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Welcome to Biomath 2021

Biomath is an established series of conferences devoted to recent research in life sciences based on applications of mathematics as well as mathematics applied to or motivated by biological studies. Biomath 2021 is special as it happens in a world significantly changed by the Covid-19 pandemic. The conference takes place in a hybrid mode with some participants being in person at the conference while others taking part online. Unfortunately, Biomath 2020 could not take place due to the pandemic. We expect to learn from the new format of Biomath 2021 so as to enrich future conferences with new opportunities for the interactions of participants.

Biomath 2021 maintains the international character of the series as it has participants from 14 countries: Brazil, Bulgaria, Cameroon, Eswatini, France, India, Indonesia, Japan, Morocco, South Africa, Spain, Ukraine, United Kingdom, United States of America.

An international and interdisciplinary meeting of this kind needs the support of many. We acknowledge the support of the University of Pretoria and specifically the Department of Mathematics and Applied Mathematics and SARChI Chair M^3B^2 - the hosts of the conference. Further, we need to acknowledge the support of the National Research Foundation of South Africa and the Center of Excellence in Mathematical and Statistical Sciences. Biomath conference series has a strong emphasis on supporting and promoting young scientists. In this regard, we need to acknowledge the support provided by the mentioned sponsors to young scientists.

We are grateful to all members of the Program and Organizing Committees as well as to the International Steering Committee for their active assistance.

Biomath organisers pay special attention to the publication of the presented scientific communications. Original papers based on the presentations in Biomath 2021 are invited for submission to the journal Biomath. We expect that the contributions of all participants will result in high-quality publications.

Jacek Banasiak
For the Local Organising Committee

Roumen Anguelov
For the International Steering Committee

Keynote Presentations

Modeling and analysis for Sterile Insect Technique (SIT): residual fertility and nonlinear feedback control

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The Sterile Insect Technique (SIT) is a biological control method that consists of releasing males that have been sterilized using ionizing radiation. In the wild, these males mate with wild females that will not produce viable offsprings.

In this talk we present a minimalist model for SIT, assuming that residual fertility can occur in the sterile male population after radiation. Assuming that we are able to get regular measurements from the biological system along the control duration, such as the size of the wild insect population, we investigate different release strategies that involve either continuous or periodic impulsive releases, in open- and closed-loop forms. We show that a combination of open-loop control with constant large releases and closed-loop nonlinear control leads to the best strategy in terms of both number of releases and total quantity of sterile males to be released. Additionally, we show that SIT fails if the residual fertility is greater than a threshold value that depends on the wild population biological parameters. Moreover, even for small values, the residual fertility induces the use of such large releases, that SIT alone is not always reasonable from a practical point of view.

We provide applications against a mosquito species, Aedes albopictus, and a fruit fly, Bactrocera dorsalis.

The importance of getting the "bio" right in "biomathematics"

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A paper that is worth publishing in the world of mathematics, as applied to the biological sciences, should satisfy at least one of two criteria: (i) It should say something that is new mathematically, (ii) It should make a useful contribution to biology. Unhappily, journals of applied mathematics are increasingly clogged with papers that satisfy neither criterion: too often they are of no interest mathematically and - worse - make no sense biologically. This is particularly the case in the world of mathematical epidemiology, which is typified by the "Pick a Box" approach to mathematics - where the identical formulaic approach is applied to every disease known to man, in hundreds if not thousands of published works. The problem is that workers are running out of diseases to which they can apply their tired approach. Not to be thwarted, however, yet more papers are appearing where the method is applied to combinations of diseases diseases taken two at a time - co-infections - often with scant regard for the possibility that the diseases might ever even have occurred in a single person at the same time.

Modellers ignore biological reality at their peril, however, and I shall illustrate how badly things can go wrong through the discussion of a recently published paper. It was suggested in the paper that rates of diffusion in populations of tsetse flies (Glossina spp) increased as population densities decreased. That is to say, it was hypothesised that tsetse exhibited negative density dependent dispersal. The theory underpinning the development of this hypothesis is sufficiently complex that few biologists will understand it. Application of the theory to available data did, however, produce an extremely high negative correlation coefficient between population density and rates of dispersal. The authors appear to have been entirely seduced by this high correlation and by the fancy mathematics - and provided a plethora of post hoc rationalisations in support of the idea that there was already solid published evidence in support of their hypothesis. Careful consideration of the data shows, however, that the observed correlation is entirely an artefact - consequent on multiple errors of analysis and interpretation. The most serious of these errors results from a misunderstanding of the way in which traps sample tsetse, resulting in large errors in estimates of the areas covered by the traps, and occupied by the sub-populations being sampled. Our modelling studies show that these errors result in the false signal of negative density dependent dispersal - even in situations where we have specifically assumed that rates of dispersal are independent of density.

Mathematics can make important contributions to the world of medicine - and of biology in general - but these contributions will be much more valuable, and relevant, and less prone to absurd conclusions if and when applied mathematicians engage with biomedical data and take careful note of biomedical realities.

Mathematical models of living tissues and free boundary problem

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Tissue growth, as it occurs during solid tumors, can be described at a number of different scales from the cell to the organ. For a large number of cells, 'fluid mechanical' approaches have been advocated in mathematics, mechanics or biophysics. Since the 70's the mathematical modeling has been progressing regularly, posing new mathematical questions.

We will focuss on the links between two types of mathematical models. The 'compressible' description describes the cell population density using systems of porous medium type equations with reaction terms. A more macroscopic 'incompressible' description is based on a free boundary problem close to the classical Hele-Shaw equation. In the stiff pressure limit, one can derive a weak formulation of the corresponding Hele-Shaw free boundary problem and one can make the connection with its geometric form.

The mathematical tool to perform the incompressible limit is the Aronson-Benilan estimate and we will show why a L^2 version is needed. We will also show that a L^4 estimate on the pressure gradient can be derived.

Multiscale modelling and analysis of plants: Interplay between mechanics, chemistry and growth

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In this talk we shall consider multiscale modelling and analysis of different aspects of plants development and growth. We shall discuss the interactions between the transport of plant hormone auxin and plant root growth and formation of the 'reverse fountain' in plant root tips. In multiscale modelling of the interplay between the mechanics, microscopic structure and chemistry in plant tissues we assume that elastic properties of cell walls depend on the chemical processes, whereas chemical reactions depend on mechanical stresses within the cell walls and tissues. For plant growth we will consider macroscopic density-based models and microscopic description of growth processes on the level of individual plant cells. Multiscale analysis techniques are applied to derive macroscopic tissue level models from the microscopic cell level description of the biological and physical processes. Numerical solutions for macroscopic models will demonstrate the dynamics of plant growth and development and the heterogeneity due to interactions between mechanical stresses, microstructure, and chemical processes.

Intra and Inter cellular communications lead to glycolytic synchronisation waves in yeast cells

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Glycolysis is the main metabolic pathway for glucose degradation and is one of the best studied models for biological oscillations. In yeast, the glycolytic oscillations are not only visible at a cellular level, but also lead to synchronisation in populations.

I will present the construction and validation of a detailed mathematical model for glycolysis, starting at the individual enzyme- catalysed chemical reaction step, with a focus on the phosphofructo kinase. The de-stabilising kinetics of this enzyme, caused by substrate inhibition and product activation, lead to oscillations in the enzyme activity that are transduced through the glycolytic pathway via co-factor coupling. The intra-cellular oscillations are observable via NADH fluorescence in individual cells, and inter-cellular communication via acetaldehyde (an intermediate in the glycolytic pathway that quickly permeates the cellular membrane), leads to synchronisation of the oscillations in a yeast population.

The mathematical model has been developed over a 20 year period in my group, and is strongly based on experimental data obtained in a collaboration between Stellenbosch University, Vrije Universiteit Amsterdam, and Gothenburg University. For each of the individual reaction steps, and for the pathway dynamics leading to oscillations, multiple data sets for model construction and validation were generated. These include bifurcation parameter scans, quenching experiments, phase response curve analysis, and microfluidic cell analysis for wave propagation.

For mathematical modelling it is important to find a good level of abstraction; core models are good for a conceptual understanding and mathematical representation, but often miss the link with experiment. Detailed models often have hidden variables and non-identifiable parameters. A good basis for deciding on the level of abstraction in a model is an evaluation of our understanding of the system and its experimental accessibility. In my talk I will stress the importance of iterating between theory, model and experiment.

Discrete-time infectious disease models

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The number of outbreaks of emerging and re-emerging infectious diseases is growing, and the ongoing COVID-19 pandemic is one of the latest examples. In this talk, we will introduce a discrete-time Kermack-McKendrick infectious disease model and its extensions and then use these models to introduce a framework for studying disease transmission dynamics in discrete-time epidemic models. For these models, we will study the epidemic threshold parameter, the basic reproduction number, then derive the final size equation, and illustrate herd immunity.

Invited Presentations

Modelling a dynamic pandemic: Lessons from COVID-19 in South Africa

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Every new infection that invades a population brings along huge information deficiencies as the epidemic evolves. This has been the case with the current COVID-19 pandemic. In this talk we explore the modelling challenges, success and future scenarios given the evolving vaccination landscape. The aim is to generate debate, highlight modelling pitfalls and interrogate previous and current models. We look at the various models to date, the possible modelling of different variants and how we can approach multiple peaks. The models presented will be of a deterministic type. We explore the models using data from South Africa. We look at the various simulations scenarios and the implications to public health.

Contributed Talks

Immune system response: a mathematical exploration of COVID-19 anomaly

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The ongoing COVID-19 pandemic has infected many populations groups leading to different disease outcomes that range from asymptomatic illness to fatality. Due to the unprecedented nature of the pandemic, studies of the immune system response to COVID-19 are still not definitive for the different degrees of severity exhibited by different patients. Some studies have attributed the different outcomes to cytokines storm by the immune response while others have associated the disease?s severity to preexisting conditions. Some studies also suggest genetic predisposition, a theory that is likely to suffer from scrutiny given that many infected pairs of identical twins have presented with very different outcomes for COVID-19. This paper presents a mathematical model of the immune response to COVID-19 by attempting to capture the viral load generated by the virus and the collective response that is mounted against it. The model is then used to explore the anomalies presented by the disease as observed in similar patients.

Solving population dynamics models via Sumudu transform

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The progressions of a disease through a set population are governed by differential and integral equations. For instance, modeling of the spread of infectious diseases, population dynamics or electrodynamics problems are guided by differential equations. Finding the conditions for certain differential equations has been demonstrated in the literature by several authors (See e.g, Ademola et al. [1] and references therein). Such mathematical models which generally are nonlinear, often defy analytical methods and the exact solutions are consequently rare to obtain. How to obtain the solutions of nonlinear equations has been a subject of research for decades and it has recently attracted much attention (See e.g, Aibinu et al. [2] and references therein). The Sumudu transform is a simple modified form of Laplace transfom. There are reports on applications of Sumudu transform for obtaining the solutions of several forms of differential equations (See e.g, Nisar [3] and references therein). This study will demonstrate how to construct the solutions of a most general form of population dynamics models via a blend of variational iteration method with Sumudu transform. Results or outcomes from this type of research can help inform best practice in applicable areas and address certain United Nations Sustainable Develop Goals. This study also has applications in other fields such as engineering, Physics, Chemistry and Economics.

Keywords: Population dynamics, models, Sumudu transform.
Mathematics Subject Classification: 35K55; 35B10; 35B40; 35K57.

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Numerical Method for the Nonlinear Age-structured SIPCV Model of Cervical Cancer Cells and HPV Dynamics

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Advanced models for the infectious disease dynamics are based on the age-structured epidemic models [1]. In this work we develop the numerical method for simulation the dynamics of age-structured sub-populations of susceptible, infectious, precancerous and cancer cells and unstructured sub-population of human papilloma virus (HPV), (SIPCV model [2]). The features of our SIPCV model are: (i) death rates of infected, precancerous and cancerous cells do not depend from the quantity of HPV since the immune system of organism is tolerant with respect to its own cells; (ii) death rate of HPV depends on the virus quantity, since the immune response of the organism to the virus population growth is taken into account; (iii) interaction between susceptible cell population and HPV is described by Lotka-Voltera incidence rate and result in the growth of infected cells; (iv) infected cells partially move to the precancerous sub-population and partially apoptose when viruses leave them; (v) cells of precancerous sub-population move to the cancer sub-population with density-dependent saturated rate; (vi) two time-delay parameters describe the time between HPV entry into a host susceptible cell and production of new viruses and a duration of the first phase (CIN I and CIN II stages) of immune response to HPV population growing. Using a method of characteristics, we obtain the explicit recurrent formulae for the solution of SIPCV model and prove the theorem of existence and uniqueness of solution. Explicit recurrent formulae allow us to develop the effective numerical method of second order of approximation. We prove the convergence of numerical solution to the exact one with the second order of accuracy. Numerical experiments reveal two types of the asymptotically stable dynamical regimes corresponding to the localization of dysplasia and cancer tumor in biological tissue without metastases and two unstable dynamical regimes which are related to the cancer tumor growth and formation of metastases in organism. Overall, the numerical method provides the reliable and accurate theoretical instrument for simulation and study of age-structured SIPCV epidemic models.

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Dynamics of SEIR model in random environment

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Mathematical models have been used to describe natural phenomena and they have been long investigated in science and engineering. Data are often rarely obtained or only partially observed in the field of life sciences, approaches by differential equations play an important role to quantify observations such as evaluating the effect of treatment and to predict future behavior of the system such as estimation of the treatment outcome or long term dynamics of infectious diseases epidemics. Moreover, numerical simulation based on differential equations and stochastic processes gives us new insight into system behavior under different scenarios and such approaches are often used in optimization of treatment schedule of diseases or developing health countermeasures in policy making.

Mathematical modeling in epidemiology has long history and one of the most important works is SIR model which was introduced by Kermack and McKendrick in 1927. They described the interaction among susceptible, infected and recovered individuals in a population. The model itself is quite simple, however, it can be used to estimate the threshold value for the future behavior of the infectious disease outbreaks as well as estimate transmission potential of the corresponding pathogens. To account for various transmission patterns or structure of the population, many mathematical models have been later developed based on the SIR model.

Most of the models appeared in literature are deterministic and the averaged values are usually employed in the population level analyses. However, uncertainties are often observed in epidemiology and parameter values often show fluctuations. In addition, it is well known that contact pattern of individuals depends on the age of contactor and contactee. To deal with heterogeneously mixing population and it is necessary to account for age-dependent heterogeneity when we deal with population with various demographic background. Furthermore, human behavior and environment make the dynamics more complicated and some infectious diseases show periodic patterns which are caused by seasonal effects. For example, the number of influenza cases increases during winter season while the peak of malaria incidence appears during and after rainy season in warm countries. Incidences of childhood diseases also show similar patterns due to school years and the number of measles cases elevates when school year starts and decreases during winter holidays.

In this study, we focus on a system of ordinary differential equations with an SEIR (Susceptible-Exposed-Infected-Recovered) type of structure. Concerning above mentioned time-dependencies and heterogeneities appeared in infectious disease transmission, we develop an SEIR model with randomness due to fluctuations of birth and death rates and contact patterns between susceptible and infected populations. The formulated model is now a system of random ordinary differential equations and it is studied by the theory of random dynamical systems and dynamical analysis. First the existence, uniqueness, positiveness and boundedness of solutions are discussed. Then the sufficient conditions under which the prevalence of infectious diseases decreases monotonically to zero, as well as conditions under which an epidemic occurs are shown. Lastly, the numerical simulation under given disease-free and endemic scenarios will be presented as an illustrative example.

Beyond the Next Generation Matrix Method

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The Next Generation Matrix method has been one of the most popular methods for establishing the stability of the disease-free equilibrium. It has, however, some drawbacks - for instance it is not directly applicable for problems with the immigration of infectives. In this talk, we shall discuss some ways of dealing with such problems, based on perturbation techniques.

Grapevine leafroll-associated virus 3: modeling and assessing the effects of control measures

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Most plant viruses are vector-borne. Grapevine Leafroll Disease (GLD) is the most economically damaging grapevine viral disease, being responsible for 60% of yield losses in grape production. It affects grape quality and vine health, often resulting in shorter vineyard life spans as well as the late maturity of grapes, all of which affect the sale to market and overall wine quality. The disease is found in almost every grape-growing region in the world, in particular, in the wine-making industry in South Africa where the infection rate is high. In this talk, we propose an age-structured mathematical model for the transmission of Grapevine leafroll-associated virus 3 (GLRaV-3). We investigate the dynamics of transmission and assess the effectiveness of roguing as the main control strategy for GLRaV-3 spread.

Stability analysis of an in-host high-risk human papillomavirus (HPV) vaccination model

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High-risk human papillomavirus (HPV) types 16 and 18 are the major causes of cervical cancer in women. HPV is a widespread sexually transmitted infection that is given less attention, with many men and women living and spreading the infection through unsafe sexual practices. We present a mathematical model for the transmission dynamics of HPV in-host in the presence of an immune response represented by Cytotoxic T-Lymphocyte cells (CTL) and vaccination. The model exhibits exhibits the following, the disease-free equilibrium, CTL-inactive endemic equilibrium, CTL-active endemic equilibrium, effective reproduction number and CTL reproduction number . The local and global stability dynamics of the equilibrium points are established. Sensitivity analysis is carried out and it was established that an increase in the transmission rate and the mature rate of latently infected cells effectively increased the infection while an increase in vaccination reduces infection. Numerical simulations confirmed the stability of the stability of the equilibrium points thereby supporting the theoretical work presented. Results also show that the HPV vaccine is effective in the reduction of new infections if the efficacy is above 85% as indicated by the contour plot. Finally, while the immune response plays an important role in the reduction of HPV infection in-host research clearly shows that the action of the immune response alone is not sufficient and there is need to promote the full uptake of the HPV vaccine by women and girls within developing countries.

Vector-borne diseases control using Sterile Insect Technique with accidental releases of sterile females

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According to the world health organization, the major vector-borne diseases (VBD) together account for around 17% of the estimated global burden of communicable diseases. Every year, there are nearly 700,000 deaths from VBD. It is important to emphasize that more than 80% of the global population live in areas at risk from at least one major VBD. Despite the progress in knowledge on VBD, for most of them, the major problem is the absence of effective drugs and vaccines. That is why, in the last decades, the development of (sustainable) vector control methods has become one of the most challenging issues to reduce the impact of VBD and, also, limit their spreading.

In this talk, we focus on the Sterile Insect Technique (SIT) within an epidemiological context [1], with a main focus on Dengue. SIT is a technique to control vectors of diseases by releasing sterile males only. However, sex-separation being a complex process, females can also be sterilized and released. Since only females are vectors, it could be problematic when arthropod viruses are circulating. We develop and study an entomological-epidemiological model that includes releases of sterile insects and mechanical control, i.e. the removal of breeding sites. Qualitative analysis of the model highlight a threshold number of treated males above which the control of wild population is always effective, using massive releases. We show that if R0, the basic reproduction number of the epidemiological model without SIT, is above a certain threshold, then, the epidemiological risk can only be controlled using (very) massive SIT releases. Otherwise, when SIT occurs, the SIT-R0, that shapes the stability property of the (periodic) disease-free equilibrium, can be taken below one using non-massive SIT releases. However, practically, it seems more efficient to consider massive releases, followed by small releases [2]. Of utmost importance, our results reveal that outside an epidemic period, the release of sterile females is not an issue, as long as the number of sterile males is above the critical threshold. Within an epidemic period, we show that the releases of sterile females do not really influence the SIT strategy, as long as their proportion (to the total amount of released sterile insects) is quite low, i.e. no more than 5% (IAEA standard requires 2%). Our theoretical results will be illustrated with an example based on an ongoing SIT project in Réunion island (France), where Dengue is circulating [1].

Key words: Vector-borne disease, Sterile Insect Technique, Sterile female, Mechanical control, Monotone system, Dengue

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Dynamics of microbial population with quiescence state under nutrient-limiting conditions

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Majority of microorganisms have the ability to resist stressors such as antibiotics, temperature and desiccation and anaerobic conditions by entering a state of low no physical or/and metabolic activity - dormancy. In this work, we present a system of reaction-diusion equations modeling growth and decay of microorganisms that explicitly accounts for their ability to switch between active and dormant states in response to a limiting-nutrient. We show that traveling-wave solutions may exist, with the traveling speed dependent on the nutrient input.

On residual fertility and remating in the Sterile Insect Technique against fruit flies

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The fruit fly ceratitis capitata, also called the medfly, is a very destructive pest all around the world against a wide range of hosts, including stone fruits and citrus. Several operational control programs have been launched against the medfly in California, Central America, in Southern-Europe (Spain, Croatia) and in South Africa, using the sterile insect technique (SIT). SIT is an environmentally-friendly insect pest control method involving the mass-rearing and sterilization, using radiation, of males that are repeatedly released to mate with wild females resulting in no viable offspring. A new SIT project against medfly is now ongoing in Corsica (a French island in the Mediterranean Sea), CeraTIS-Corse. A new and very destructive pest, the oriental fruit fly, bactrocera dorsalis, has appeared in Réunion island (a French overseas department in the Indian Ocean) in 2017. Since then, it has invaded the whole island, infesting most of the crops from the sea level till 500 m. The damages are important, in particular in Mango orchards where crop yields have been reduced by 50% to 80%. A feasibility SIT project, GEMDOTIS, is ongoing in La Réunion.

While conceptually very simple, in practice, SIT is very complex. In particular, it requires a very good knowledge of the targeted pest ecology and biology. It is also crucial to ensure that the released sterile males are of very good quality to disperse and compete against wild males. However, release strategies often seek for a balance between the quality of the males and the minimum level of sterility acceptable. In [1], using a generic model we studied the impact of residual fertility (RF), i.e. irradiated males are not fully sterilized, that is, a proportion, say ?, of sperms is always fertile. At the population level, this means that a proportion, ?, of sterile males is able to have progeny. In [1], we show that RF is strongly linked to the basic Offspring/Reproduction Number of the pest, N, i.e. the average number of female offspring produced by one female during her entire life. In other words, we showed that SIT is effective if and only if $\varepsilon N < 1$ [1].

In this talk we consider a more complex model, where remating, i.e. the ability of female to be inseminated multiple times, after a so-called "refractory" period, can occur. We also consider that the frequency of remating is higher for females previously mated with sterile males. We study the impact of remating coupled to RF to explain SIT failures or mitigated results obtained in some countries. Our results highlight the importance of a very good knowledge of the targeted species reproduction biology. We illustrate our results on Ceratitis capitata and Bactrocera dorsalis and the consequences in terms of efficiency [2].

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Sampling for rabies vaccination coverage in Tanzania

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Spatial statistics is a hugely growing field as the acquirement of data via satellites is increasing. Applications in remote sensing and geolocated data are prominent, providing much scope for improved analysis. A case example of this is geolocated households in rural Tanzania. Efforts are being made to contain rabies in Tanzania, reported in the southern highland regions, since 1954, and endemic in all districts in Tanzania currently. It has been determined that mass vaccination of at least 70% of an animal population is most effective in reducing transmission of rabies. Current vaccination campaigns in Tanzanian villages have many administrative and logistical challenges. Animals roam freely, making a full population vaccination impossible. Spatial sampling of households in villages is proposed, where optimality is measured through the distance traversed by the vaccinator by foot for vaccinating at each sampled household. The walking distance is attained by incorporating a driving network between optimally determined stopping points from which the vaccinator then walks for executing vaccinations, while ensuring the 70% coverage of the animal population. A systematic regular spatial sampling is found to be optimal. The vaccination scheme proposed, provides an effective way to manage a vaccination campaign.

The pandemic state of Coronavirus (COVID-19), insights from a mathematical model

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Coronavirus (COVID-19), a novel, highly contagious, viral disease, was first identified in Wuhan, the capital of Hubei, China in December 2019 and quickly spread to more than 220 countries around the world causing in excess of 170 million infections with more than 3.5 million deaths globally. In this talk, a model for the transmission dynamics of the novel COVID-19 in a population is presented. In the absence of disease-free equilibrium for the model, an invasion reproduction number is computed and used to analyze the stability of the equilibrium for the model.

The model is fitted with the cumulative number of daily reported deaths with the system plot, the system is used to assess the most effective measures in controlling the disease in South Africa. The impact of non-pharmaceutical interventions is assessed via a threshold analysis approach. Analysis of the model demonstrates that COVID-19 can be controlled effectively by reducing contact between individuals via social-distancing, monitoring close contacts, self-isolation and quarantining of suspected exposed individuals. Sensitivity analysis using data available were used to assess the parameters that have the most influence on coronavirus transmission. The analysis show that quarantine and isolation are the most effective control strategies in combatting the outbreak.

Patterns in Plant Pigmentation

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Red, blue, and purple colors in plants are typically due to plant pigments called anthocyanins. In a plant cell, an equilibrium is established between anionic and cationic forms of anthocyanins as well electrically neutral colorless forms called hemiketals. In typical pH ranges in cells, the colorless hemiketal would be expected to be the dominant form. Why then, do plants, in fact, display colors? We propose that this is part due to aggregation of the colored forms of anthocyanins.

In previous work, Ding and colleagues [1] have produced a reaction-diffusion model for patterns of varying anthocyanin concentration in plants. We augment this model to include aggregation. We show that nonlinear effects due to aggregation combined with a spatially varying total concentration allow for a spatial pattern of colored and uncolored species. Hence, the combination of an activator-inhibitor system and aggregation is suggested to be the biological framework for colorful spotted pattern formation of plants. These patterns are of importance for pollination.

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Molecular mechanism of the anti-inflammatory action of heparin: a computational perspective of the COVID-19 case

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We perform in silico study of the ability of low-molecular-weight heparin (LMWH) to inhibit both IFNγ and IL-6 signalling pathways. While heparin's binding affinity to these cytokines is well-known, the molecular mechanism of its impact on their biological activity has not been studied in detail. Our results show that LMWH is able to fully inhibit the interaction of IFNγ with its cellular receptor, thus blocking the IFNγ signalling pathway. It also influences the biological activity of IL-6 by preventing the formation of the IL-6/IL-6Rα/gp130 signalling complex. These findings shed light on the molecular mechanism of the anti-inflammatory action of LMWH, relating it to the impairment of the biological activity of these cytokines, and underpin heparin's ability to influence favourably conditions characterised by overexpression of the latter. Such conditions are associated with autoimmune diseases, but also with inflammatory processes, in particular with COVID-19. Our results put forward heparin as a promising means for prevention and suppression of the development of severe CRS in acute COVID-19 patients and encourage further investigations on its applicability as an anti-inflammatory agent.

Acknowledgements: This work was supported in part by the Bulgarian National Science Fund under Grant KP-06-DK1/5/2021 and by the Bulgarian Ministry of Education and Science, under the National Research Programme "ICTinSES" (D01-205/23.11.2018, DCM # 577/17.08.2018).

Automated Feature Extraction from Large Cardiac Electrophysiological Data Sets

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Rationale: A new multi-electrode array-based application for the long-term recording of action potentials from electrogenic cells makes possible exciting cardiac electrophysiology studies in health and disease. With hundreds of simultaneous electrode recordings being acquired over a period of days, the main challenge becomes achieving reliable signal identification and quantification.

Objective: We set out to develop an algorithm capable of automatically extracting regions of high-quality action potentials from terabyte size experimental results and to map the trains of action potentials into a low-dimensional feature space for analysis.

Methods and Result: Our automatic segmentation algorithm finds regions of acceptable action potentials in large data sets of electrophysiological readings. We use spectral methods and support vector machines to classify our readings and to extract relevant features. We are able to show that action potentials from the same cell site can be recorded over days without detrimental effects to the cell membrane. The variability between measurements 24 h apart is comparable to the natural variability of the features at a single time point.

Conclusions: Our work contributes towards a non-invasive approach for cardiomyocyte functional maturation, as well as developmental, pathological and pharmacological studies. As the human-derived cardiac model tissue has the genetic makeup of its donor, a powerful tool for individual drug toxicity screening emerges.

Contact Tracing for COVID-19

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Contact tracing is critical to controlling COVID-19, but most protocols only "forward-trace" to notify people who were recently exposed. Using a stochastic branching-process model, we find that "bidirectional" tracing to identify infector individuals and their other infectees robustly improves outbreak control. In our model, bidirectional tracing more than doubles the reduction in effective reproduction number, R_{eff}, achieved by forward-tracing alone, while dramatically increasing resilience to low case ascertainment and test sensitivity. The greatest gains are realized by expanding the manual tracing window from 2 to 6 days pre-symptom-onset or, alternatively, by implementing high-uptake smartphone-based exposure notification; however, to achieve the performance of the former approach, the latter requires nearly all smartphones to detect exposure events. With or without exposure notification, our results suggest that implementing bidirectional tracing could dramatically improve COVID-19 control.

COVID-19 intervention model: An initial aggressive treatment strategy for controlling the infection

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The novel coronavirus (COVID-19) outbreak emerged in December 2019. The disease has caused loss of many lives and has become an unprecedented threat to public health worldwide. We develop simple COVID-19 epidemic models to study treatment strategies to control the pandemic. The results shows that eradication of the disease is possible if the efficacy of treatment is perfect. We also investigate the existence of a dual-rate effect. Conditions under which the effect occurs are derived. When the effect is present, a tactic to control the infection might be to initially treat infected individuals aggressively at a relatively high rate to drive the prevalence to a lower region that can be maintained in the long run at relatively moderate rate and cost.

Comparison theorems for parabolic operators in variational form

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IIn this talk we discuss the properties of a parabolic differential operator which is commonly used in Partial Differential Equations (PDEs) arising in many areas for example Mathematical Physics and Theoretical Biology. We derive results regarding order/ comparison for the variational formulation. The solutions of the classical formulation in variational form are called weak solutions. We show that the comparison theorem for weak solutions can be recast in a general framework; namely, in terms of inverse monotone operators.

Efficacy analysis of COVID-19 control measures: Insights from mathematical modelling

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World over, economies are still grappling with the novel coronavirus, COVID-19, that has long been declared a pandemic by the World Health Organisation. The discovery of vaccines has shed a glimpse of hope that the pandemic shall soon subside. Nonetheless, to-date several countries in Africa are still to vaccinate a considerable number of individuals to curtail the disease. More still, several challenges still remain; ranging from securing the vaccines, to their distribution. It is therefore highly imperative that the non-pharmaceutical interventions are still adhered to. In this study, we investigate the dynamics of COVID-19 in Eswatini and determine the efficacy of the different control measures via dynamic mathematical modelling and sensitivity analysis; using data from Eswatini.

The Two-step Exponential Decay Reaction Network: Relation to Epidemiological SIR Models with Gompertz Type Infection Contact Patterns

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The following topics are discussed:

- Bateman equations
- One-step exponential growth-decay model
- chemical reaction network theory
- Two-step exponential growth-decay model
- Logistic and Gompertz growth-decay models

Formulated as chemical reaction networks

- Kermack-McKendrick epidemiological SIR model and its relation to the logistic model
- G-SIR model - a SIR-type epidemiological model with Gompertzian disease spread mechanism
- Comparison of the discussed models

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On synergistic co-infection in crop vector-borne diseases

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Major constraint to crop productivity are pests and diseases that cause major food insecurity throughout the world, especially in Southern Countries. The Food and Agriculture Organization estimates that pests and diseases are responsible for about 25% of crop loss. A new deadly disease of maize was reported in many Southern Countries, the Maize Lethal Necrosis Disease (MLND). For instance, in Kenya alone, the MLND affected around 77 000 ha, translating into an estimated loss of US $ 52 million. The MLND results from a synergistic interaction between the Maize Chlorotic Mottle Virus (MCMV) and one of several viruses from the Potyviridae family, like the Sugarcane Mosaic Virus (SCMV). In this talk, we focus on modelling and analysis of MLND. However, our model is sufficiently generic to be applied to different co-infection vector borne diseases. A theoretical analysis shows that different equilibria and thresholds exist: the basic reproduction numbers and the invasion reproduction numbers. We show that these thresholds drive the dynamics of the MLND system. In particular, the invasion reproduction numbers are essential for the emergence or not of the MLND. We illustrate our results through numerical simulations and discuss potential control methods. This work has been published in [1].

Key words: Crop disease, synergistic interaction, basic reproduction number, invasion reproduction number, numerical simulations.

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Effects of Transplacental and Direct Transmission on the Probability of Bluetongue Virus Persistence in Temperate and Tropical Regions

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Bluetongue virus (BTV) is an important concern for the ruminant livestock industry owing to its high morbidity rate. It is mainly transmitted by a midge to a host (vectorial transmission) but even though its replication in the midge ceases during winter in temperate countries, outbreaks re-emerge in the next season. Transplacental and direct transmission have been proposed as mechanisms that facilitate its overwintering (persistence), but to date, their effects on the probability of BTV persistence are not fully understood. In addition, the effects of these mechanisms on the probability of BTV persistence in tropical regions where the virus is endemic are not clear. A deterministic model that accounts for BTV transmission to cattle is formulated and analysed. Using the next generation approach the basic reproduction number (R_0) is determined. When $R_0 < 1$, the model exhibits a backward bifurcation indicating that the virus persists. When $R_0 > 1$, a continuous-time Markov chain (CTMC) model derived from the deterministic model is used to estimate the probability of BTV persistence. By approximating the CTMC model with a multitype Galton-Watson branching process, it is shown that both mechanisms can have a high and a low positive effect on the probability of BTV persistence in temperate and tropical regions, respectively. These results indicate the importance of transplacental and direct transmission for BTV persistence in temperate regions, but not in tropical regions where vectorial transmission is the dominant mechanism as expected.

Keywords: Bluetongue virus; Transplacental transmission; Direct transmission; Persistence; Overwintering

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The estrogen paradox in breast cancer treatment, A mathematical modeling approach

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In this work, we formulate an ODE-based mathematical model that proposes an explanation of the mechanisms behind the estrogen paradox, whereby estrogen is a risk factor for breast cancer development, while it can also cure it. The key feature of the model is the protein p53 which is known to play an important role in breast cancer suppression.

We perform a global stability analysis and bifurcation and carry out numerical simulations of various scenarios related to the estrogen paradox. The findings from the mathematical and numerical analyses suggest that the apparent paradoxical role of estrogen could be the result of some interplay between estrogen and p53.

Forecasting using extended dynamic mode decomposition

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Mathematical modelling takes a central stage in dealing with various real-world challenges such as saving lives from infectious diseases, policy-making and decision making, maximising economic growth, etc. These problems are usually nonlinear and high dimensional, posing a challenge to modellers not only on how to formulate the equations that suitably describe the system but also choose the method to solve such complex systems. Data-driven modeling concerns learning a dynamical system from repeated measurements made from an unknown dynamical system. The learnt dynamical system is meant to approximate the dynamics of the unknown. In this work, we explore different methodologies through dynamic mode decomposition (DMD) and the extended (DMD) for simpler data. When a lengthy time series is available, we explore the methods of recurrent neural networks to forecast and build high-fidelity models. We apply our methods to data from infectious diseases.

Tumorigenicity and one-dimensional diffusion in osteosarcoma

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Osteosarcoma is the most common primary malignant bone tumor, it affects children, adolescents, and older adults. According to biological and medical studies, its genetic complexity is very high; this feature makes it difficult to describe its mechanisms of appearance and evolution. For the same reason, different osteosarcoma cell lines have been generated; these have helped to describe underlying mechanisms of tumor progression through preclinical investigations. In this talk we describe the relationship between diffusion and tumorigenicity by proposing a mathematical model based on the one-dimensional Fisher-Kolmogorov equation $u_t = D(t)u_{xx} + f(u)$, $u = u(x,t)$ is the cell density, D is a difussion coefficient and $f(u)$ represents the proliferation model [1, 2]; this model supposedly is related to the power law model [3], $V(t) = \alpha t\beta$, where V represents the tumor volume. To obtain the results we implement codes in Matlab.

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Fragmentation Equations with Growth and Decay

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Fragmentation equations with transport occur in nature and also through human developed processes. They describe processes including ecology, animal groupings, fish schooling, applied physical sciences, e.t.c. Studies have been conducted to have a better insight of the process, and they have concentrated on getting exact solutions for specific cases and building on the existence and uniqueness of solutions. In this talk, we prove the existence of solutions using semigroup theory in a Banach space settings. The space takes into account that the mass and number of particles remain controlled throughout the fragmentation process. A regularising effect property is observed from a semigroup, where high order moments are controlled by the low order moments. As an illustration, we provide explicit solutions for the power law coefficients and further show that this computations satisfies the regularising effect.

Global stability of cervical cancer cell model based on age structured

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Cervical cancer was the fourth most common cancer diagnosed in women, moreover in 2020, it was estimated 604.000 new cases of cervical cancer and 342.000 deaths worldwide [1]. Human Papillomavirus (HPV) infection is one of the causes of cervical cancer [2]. In the early stages of HPV infection, the non-invasive lesions of abnormal cervical epithelial cells are found. The virus starts to enter and infect epithelial basal cells when the cells are at a certain maturity. Cell maturity is closely related to the age of the cell which is passed in four phases, i.e. G1, S phase, G2 and M phase (mitosis). Virus HPV genome replication is highly dependent on when the host cell is in the G1 phase towards the S phase. Proteins from HPV, E6 and E7, will inhibit the cell from entering the G1 phase [3]. Hence this becomes the concern of researchers to reduce the death risk of cervical cancer due to HPV infection in the cells. Study of transmission between cells is done to determine the behavior of cervical cancer cells in the cervical epithelial tissue.

In this study, we consider a qualitative study of an age dependent mathematical model for the development of cervical cancer at the tissue level as modified from the ones in [4, 5]. Based on [4], the interaction between cells occurs at any time. The reality of the abnormality of cells is at certain age, so we add a new variable that represents the age of cells. Moreover, by the fact that the virus can be reproduced and spread in the tissue since the first infection, the free virus compartment in [4, 5] can be fused in the transmission rate parameter. Hence, in this paper, we propose and analyze a mathematical model of cervical cancer cell in cervix tissue level based on age structured. The model is a four-dimensional system of non-linear partial differential equations with a six-dimensional parameter space that describes the cancer development in the cervix i.e. susceptible, infected, pre cancer and cervical cancer cell population. A cell has ability to be infectious or become abnormal in a certain interval of the cell cycle. Therefore, we assume that the age of abnormality will not start from zero. The steady state conditions and its stability analytically are important to be investigated, and we focus our study to the existence conditions of the global stability for the disease-free equilibrium point and its characteristics. Lastly, we show the dynamics of the system with age structures numerically.

Keywords: cervical cancer cells, age structured, global stability.

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Complex dynamics of prey predator model with disease in predator and cost of predation fear

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In prey predator system, the impact of fear on prey population receive significant attention by the researchers recently. The study of a prey predator system with disease in predator in the presence of fear has not yet been studied. We model a prey predator system with density dependent disease transmission in predator and predator induced fear in prey. We consider two important mechanisms where fear on prey can be detrimental to the prey due to low reproduction and disease in predator can be beneficial to the prey population due to low predation risk. In this study, we try to investigate the simultaneous effect of disease transmission and the cost fear on the system dynamics. We study the dynamics of such system around the equilibrium points by stability and bifurcation analysis. Numerical results reveal that high strength of fear and disease transmissions have the ability to stabilize the system by excluding limit cycle oscillations. We show that the high strength of disease transmission not only control or eradicate the predator, but also allow the prey species to recover. The study indicates that infectious diseases may act as a biological control to control of undesirable species. In the presence of fear, half saturation constant make an important role to shrink or expand the oscillatory region. Also, we identify a scenario in which disease transmission rate produces bubbling effect around endemic equilibrium. We validate our analytical findings through numerical simulations.

Low order analytic perturbations of positive semigroups

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In the talk, we discuss smoothing properties of positive linear semigroups, generated by a sum of two closed and densely defined operators. In the general settings of AL spaces and under the assumption that the lower order operator is positive and sectorial, we show that the resulting non-analytic semigroup has essentially the same regularizing properties as the analytic semigroup generated by the low order sectorial perturbation.

Our result is relevant for the study of semilinear equations arising in context of population dynamics, demography, epidemiology, e.t.c., where the linear processes (e.g. aging, transport, e.t.c.), coupled with strong nonlinearities, make it impossible to use the standard analytic semigroup framework.

Keywords: Positive semigroups, Perturbations, Smoothing

Mathematical modelling analysis of the mitigation strategies for COVID-19

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A mathematical model for the transmission dynamics of COVID-19 disease is formulated and analysed. In the presence of reinfection, the model exhibits a backward bifurcation when the basic reproduction number is equal to unity. In the absence of reinfection, the model is without backward bifurcation and the disease-free equilibrium is globally asymptotically stable when the basic reproduction is less than unity. Using a secondary data, the model is validated and the values of parameters used in the model are estimated. The sensitivity analysis of the basic reproduction number with respect to changes in any value of the parameter involved in its formula is presented. Some mitigation strategies are proposed.

Investigating the Impact of Transmission-Blocking Anti-malarial Drugs: A Mathematical Modelling Approach

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Background: Despite all efforts in the fight against malaria, the disease continues to wreak havoc, especially in Sub-Saharan Africa. Recently, promising clinical advances have been made in the development of antimalarial drugs that block the parasite transmission and also cure the disease, and has prophylactic effects, called transmission-blocking drugs (TBDs). Moreover, to effectively control and eliminate malaria, it is important to note here that alongside vector control, the community-based treatment of asymptomatic carriers of Plasmodium with TBDs is needed. This calls to study, qualitatively and quantitatively, the impact of control with TBDs treatment on both asymptomatic and clinical (symptomatic) infections towards the effect of malaria control and elimination.

Aim: Our main aim is to explore the potential effects of TBDs on malaria transmission in the effort to control and eliminate the disease using mathematical models to ascertain how the presence of TBDs can mitigate the transmission of malaria parasites on both asymptomatic and symptomatic carriers in a defined hotspot of malaria. Our special focus is on the effects of the treatment coverage and the efficacy of TBDs along with the protective effect and waning effect of TBDs.

Methods: We propose and analyze a mathematical model for malaria transmission dynamics that extends the SEIRS-SEI type model to include a class of humans who are undergoing the treatment with TBDs and a class of those who are protected because of successful treatment. Before we proceed with an analysis of the model's stability, sensitivity, and bifurcation behaviors, we start by ensuring that the model is well-posed in a biologically feasible domain. We compute a control reproduction number, $\mathcal{R}_T$, and discuss the model's bifurcation behavior (which is relevant in determining the level of control that needs to be put into place to achieve disease elimination or control). The mathematical and epidemiological implications of the TBDs are assessed using different approaches. Furthermore, we fit the model to data obtained from the Institute for Health Metrics and Evaluation-Global Burden of Disease (IHME -GBD) by using a non-linear least-squares minimization and curve-fitting package in python known as "lmfit" and use the validated model to explore the model's predictions under various scenarios.

Results and discussion: Mathematical analysis indicates that the model exhibits a forward and backward bifurcation under certain conditions. Thus, the disease can be eliminated when the control reproduction number is less than the critical quantity, otherwise, the disease will be stabilized at an endemic equilibrium point at which its expression is given. Results from our analysis show that the effect of treatment coverage rate on reducing reproduction number depends on other key parameters such as the efficacy of the drug. The projections of the validated model show the benefits of using TBDs in malaria control in preventing new cases and reducing mortality. In particular, we find that treating 35% of the population of Sub-Saharan Africa with a 95% efficacious TBD from 2021 will result in an approximately 82% reduction in the number of malaria deaths by 2035.

Keywords: transmission-blocking antimalarial drug, mathematical modeling, data fitting, treatment coverage, drug efficacy, bifurcation analysis, numeral simulation.

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