NEWSLETTER
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ISSUES 17 (JANUARY - APRIL 2025)

Welcome to the Newsletter e-Science Putra. This issue presents the research activities from January to April 2025 which highlight the latest research findings by the selected faculty members.

HIGHLIGHTS

- Utilizing Artificial Intelligence to Discover Drugs for Dengue
- Mr MoleC™: An Innovative and Sustainable Biorepellant for Integrated Pest Management (IPM)
- Synthesis, Reaction Mechanism and Applications of 45S5 Bioactive Glass
- Major Histocompatibility Complex genes in Malayan Tapir
- Detection of Structural Perturbations in Time Series Data Using Impulse Indicator Saturation Technique

UTILIZING ARTIFICIAL INTELLIGENCE TO DISCOVER DRUGS FOR DENGUE

Assoc. Prof. Dr. Bimo Ario Tejo
Department of Chemistry, Faculty of Science, Universiti Putra Malaysia
Expertise: Computing Chemistry, Medicinal Chemistry
Email: bimo.tejo@upm.edu.my

Dengue fever is caused by four distinct serotypes of the dengue virus (DENV1–4) and is transmitted primarily through the bite of infected Aedes aegypti and Aedes albopictus mosquitoes. It remains a significant public health concern, particularly in tropical and subtropical regions like Southeast Asia. With an estimated 390 million dengue infections worldwide annually, around 96 million of these cases exhibit varying degrees of clinical severity. At present, there are no effective vaccines or antiviral drugs for dengue, with the only available vaccine, Dengvaxia (CYD-TDV), showing efficacy in seropositive patients but posing a heightened risk of severe disease in dengue-naive individuals. The search for effective treatments has long been difficult and costly.

Artificial intelligence (AI)-based approaches are transforming the drug development process, offering a more efficient and cost-effective method of discovering new therapies. By analyzing large datasets containing molecular structures, biological interactions, and chemical properties, AI can predict drug-target interactions, identify promising candidates, and optimize drug efficacy while minimizing side effects. This accelerates drug discovery and reduces development costs. Our research group is focused on expediting the identification of drug candidates for dengue virus treatment. Using a combination of machine learning-based quantitative-structure activity relationship, molecular docking, and molecular dynamics simulations (Figure 1), we have successfully identified potent inhibitors, such as bromocriptine, ergotamine, and amphotericin B, from repurposed drug databases targeting the dengue virus's NS3 protease (Figure 2). Additionally, we are creating a novel framework for discovering anti-dengue peptides, integrating deep learning, structural prediction, molecular docking, and simulations. We are also utilizing generative AI to design new anti-dengue peptides by incorporating both sequence and three-dimensional structural features.

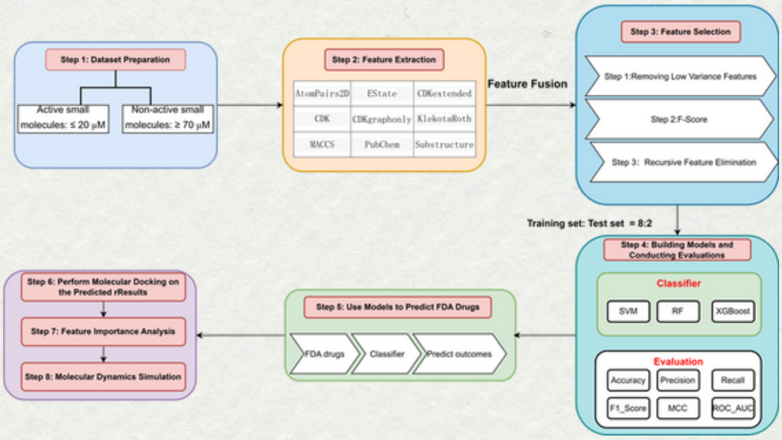

Figure 1: The workflow for predicting repurposed drugs targeting the NS3 protease of dengue virus using machine learning, molecular docking, molecular dynamics simulation approaches (adapted from Chongjun et al., 2024)

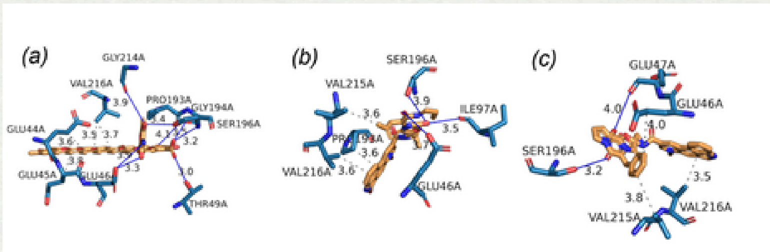

Fig. 2: Molecular interaction profiles of the top NS3 protease inhibitors: (a) amphotericin B; (b) bromocriptine; (c) ergotamine (adapted from Chongjun et al., 2024)

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MR MOLEC™: AN INNOVATIVE AND SUSTAINABLE BIOREPELLANT FOR INTEGRATED PEST MANAGEMENT (IPM)

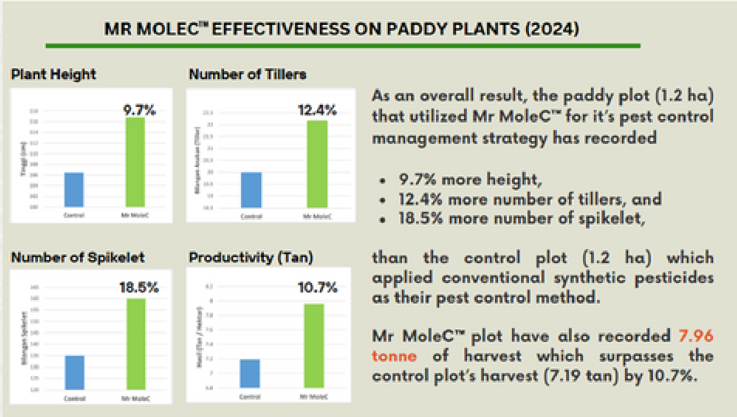
Assoc. Prof. Dr. Nur Kartinee Kassim
Department of Chemistry, Faculty of Science, Universiti Putra Malaysia
Expertise: Natural Product Chemistry
Email: kartinee@upm.edu.my

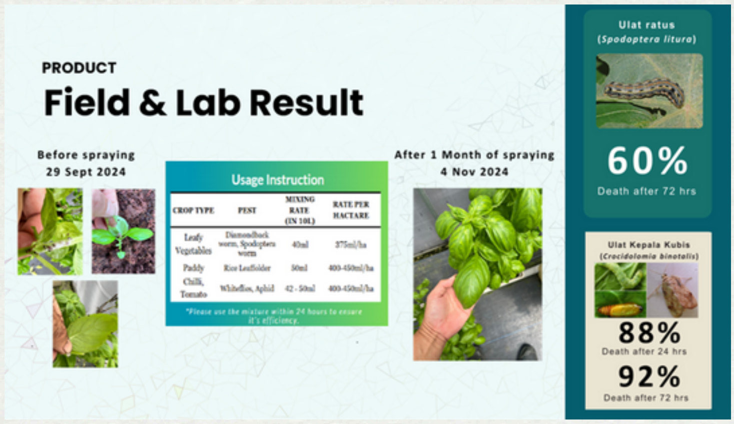
Hilda Carol Ahkui [1], Siti Aisah binti Salmin[2], and Luqman Hadi bin Iskandar[2]
[1]Institute of Tropical Agriculture and Food Security, Universiti Putra Malaysia, 43300 UPM, Selangor Darul Ehsan, Malaysia
[2]Chemistry Department, Science Faculty, Universiti Putra Malaysia, 43300 UPM, Selangor Darul Ehsan, Malaysia
Corresponding author: kartinee@upm.edu.my

As the global population continues to rise, farmers have increasingly relied on chemical pesticides to protect crops from pests and diseases. However, this widespread use of chemical pesticides has led to serious environmental pollution, health risks, and pesticide resistance. Common agricultural pests such as whiteflies, armyworms, and thrips have developed significant resistance towards these pesticides, making pest management more challenging and costly. While biopesticides exist in the market, they are often expensive, difficult to access, and not always effective. To address this gap, Mr MoleC™ serves as a solution that acts as both repellent and anti-feedant, offering a sustainable and efficient alternative to conventional pesticides. Mr MoleC™ contains plant active ingredients and fully organic formula that contribute to its effectiveness, working synergistically to deter pests, preventing crop damage and enhancing plant health.

In vivo trials have demonstrated that Mr MoleC™ effectively controls pest populations. It achieved a 60% mortality rate for Spodoptera litura (second instar larvae) after 72 hours and an 88% mortality rate for Crocidolomia binotalis (second instar larvae) within 24 hours. These results highlight its potential as a powerful tool for pest control. A field trial conducted at Tanjung Karang, Selangor on a 1.2-acre plot further reinforced the benefits of Mr MoleC™. The treated paddy plants exhibited a 9.7% increase in height, 12.4% more tillers per plant, and an 18.5% increase in spikelet numbers. The yield from the treated plot was 7.96 tonnes, marking a 10.7% increase compared to the control plot, which produced 7.19 tonnes. Additionally, the revenue from the treated plot was RM 9,921.34, compared to RM 8,961.82 from the control plot. These figures demonstrated the economic benefits of Mr MoleC™, making it a valuable solution for low-income and small-scale farmers, as well as eco-conscious users. The application of Mr MoleC™ is straightforward, with a recommended dosage of 5ml per litre of water. A 450ml volume is sufficient to treat one hectare of land, making it a cost-effective and efficient pest management solution. The in vivo research team was led by Assoc. Prof. Dr. Nur Kartinee Kassim and the field research was led by Miss Hilda Carol from ITAFOS.

Currently, this technology is licensed to TerraDeca Sdn. Bhd., a start-up company under Innohub Programme of Universiti Putra Malaysia for the commercialization purposes. With its innovative approach, proven effectiveness, and economic benefits, Mr MoleC™ is set to revolutionize Integrated Pest Management by offering a sustainable, accessible, and highly effective bio-repellant solution.





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SYNTHESIS, REACTION MECHANISM AND APPLICATIONS OF 45S5 BIOACTIVE GLASS

Dr. Mohd. Hafiz Mohd. Zaid
Department of Physics, Faculty of Science, Universiti Putra Malaysia
Expertise: Material Science, Glass, Ceramic, Composite and Nanomaterials
Email:mhmzaid@upm.edu.my

A class of reactive surface glasses known as "bioactive glasses" releases ions into the surrounding environment, which can cause a variety of biological reactions. The most desirable reaction from the glass is to release sodium (Na+), calcium (Ca2+), and phosphate (PO43) ions, which will induce the development of new bone, apatite, or hydroxyapatite (HA) [1]. In the late 1960s, Larry Hench made the discovery of bioactive glass in response to a request from a Vietnam-era Army colonel to create a substance that could endure touch with human tissue in order to aid his wounded soldiers. In summary, 45S5 Bioglass®, which contains 45% SiO2, 24.5% CaO, 24.5% Na2O, and 6% P2O5, is the first bioactive glass that fabricated by Hench and team. It can easily combine hard and soft tissues together and has a high bioactivity property [2]

The structure of the bioactive glass is like any glass structure, consisting of a network former with selective network modifier oxides. As demonstrated in Fig. 1, there are generally five phases in the reaction mechanism that lead to the development of apatite and a crystalline phase on the surface of bioactive glass - in this case, silicate-based glass - when it is immersed in an aqueous solution [3]. During the in-vitro research, the solution's pH is buffered between 7.25 and 7.40 at 37 °C. This is due to the fact that the typical temperature of the human body and mouth cavity is between 36.7 and 37.5 °C. Meanwhile, The pH range of saliva is 6.20 to 7.60, and that of the human body is 7.35 to 7.45. Moreover, bioactive glasses are successfully utilized in the dental field, for instance, in dental restoration, tooth replacement, dental inlays, crowns, bridges, and veneers. As can be seen, many studies have been done by researchers on the usage of bioactive glass. This is a highly researched field, as seen by the increasing number of papers on bio-glasses, their properties, and their applications. Bioactive glass and glass-ceramics are therefore used in a wide range of healthcare applications today, including bone formation, dentistry, soft tissue healing, diagnostic imaging, cancer treatment, and delivering medications, as demonstrated in Fig. 2.

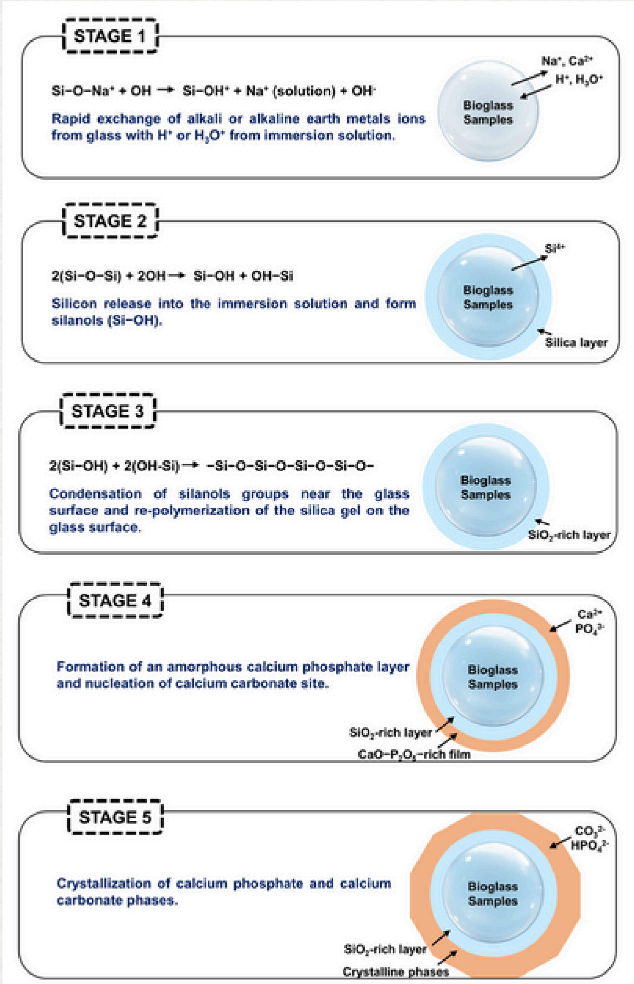

Fig. 1. Schematic diagram of the reaction mechanism of surface reactions of bioactive glass.

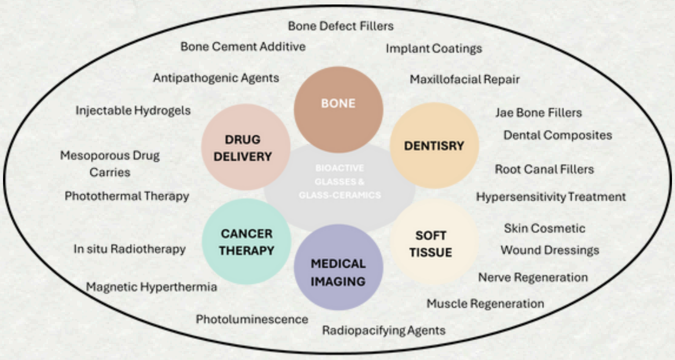

Fig. 2. The various applications of bioactive glasses

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MAJOR HISTOCOMPATIBILITY COMPLEX GENES IN MALAYAN TAPIR

Assoc. Prof. Dr. Geetha Annavi
Department of Biology,
Faculty of Science,
Universiti Putra Malaysia
Expertise: Wildlife Genetic and Behaviour Ecology
Email: geetha@upm.edu.my

The Malayan tapir (Tapirus indicus), an endangered species endemic to Southeast Asia, faces several serious threats, including habitat loss, hunting, road kills, coupled with low reproduction rate all of which contribute to its endangered status. The current population size is estimated at 2500 individuals across their geographical range. The declining population trend increases the risk of inbreeding, which could result in the reduction of genome-wide genetic variation and negatively affect the gene responsible for immune response. Major Histocompatibility Complex (MHC) genes (Class I and Class II) are responsible for encoding MHC molecules in the cells that recognise pathogenic peptides and present them to T-Cells on the cell surface for adaptive immune response. Individuals that are heterozygotes at the MHC gene are deemed to be advantageous to survival as their MHC molecules can recognise a wide range of pathogens.

We designed and characterised 5 MHC markers using seven individuals, and reported at least one Class I gene and four Class II genes in the Malayan tapir population in Peninsular Malaysia. Five alpha1 (α1) and four alpha2 (α2) domain sequences from Class I alleles, along with two DRA, two DQA, three DRB, and three DQB domain sequences from Class II alleles, were isolated. The α1 and α2 domains of Class I, along with the DRB domain of Class II, exhibited signs of selection, showing a higher rate of non-synonymous substitutions compared to synonymous ones.

Within the DRB gene, 24 codons were identified as being under selection, with 10 of these codons forming part of the Antigen Binding Site. Phylogenetic analysis revealed that the gene sequences generally form species-specific monophyletic groups, except for the Class I and DRB genes, which show intermixed relationships in their trees, suggesting the potential occurrence of trans-species polymorphism in allelic lineages.

Credits to Kalai Arasi Arumugam (MSc, UPM 2018)

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DETECTION OF STRUCTURAL PERTURBATIONS IN TIME SERIES DATA USING IMPULSE INDICATOR SATURATION TECHNIQUE

Dr. Farid Zamani Che Rose
Department of Mathematics and Statistics, Faculty of Science, Universiti Putra Malaysia
Expertise: Time Series Analysis
Email: faridzamani@upm.edu.my

Time series data are often subject to structural perturbations, which refer to unexpected changes that can distortstatistical analysis and forecasting. These perturbations can take various forms, including outliers (temporary spikes or drops in data), location shifts (permanent changes in the mean level), and structural breaks (changes in trend or variance that alter the underlying data-generating process). Ignoring these disturbances can lead to biased parameter estimation, incorrect model specifications, and reduced forecasting accuracy, particularly in economic and environmental applications where sudden changes frequently occur.

The Impulse Indicator Saturation (IIS) technique introduced by Hendry (1999) provides a systematic approachto detecting and adjusting for structural perturbations, ensuring that time series models remain robustand reliable. At first this technique was introduced as a procedure for testing parameter constancy. IIS is a generic test for an unknown number of breaks, occurring at unknown times anywhere in the sample,with unknown duration,magnitude, and functional form. IIS detects outliers by including an impulse dummy for each time point with

the function $\sum_{j=1}^{T}\gamma_j I_{j,t}$ where $I_{j,t}$ equal to unity when $j = t$ and zero otherwise. How does IIS works? In brief, the algorithm is as follows:

1. Order the T impulse indicators $\{I_{1,t}, I_{2,t}, \ldots, I_{T,t}\}$ by date i, and set a significance level of α.
2. Partition the indicators into two blocks, which are represented by their sets of indexes: $\kappa_1 = \{1, \ldots, (T/2)\}$ and $\kappa_2 = \{(1+T/2), \ldots, T\}$ as depicted in Figure 1.
3. Estimate and record the two $T/2$ subsample parameter estimates.
4. Apply a model selection method to each block, and record the sets of indexes for the indicators significant at α, denoted κ_1 and κ_2.
5. Form their union $\kappa = \kappa_1 \cup \kappa_2$.
6. Apply model selection at α to the impulse indicators with dates in κ.

These methods collectively enhance model estimation by filtering out distortions and improving the accuracy of statistical inference and forecasting. The IIS technique enables researchers to detectstructural changes without pre-defining breakpoints, making it valuable in situations involving unknown shocks.By incorporating IIS, analysts can identify anomalies, improve model accuracy, and strengthen forecasting in dynamic, data-driven environments.

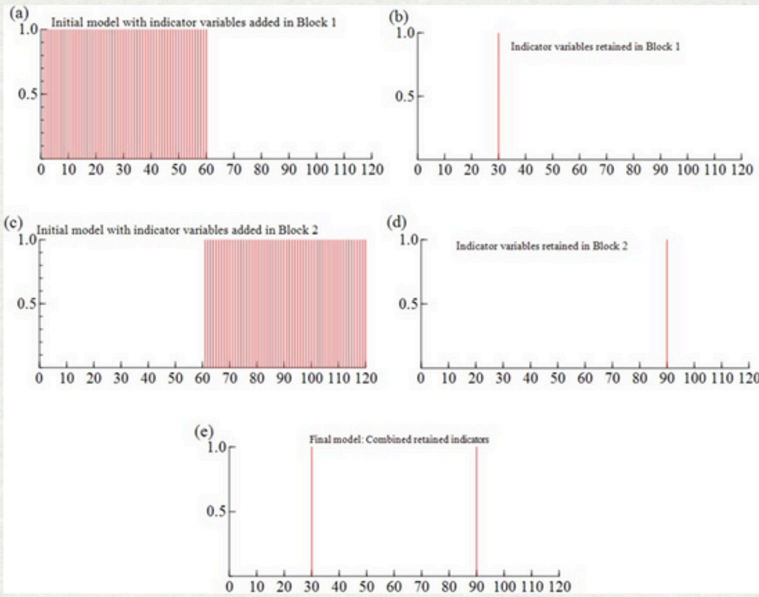

Figure 1: The impulse indicator saturation algorithm depicted when the additiveoutlier located at t = 30, t = 90 and T = 120 observations.

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Science is much more than just a body of KNOWLEDGE.
It is a way of THINKING.

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FACULTY OF SCIENCE, UNIVERSITI PUTRA MALAYSIA, 43400 UPM SERDANG, SELANGOR DARUL EHSAN, MALAYSIA
+603 97696601/6602/6603 www.science.upm.edu.my fs_tdps@upm.edu.my