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Nonlinear Theory and its Application to Personalized Medicine

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Abstract—In this plenary talk, I review our recent research on nonlinear theory and its application to personalized medicine based on dynamical systems modeling. First, we use hybrid dynamical systems to mathematically describe intermittent hormone therapy of prostate cancer that is an important model disease for mathematical analysis, and realize personalized medicine for diagnosis, therapy, as well as prognosis of prostate cancer, using mathematical modelling. Second, we extend the concept of the conventional biomarkers to that of dynamical network biomarkers (DNB) which can detect in a personalized way early-warning signals of imminent bifurcation from a healthy state to a disease state. Since the DNB can predict sudden deterioration of each patient's disease in advance, it may open a new way for personalized and preemptive medicine.

1. Introduction

Mathematical engineering is a transdisciplinary research field where mathematical models are built and theoretically analysed in order to understand, optimize, control, and predict real-world systems in different fields. We have been developing nonlinear theory of modelling complex systems and its wide-ranging applications in science and technology from the viewpoint of this mathematical engineering [1–3] and chaos engineering [4, 5].

Here, we aimed not only to systematize methodology for mathematically modelling of real-world complex systems on the basis of (1) advanced control theory of complex systems by fusion of dynamical systems theory and control theory [2, 3], (2) complex networks theory, and (3) nonlinear data analysis as well as data-driven modelling, but also to provide possible solutions for complex real-world problems with high importance and urgency for society, such as treatments of complex diseases like cancer and HIV [3, 6–8], optimization and control of power grids, communication networks, and traffic flow systems [9, 10], and development of novel nonlinear electronic and optical technologies such as chaos chips, neurochips, quantum neural networks, and AD converters based on β encoders [11, 12]. In this talk, I concentrate on our recent research of nonlinear theory and its application to personalized medicine.

2. Personalized Hormone Therapy of Prostate Cancer Based on Mathematical Modeling

There exists an excellent biomarker called PSA (prostate-specific antigen) for prostate cancer. Then, prostate cancer can be an important model disease for mathematical modelling of diseases because goodness of each mathematical model can be quantitatively evaluated by measured values of PSA. We made different kind of mathematical models for prostate cancer [3,7,8], and found that in particular, a three-dimensional piecewise-linear hybrid system works well to describe time evolution of PSA quite quantitatively [8]. Further, personalized fitting of model parameters and prediction of disease progression are also made possible on the basis of mathematical methods and PSA data [13–15].

3. DNB (Dynamical Network Biomarkers) as Early Warning Signals of Diseases

Recently, early-warning signals for critical transitions of various nonlinear systems have been intensively studied in the field of nonlinear science [16, 17]. We have extended this concept to that of complex systems, especially biological complex networks [18], and formulated DNB (Dynamical Network Biomarkers) that can detect early-warning signals for imminent bifurcation from a healthy state to a disease state as a new kind of biomarkers for complex diseases [19–21]. Since the DNB can predict sudden deterioration of such complex diseases in advance on the basis of bifurcation theory, early treatments can be started as preemptive medicine in a personalized way before bifurcation to a disease state will emerge.

4. Conclusion

Nonlinear theory is effective for real-world systems because most of them are nonlinear. Since complex biological systems are highly nonlinear and large-scaled, I believe that nonlinear theory can greatly contribute to realization of personalized medicine.

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