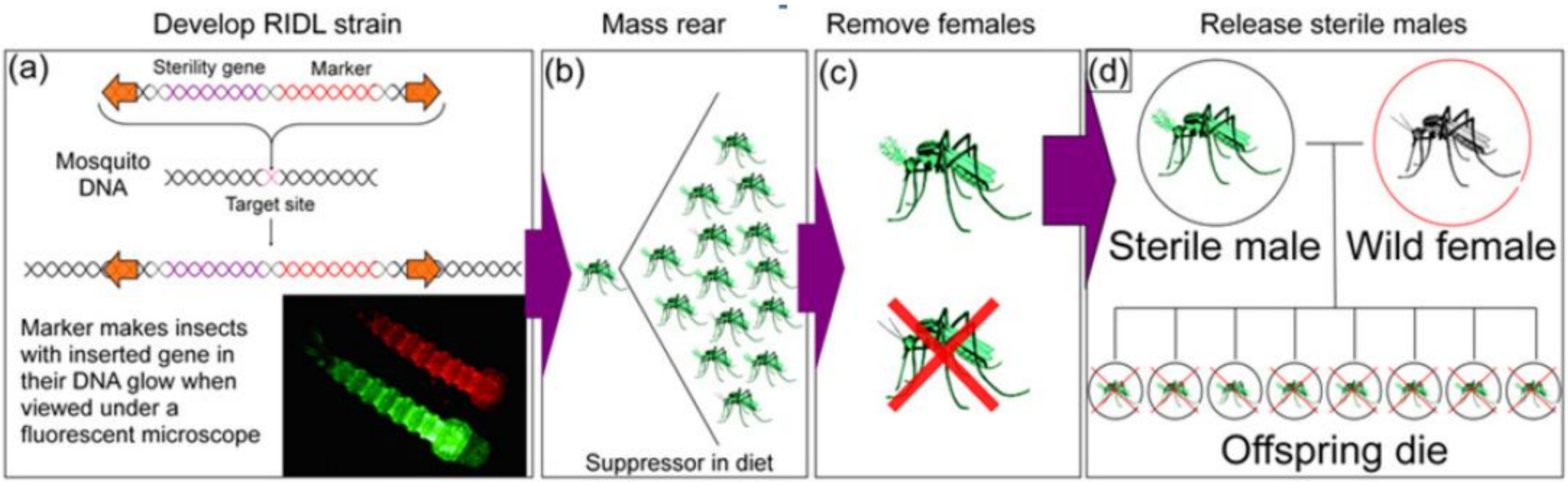
- **Classical Sterile Insect Technique (SIT)**
  - Radiation
  - No marking system
  - No sexing system
- **Genetic technologies provide**
  - markers,
  - genetic sexing,
  - genetic sterilization and





RIDL: Releasing Insects carrying Dominant Lethal

- Genetic sexing
- Genetic marker
- Genetic sterilization



https://www.researchgate.net/publication/234913747_Mini-review_Genetic_enhancements_to_the_sterile_insect_technique_to_control_mosquito_populations/figures?lo=1

Population Replacement

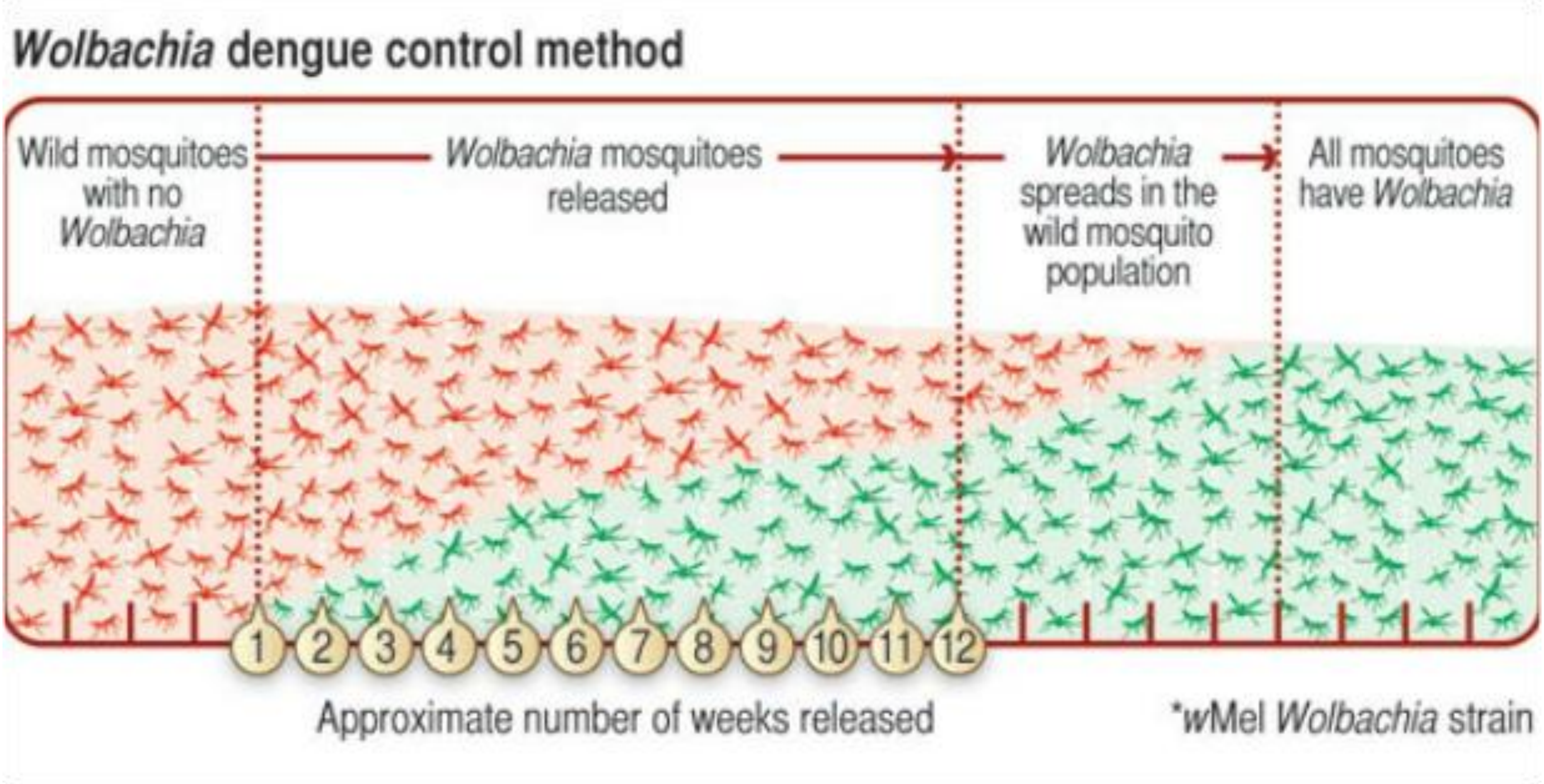
Population replacement

- ....replacing populations of insect disease vectors with genetically modified populations refractory to pathogen transmission

Wolbachia infections

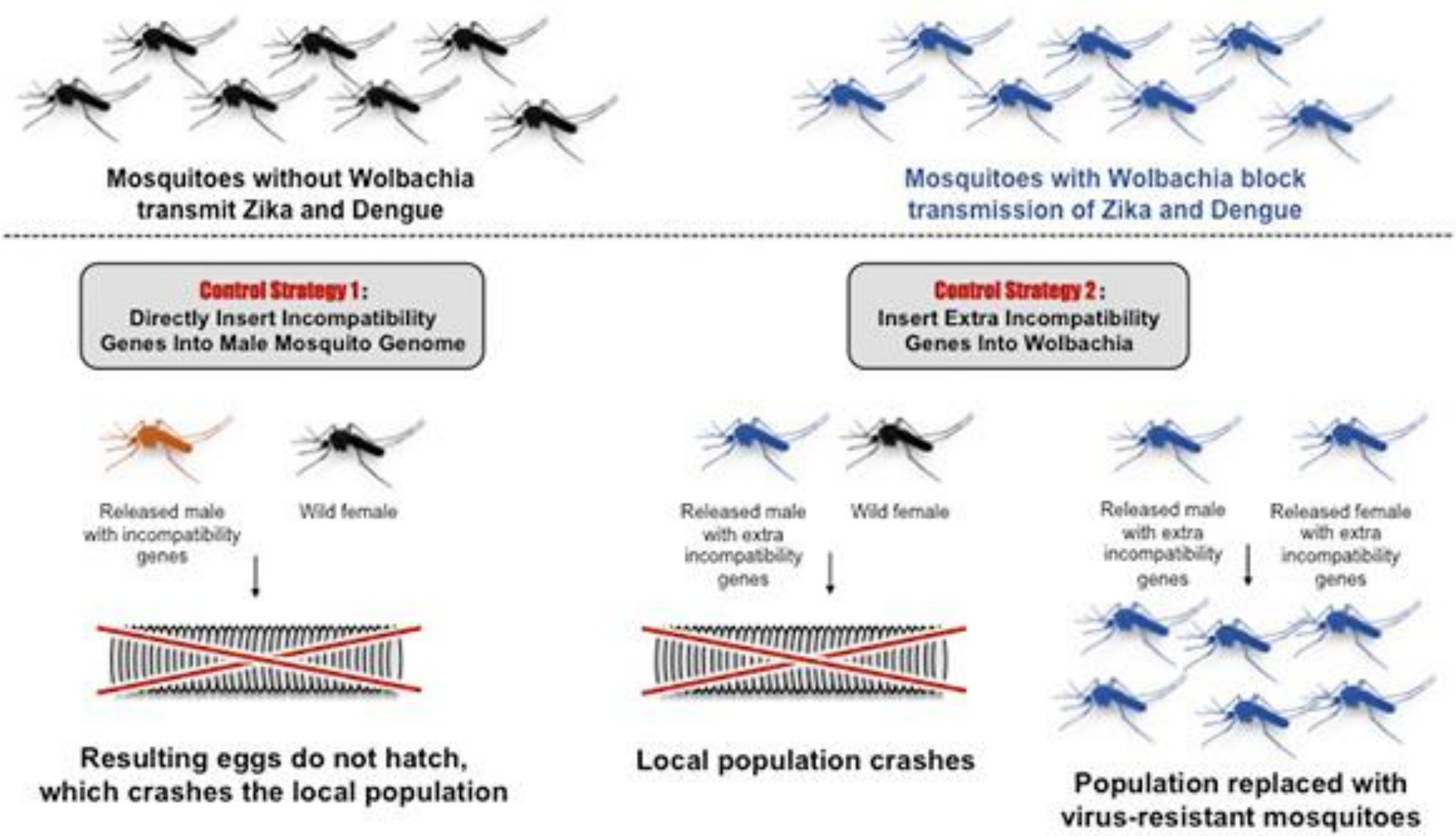
- **Endo symbiotic gram negative bacterium**
- **Causing Cytoplasmic Incompatibility (CI)**

Wolbachia in dengue control



http://www.zino.pt/mosquito-aedes-aegypti-blog/wolbachia-bacteria-reduce-
aedes-aegypti-capacity-to-transmit-dengue#.WhZoOtKWZ0w

Releasing *Wolbachia* infected dengue mosquitoes



https://news.vanderbilt.edu/2017/02/27/new-tool-for-combating-mosquito-borne-disease-insect-parasite-genes/

Advantages of using *Wobachia*

- **Population reduction-** releasing males
- **Population replacement** – releasing both
- **Paratrangenesis** – GM *Wolbachia* transformed mosquitoes

CRISPR/CAS9 SYSTEM

CLUSTERED REGULARLY INTERSPACED SHORT PALINDROMIC REPEATS

GMM- from Sri Lankan perspective

GMM and Disease Control

- Many countries are ready to explore this strategy
- RIDL *Ae. aegypti* by Oxitec
- Dengue control Unit, SL explores the possibility of using RIDL

GMM major constrains

- Presence of two or more vector - vector species that is not transformed will carry away the transmission momentum.
- At the same time elimination of one vector species and ecological changes might result in the emergence of new vector species.
  - *An annularis* has been shown to transmit malaria with a very high entomological inoculation rate during the peak transmission season

Major Constrains....

- **The dengue vector mosquitoes *Aedes aegypti* and *Ae albopictus* occupy the same ecological niche.**
- **The replacement or suppression of one vector species may aid in the propagation of another potential vector species.**
- **Ethical Concerns**
- **Biosafety**
- **Sustainability**

Positive aspects

- The island nature of the country makes it easier to use GMM to control transmission of mosquito-borne diseases.
- Considering the human suffering in terms of morbidity and mortality - releasing GMM into the environment can be incorporated into other conventional vector control measures provided that a proper mechanism is established in the country.

What is required?

- ….extensive studies to be carried out to
  - establish population biology,
  - gene flow,
  - population genetics,
  - entomological inoculation rate and
  - pathogen transmission before releasing only a single genetically modified vector species in areas where prevalence of another potential species is prevalent

What is required?

- A regulatory mechanisms
  - The Cartagena Protocol – ensures the safe handling, transport and use of living modified organisms (LMOs) resulting from modern biotechnology that may have adverse effects on biological diversity, taking also into account
  - National Biosafety Framework of Sri Lanka