

Genetically Modified Mosquitoes for Malaria Control:

Hopes & Challenges

Christophe Boëte



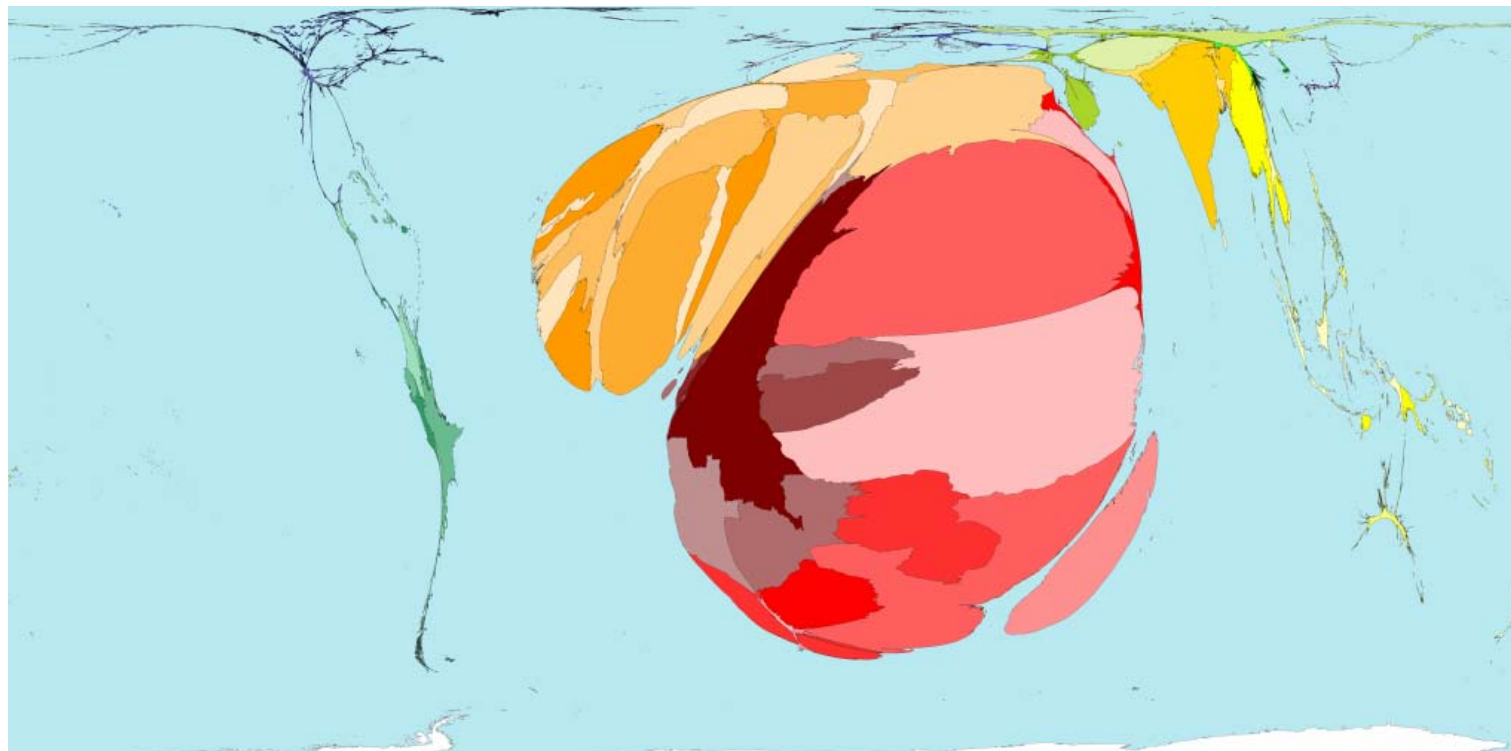
COMBAT HIV/AIDS,
MALARIA AND OTHER
DISEASES



REDUCE
CHILD MORTALITY

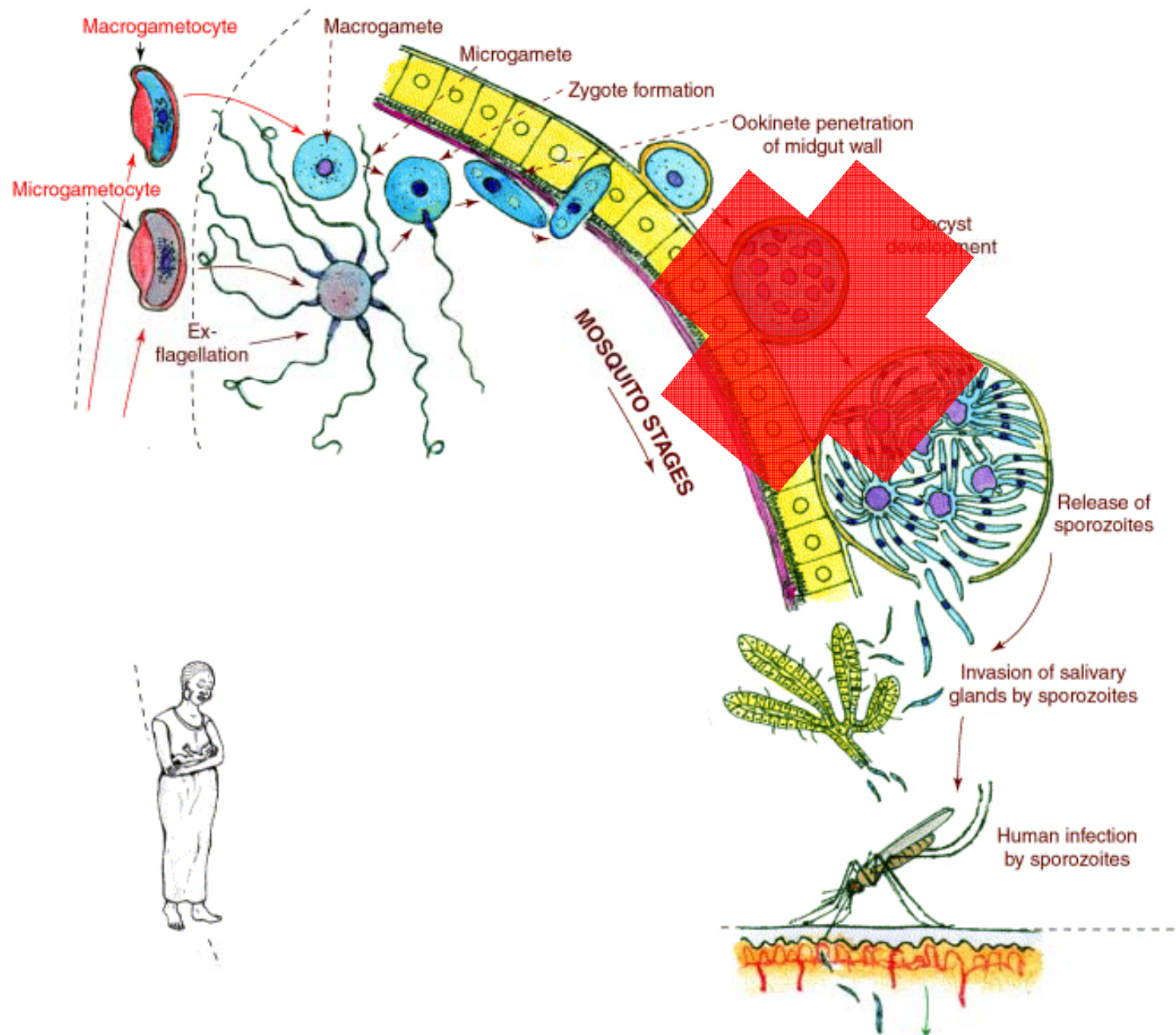


IMPROVE MATERNAL
HEALTH



Territory size shows the proportion of all people living with malaria worldwide, that live there. (2003)

Malaria life cycle



Historical Perspective: The Road to GM Mosquitoes

- *Advances in Molecular Biology*
- *Drosophila*

*Extrapolation for Vectorial
Diseases*

3 major milestones:

- Stable Transformation of anopheline mosquitoes by 2000
- Engineering of a mosquito unable to carry malaria by 2005
- Controlled experiments to understand how to drive this genotype into wild populations by 2010

- Studying Mosquito Immune Responses



mechanistic approach

Anopheles gambiae
Anopheles stephensi

P. berghei



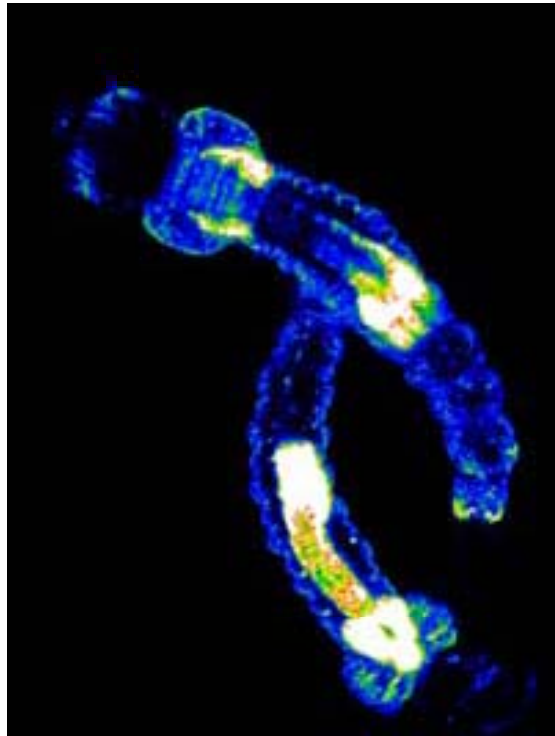
Resistance

Serpin 6, TEP1, SM1 peptide:
efficient *against P. berghei* ...
not against *P. falciparum*...

GM Mosquitoes: Sustainability and Advantages

- No need for insecticides - 'Green Strategy'
- Sustainability (release then 'natural' spread)
- No need to involve a lot of work force
- Less use of drugs with side effects
- Mosquitoes ('friendly ones') still present in the ecosystem

Ecological Issues: Spreading the 'good' gene(s)...



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- Insertion of alleles conferring resistance against malaria
- Link with a transposable element

BUT

- Is resistance going to spread?
- Which effect on the epidemiology?

- Moving from the lab to the field...



- *evolutionary biology*
 - *epidemiological questions...*
- Any relevance in the real world?*

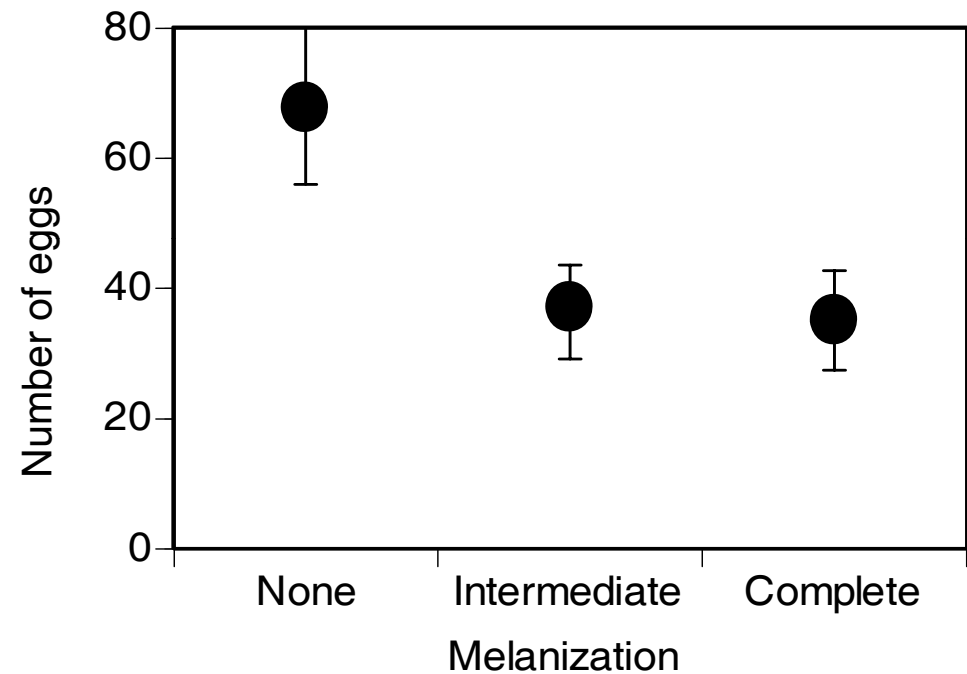
BENEFIT of resistance against Malaria



Ookinetes decrease fecundity
Sporozoites increase mortality

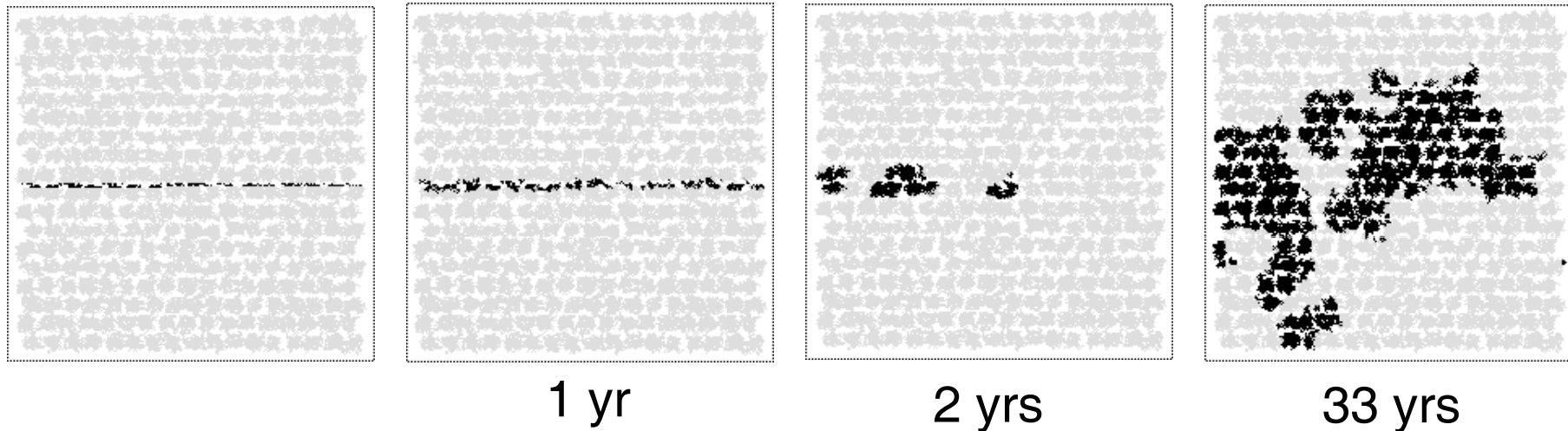
COST of the Resistance

An. gambiae inoculated with Sephadex beads.

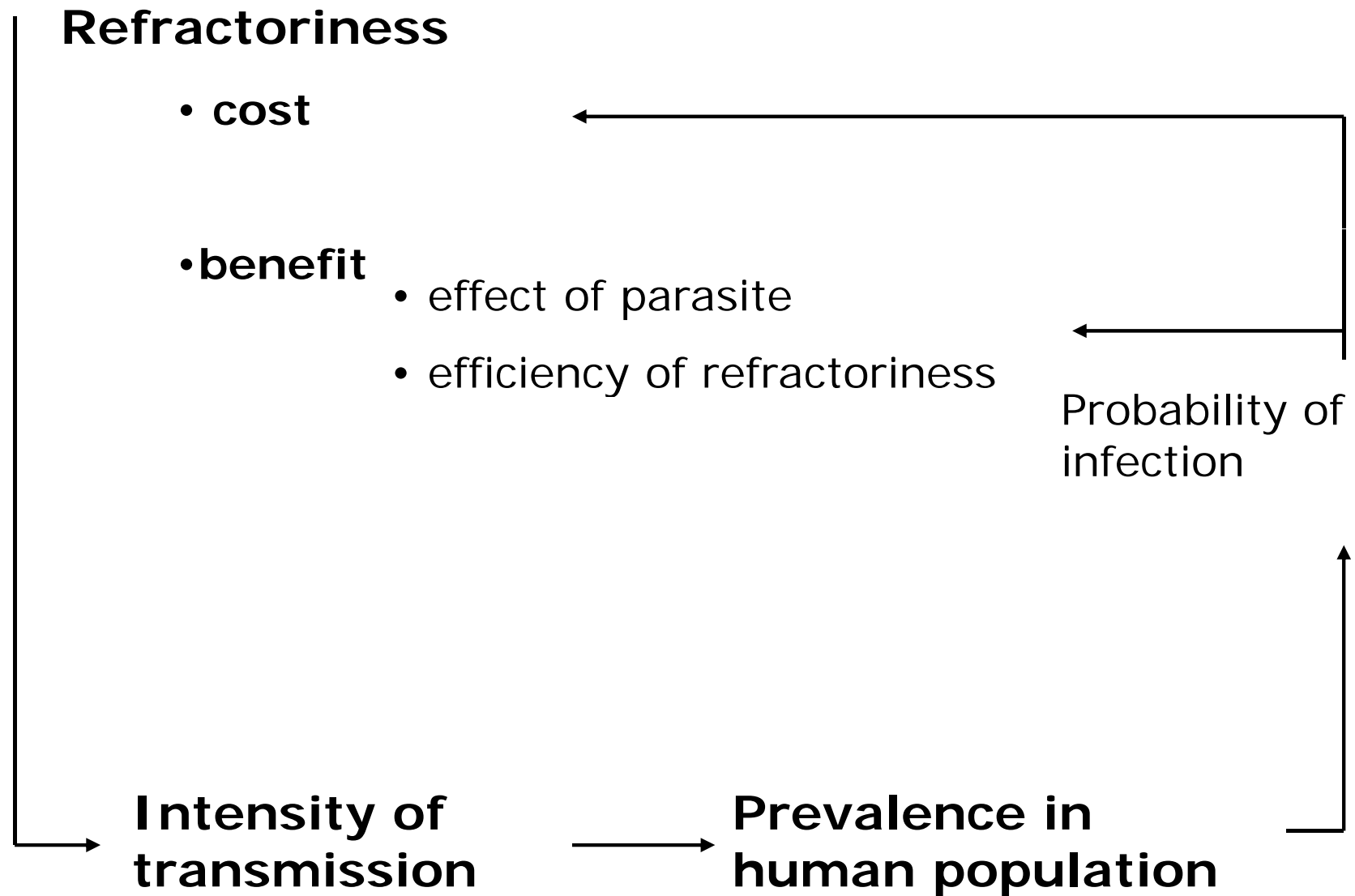


Schwartz, A. & J.C. Koella, *J. Med. Entomo.* 2002

- *Wolbachia*
- Transposable element



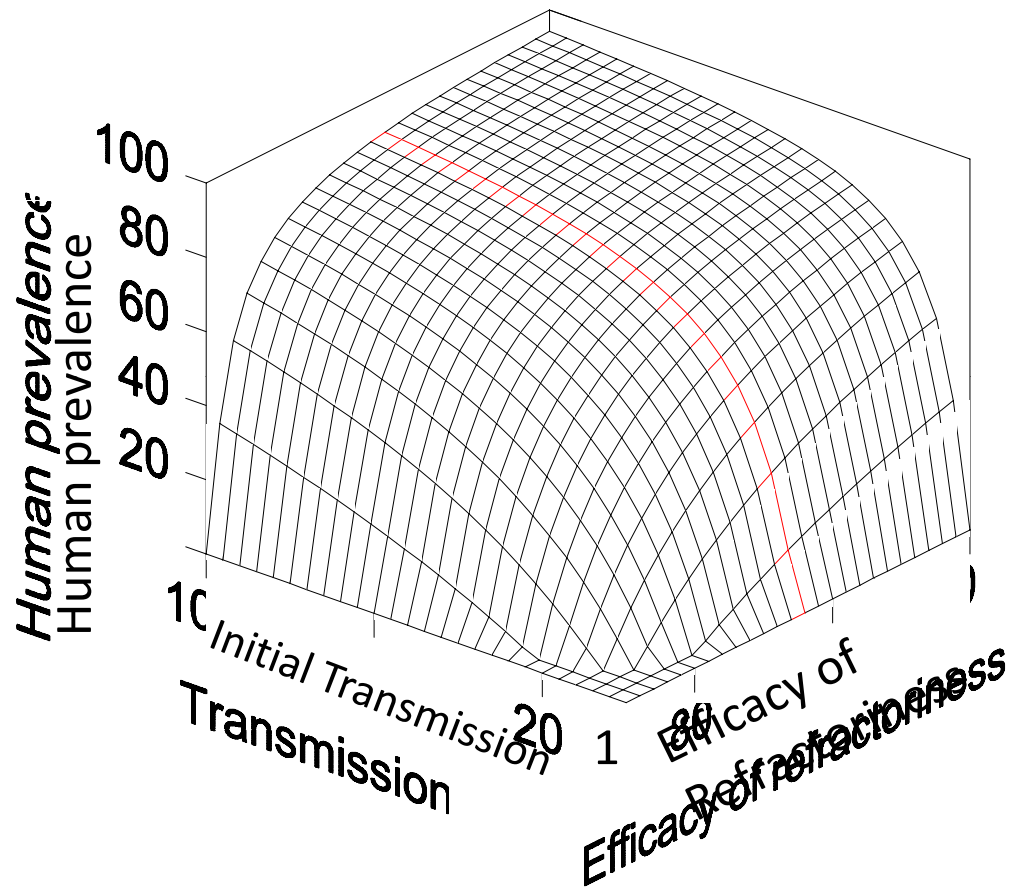
Kiszewski, A.E. & Spielman, A. , 1998 J. Med. Entomol.



Epidemiological Consequences

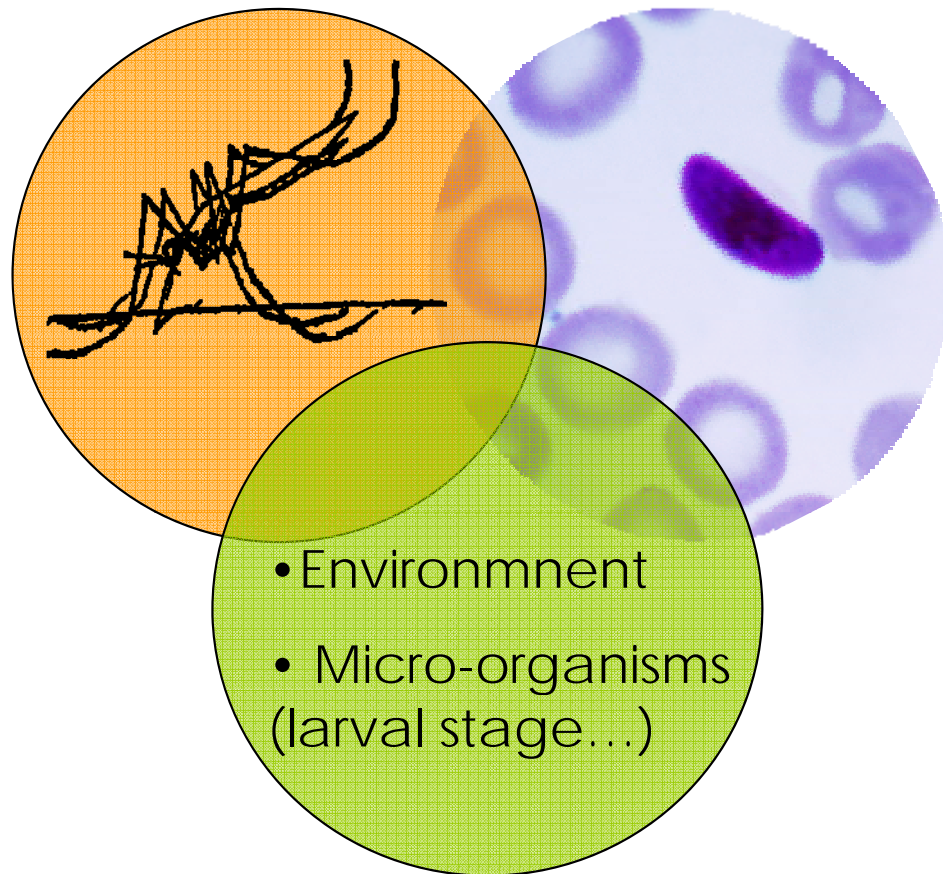
Spread of resistance

Impact on the Human Prevalence



Major issue: **EFFICACY**
of **RESISTANCE**

Ecological Issues: The Efficacy of the 'good' gene(s)...



Larval Life and influence of soil microbes on the adult life

Gene x environment interactions
(abiotic conditions)

The other parasites... (*P. vivax*, fungi, microsporidia...)

How many species to transform?

A population suppression method shares also similar issues...

Transgenic Mosquitoes: Controversy in Public Health

Technological Issues...

Ecological Issues: Spreading the 'good' gene(s)...

Epidemiological Outcomes...

Evolutionary Questions...

Next Move?

Need to develop principles for safety and efficacy

Guidelines for trials, regulations of GM Mosquitoes

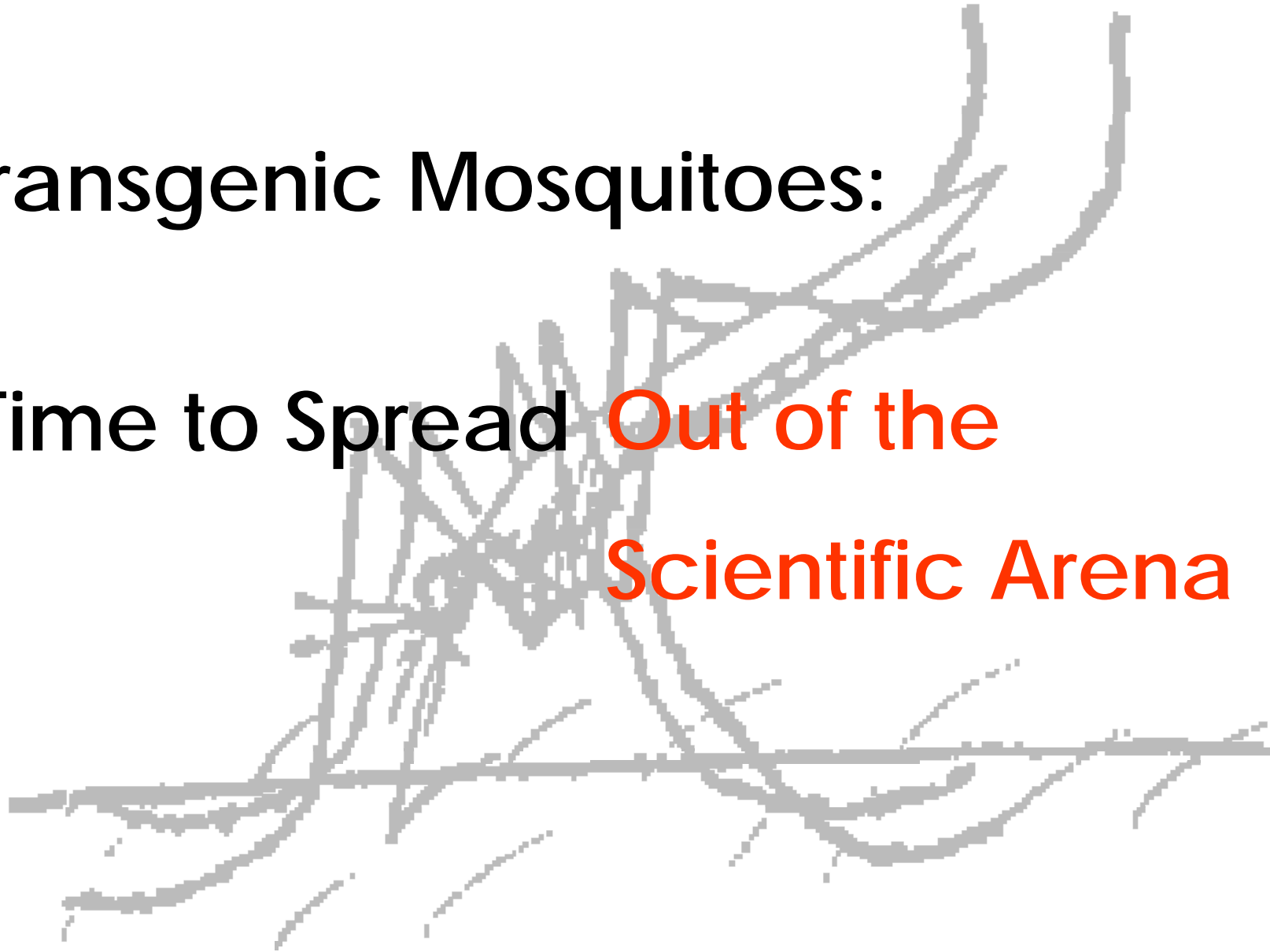
Outdoor field cages studies

Open releases (small scale) – Testing

Wide-scale releases – Testing + Vector Control

Transgenic Mosquitoes:

**Time to Spread Out of the
Scientific Arena**



Transgenic Mosquitoes: Controversy in Public Health

‘ Many of the biggest controversies in science of the past few years have arisen at least partly from problems in the process of communicating research results to the public. ’

Science and the Public Interest.

Communicating the results of new scientific research to the public. 2006

The Royal Society.



Transgenic Mosquitoes: What can learn from the past...



M. DOHRN/SPL

Bloody battle: the mosquito *Aedes aegypti* remains a scourge of health officials fighting dengue fever.

Mosquito researchers deny plotting secret biowarfare test

Kendall Powell, Washington
and K. S. Jayaraman, New Delhi

A recent admission by the United States that it conducted a biological-warfare test using mosquitoes in 1965 has reopened old wounds over a much larger, but aborted, mosquito research project in India.

The Indian project was run by the World Health Organization (WHO) and the Indian Council of Medical Research (ICMR), but received funding from the US government. Researchers involved had planned to release hundreds of thousands of sterile male *Aedes*

Virology in Pune when the project was cancelled. P. K. Rajagopalan, a retired entomologist who worked on the Sonipat project for the ICMR, points out that both programmes aimed to track the dispersal patterns of marked mosquitoes, and are similar enough to confirm government suspicions.

But researchers outside India vehemently deny that the Sonipat project was anything other than a legitimate public-health research project. "It was a very important species of mosquito to try to get rid of," says Scott Halstead, a dengue expert who served WHO

news

Penicillin paper restores Fleming's healthy reputation

Tom Clarke, London

Inspired by musicologists' use of fragmented scores to complete the unfinished works of great composers, a British researcher has pieced together Alexander Fleming's laboratory scribbles to recreate a paper that he says restores the reputation of the much-maligned discoverer of penicillin.

Fleming published details of the antibiotic effects of a mould that had killed off bacterial cultures in his poorly sterilized petri dishes, but never isolated penicillin from the mould or published work on its potential as a drug. Many of Fleming's contemporaries and biographers have accused him of being messy and lazy, and of losing interest in his chance 1928 discovery, even though he went on to take much of the credit for discovering the first antibiotic drug.

"I hope my version of this paper will once and for all scotch the idea that Fleming was some idle dilettante who did little to develop what is arguably the most important drug in medicine," says Milton Wainwright, the University of Sheffield microbiologist who has written the paper that Fleming could have produced,

Nature, 2002

Need for **upstream** engagement of the public

There is a need to engage the community and have two-way communication between researchers, policy-makers and local communities in order to find whether each particular community will want to have a field trial, the nature of the concerns they have, and the ways that can be designed to involve communities as partners in trials.

Macer, D. in *Boëte, C. 2006. (ed.) Genetically modified mosquitoes for malaria control. Georgetown. Eureka/Landes Bioscience.*

Public Acceptance of GM Mosquitoes for Malaria Control

Marshall, J.M. et al. Malaria J. 2010

Bamako area, Mali

80 persons (rural, urban, health professionals)

Evidence that GM Mosquitoes reduce malaria prevalence

No negative consequences for Human Health + Environment

Preference for a mosquito control programme

Perception of the Public Opinion by the Scientists

- Survey sent to more than 700 scientists
- 292 complete replies
 - Research area, location, ...



How to consult the Public on the Scientific & Technological Questions

- + 90%: in favour of communication with the public
- <60%: Intervention on the decision
 - <50% upstream of the research project

**North /
South**

Researchers from the South are more prone to accept the intervention of the public upstream than the ones from the North (65% vs 33%).

Pedagogic Workshops: Communication, Dialogue & Public Engagement

- Web of scientists in favour of a dialogue with the public
- How to favour the engagement of the public? - *Role play* -
- Formation of young researchers in scientific communication
(*capacity-building*)

Developing Structures engaged in
the **Dialogue** and the
Criticism of the
Scientific and
Technological Questions

Transgenic Mosquitoes: What to learn from the 'Oxitec' Release...

Oxitec small scale trial on Cayman Island – *Aedes aegypti*

- confidential?
- public debate?
- Oxitec private company / International Institution – WHO
Grand Challenges in Global Health?

- Trial planned in Malaysia (December 2010) – dengue
- Trial planned in Mali - Malaria

Development of New Technologies and Acceptance

The development process for most new technologies still uses a model unchanged since the 19th century – first, **optimise the technology**, then **check user acceptance**, and finally **examine any regulations governing its use**.

Given the investments made in the earlier stages, it becomes difficult to re-design a technology even when potentially harmful social effects have been subsequently identified.

Hence, when **faced with opposition to a new technology**, policy-makers are forced into **defending the technology**, a technocratic managerial response in which potential social and environmental impacts, identified outside the narrow design process, are regarded as **problems of user acceptance**.

Wakeford, T. Democratising technology Reclaiming science for sustainable development ITDG. 2004

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