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Advances in predictive modeling for bacterial behaviors from food processing to human consumption: application to quantitative microbial risk assessment

（食品加工から喫食に至る過程における細菌挙動の予測モデリング：
定量的微生物リスク評価への応用）

Control of microbial risk has become an extremely important issue among food hazards. Although the effectiveness of quantitative microbial risk assessment has been established for the evaluation and control of microbial risk, most of predictive models do not take into account the variability and uncertainty of bacterial behavior, which plays an important role in risk assessment. This thesis summarizes the results of studies on the development and validation of novel effective microbial behavior prediction models using probabilistic or stochastic method for quantitative risk assessment (QMRA).

1. Probabilistic predictive approach for *Salmonella enterica* lethality by iso-thermal heating

Changes in the survival probability of *S. enterica* populations during thermal processing were represented by a cumulative gamma distribution. The required heating time estimated by the cumulative gamma distribution was shorter than that estimated by the conventional kinetic method. While the conventional method could overestimate the required heating time, the probabilistic estimation method enables to ensure the food safety and allow the relaxation of heating conditions. This is an important finding as one of the new methods for setting the target heating time.

2. Stochastic predictive simulation for *Bacillus simplex* spore inactivation behaviors by iso-thermal heating

A Monte Carlo model was created from the survival data of *B. simplex* spores to describe the heterogeneity of the spore inactivation behavior. The developed model was compared and validated with observed data. The estimation results successfully predicted the observed changes in the survival probability of the spores and the changes in the distribution of the surviving spore counts. These results are novel findings that will contribute to the design of processing conditions for risk criteria and the improvement of

the accuracy of risk assessment models.

3. Stochastic and dynamic predictive simulation for inactivation behaviors of *Bacillus simplex* spore by non-isothermal heating

A dynamic and stochastic predictive model was developed to describe the heterogeneity of spore inactivation behavior during non-isothermal processing. The results of comparison of observed and predicted behavior on three non-isothermal conditions showed that the model successfully represented the heterogeneity in the survival spore counts. The developed dynamic and stochastic predictive model would allow to select an appropriate thermal condition to ensure both microbial food safety and quality.

4. Predictive model for invading behaviors of *Campylobacter jejuni* into human intestinal cells

Invasion behavior of intestinal epithelial cells by *C. jejuni* was investigated, and a predictive model of the invading *C. jejuni* counts was developed to reveal the infection behavior for the development of a new dose-response model. *C. jejuni* was co-cultured with monolayer-cultured intestinal cells, and the invading *C. jejuni* counts in the intestinal cells was observed. The invasion behavior of *C. jejuni* into the intestinal cells was successfully described by a differential equation model.

5. Development of dose-response model for *Campylobacter jejuni* based on human digestive systems

The dose-response relationship of *C. jejuni* was estimated by developing and integrating a predictive model based on the food digestion process and pathogen infection behavior. The results of comparison with epidemiological dose-response relationships illustrated that the predicted range successfully represented the reported actual values. Furthermore, host age and food type demonstrated higher importance than bacterial acid resistance and other factors, which leads to new insights for QMRA.

6. Elucidation of relevant factors to foodborne listeriosis on pasteurized milk from quantitative microbial risk assessment

QMRA of listeriosis by consumption of pasteurized milk in the Netherland was conducted for clarifying the cause of illness occurrence. The results of sensitivity analysis of 10 billion simulations showed that pathogenicity had the greatest relevance to the illness occurrence, which is different from the commonly analyzed results of sensitivity analysis of consumed log concentrations of pathogen. This result indicates that the conventional method may lead to results that differ from the true importance, and that a method directly describing the illness occurrence is more appropriate.