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Back to the future: the sterile insect technique against mosquito disease vectors

Rosemary Susan Lees, Jeremie RL Gilles, Jorge Hendrichs, Marc JB Vreysen and Kostas Bourtzis

With the global burden of mosquito-borne diseases increasing, and some conventional vector control tools losing effectiveness, the sterile insect technique (SIT) is a potential new tool in the arsenal. Equipment and protocols have been developed and validated for efficient mass-rearing, irradiation and release of Aedines and Anophelines that could be useful for several control approaches. Assessment of male quality is becoming more sophisticated, and several groups are well advanced in pilot site selection and population surveillance. It will not be long before SIT feasibility has been evaluated in various settings. Until perfect sexing mechanisms exist, combination of *Wolbachia*-induced phenotypes, such as cytoplasmic incompatibility and pathogen interference, and irradiation may prove to be the safest solution for population suppression.

Address
Insect Pest Control Sub-programme, Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture, Vienna, Austria

Corresponding author: Bourtzis, Kostas (K.Bourtzis@iaea.org)

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Introduction

The many pathogens transmitted by mosquitoes (Diptera: Culicidae) which feed on the blood of humans in order to mature their eggs are responsible for enormous suffering worldwide. Annual deaths from malaria alone number at least 600,000, up to 100,000 people contract dengue each year, and Chikungunya causes severe chronic joint pain in patients across the globe (World Health Organization factsheet; URL: http://www.who.int/mediacentre/factsheets/fs387/en/). Aside from causing mortality and morbidity, the economic and social burden from these diseases is significant [65], particularly in SubSaharan Africa (Multisectoral Action Framework for Malaria; URL: http://reliefweb.int/sites/reliefweb.int/files/resources/Multisectoral-Action-Framework-for-Malaria.pdf).

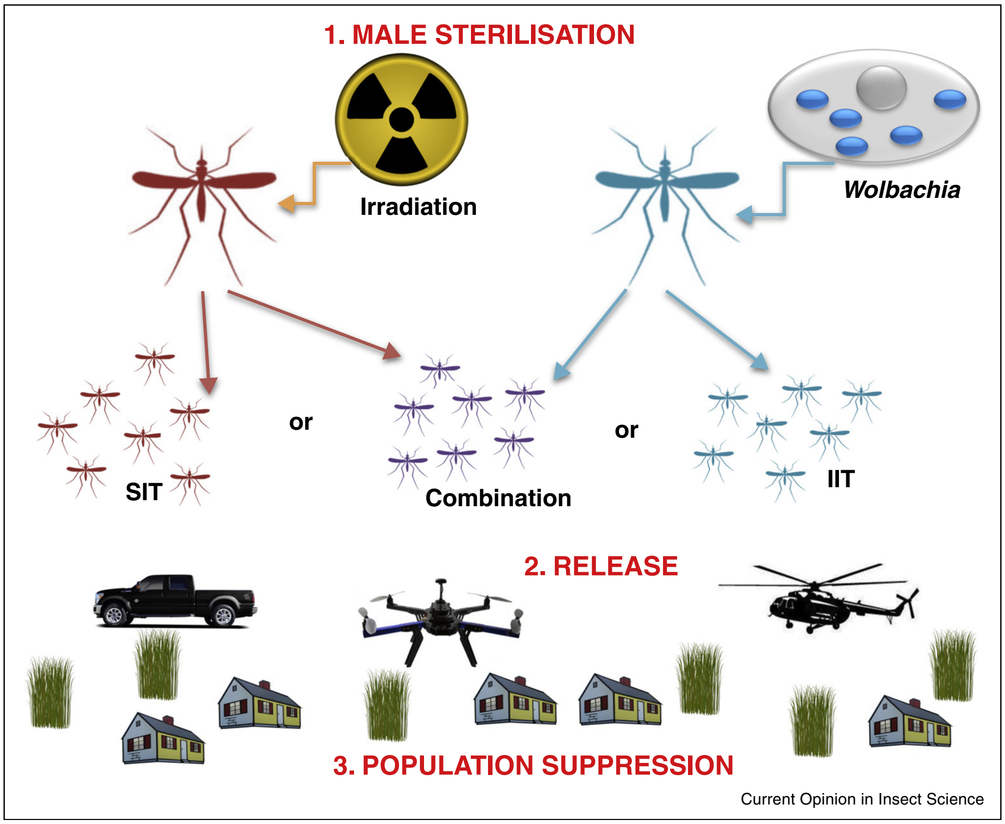
The pressure placed on humanity by these vectors is increasing. Expansion of the distribution of several invasive *Aedes* species such as *Aedes albopictus* [1] is evident in many areas, including Europe [2,3] and USA [4]. Modelling and field experiments have predicted that *Ae. albopictus* has the potential to invade large areas of Australia [5] and urbanisation is increasing its abundance in China [6]. With no effective vaccines or specific drugs to prevent or treat mosquito-borne diseases, the best line of defence is to combat the vector, to remove the contact between mosquitoes and humans and thus interrupt the disease transmission cycle. Effective mosquito control is hindered by growing insecticide resistance of malaria [7] and dengue vectors [8], even in regions only recently invaded (e.g. [9]). There is therefore increasing demand for complementary tactics that are effective, more sustainable and friendly to the environment.

One such tactic could be the sterile insect technique (SIT), which relies on the production and release of sufficient sterile males to induce sterility in the wild females which, over time, causes the target population to decline (Figure 1). The SIT has no regulatory requirements and the technique would be combined with others as part of an area-wide integrated pest management (AW-IPM) approach to reduce the vector population below the threshold required for disease transmission. Sterilisation using ionising radiation has been extremely effective and applied successfully for population suppression, containment or eradication of several major pest insect species [10].

Rather than sterilising males using irradiation, an alternative method is to exploit the natural phenomenon of cytoplasmic incompatibility (CI). In most diplodiploid species, CI is expressed as embryonic lethality after matings between *Wolbachia*-infected males and uninfected females or females infected with a different *Wolbachia* strain [11]. Proof-of-concept has been provided that CI could be used to manage agricultural pests and disease vectors through population suppression or replacement approaches [12•,13,14]. CI-based population suppression is known as the incompatible insect technique (IIT) (Figure 1).

As the key mosquito disease vectors are all relatively amenable to colonisation and rearing, and in many

Figure 1



The sterile insect technique (SIT), incompatible insect technique (IIT) or a combination of the two could be used to suppress mosquito populations. Male mosquitoes are sterilised either by the application of irradiation or (trans)infection with *Wolbachia*, or both, and then released into the target population to sterilise the wild females.

situations the natural population densities are low, the SIT, IIT, or a combination of the two are well suited for their management. The advantages of combining these tactics will be discussed in this review, alongside the current state of the art for the two approaches. Much progress has been made in recent years towards developing the required technology and methodology to bring mosquito suppression using sterility to field application; indeed pilot releases have begun in a number of sites around the world. It should be mentioned, however, that a number of other technologies have also been developed and are being tested in pilot trials including RIDL (Release of Insects carrying a Dominant Lethal) and *Wolbachia*-based population replacement strategies. However, it is beyond the scope of this review to discuss these approaches, and they have recently been reviewed elsewhere [13,15].

Developing the sterile insect technique against mosquitoes

After a period of enthusiasm in the 1960s to early 1980s [16], the use of sterile male release for mosquito control was largely abandoned. However, the growing pressures from mosquito-borne pathogens described above, and the proposed use of modern biotechnologies to sterilise or otherwise alter mosquitoes, have led to revived interest in recent years.

In the last decade, the Joint FAO/IAEA Programme and their collaborators have been the main drivers for the development of the ''SIT package'' for mosquitoes. Requests from many countries to develop and evaluate the SIT for use against mosquitoes have spurred the development and ongoing validation of mass-rearing equipment, diet and protocols for *Anopheles* and *Aedes* species. Diets have been optimised to feed the larval stages of *An. gambiae* [17], *An. arabiensis* [18], *An. stephensi* [19] and *Ae. albopictus* [20]. *Anopheles* larvae can be mass-reared efficiently in large trays fitted into a novel tilting rack system [21,22], and the system is being validated for *Aedes* species. Anopheline pupae can be separated from larvae based on differential buoyancy using custom vortex equipment [23], or the Fay-Morlan separator used for *Aedes* [24], quantified volumetrically, and allowed to emerge into adult mass-rearing cages [25]. Blood meals are offered to females using a modified hemotec membrane feeder and