# 論文の内容の要旨

# Mathematical Modeling of Disease Transmission Dynamics with Data Generating Processes
# (データ生成過程を伴う疾病伝播ダイナミクスの数理モデリング)

氏名　江島啓介

In history, fight against infectious diseases has never ended since the dawn of human being, and infectious diseases acted as the leading cause of death. To overcome the diseases, pharmaceutical approaches have been invented. However, even at the present moment emerging infectious diseases such as HIV/AIDS, Middle East respiratory syndrome coronavirus (MERS-CoV), Severe Acute Respiratory Syndrome (SARS), influenza continuously cause epidemics across the world. Accordingly, we confront with the needs to evaluate the efficacy and effectiveness of pharmaceutical or non-pharmaceutical interventions (e.g. school closure during influenza epidemic) in quantitative and qualitative manners. Despite the importance of modeling approaches to infectious disease control, the methodology has not been straightforward. The most popular and classical model that describes an infectious disease epidemic was developed by Kermac and McKendrick (hereafter I call the model as SIR (Susceptible-Infectious-Recovered) model), and the SIR model has been extended to practical problems in many ways. Apart from these progresses, a lot of quantitative questions have remained in public health. To answer the questions, this thesis has focused on the data generating

process of epidemics in order to fit models to limited data that is empirically observed. Moreover, the infectious disease modelling framework has been further extended to other health related problems that are known to be contagious.

The main contributions of this thesis are summarized as follows; (1) I constructed a transmission model of influenza during the early phase of an epidemic, investigating the required length of time to reliably estimate case fatality ratio (CFR) of influenza. The study suggested that 2-3 month would be required to reliably compare the estimated CFR with the pre-specified CFR value such as those defined by US Pandemic Severity Index. (2) I proposed a modeling method to estimate the vaccine efficacy against measles, jointly quantifying parameters governing the temporal dynamics of measles (e.g. $R_0$). The study suggested that population aged from 5-19 year should be (re-) vaccinated to prevent further epidemic in Japan. (3) I discussed the use of chance-adjusted agreement coefficients to measure the assortativity of both contact and transmission of an infectious disease. I have demonstrated that the proportion of contacts that are reserved for within group mixing, $p$ in the preferential mixing assumption has excellently corresponded to the Newman's assortativity coefficient (or the so-called Cohen's kappa). Subsequently, I have explicitly distinguished the transmission assortativity from contact assortativity, because the former captures not only the contact heterogeneity but also many other intrinsic and extrinsic factors characterizing the frequency of within- and between- group transmission. (4) I have emphasized that an appropriate model would be essential to answer public health question including vaccination problems. Examining the validity of incorporation of vaccine effect against clinical disease in epidemic models, I have shown that an explicit formulation would also help to clarify underlying assumptions that tend to be hidden in common model structures. (5) I investigated epidemiological model that describes an obesity epidemic which is known to spread via social contact and can also be acquired in a non-contagious manner. I compared the effectiveness of different types of intervention programs against obesity, identifying associated data gaps in empirical observation.

Through these five original studies, I have shown that appropriate model building approaches that explicitly account for data generating process would be essential not only for modeling researchers but also for public health practitioners. The needs for sound model building approaches have been emphasized.