Mathematics of infectious disease dynamics
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Overview: Mathematical models are an important tool for understanding infectious disease dynamics, and are increasingly used by public health workers and agencies for assessing disease risk and helping inform intervention strategies. This course provides an introduction to mathematical modeling of infectious diseases. We will learn techniques for building and analyzing disease models, and discuss calibration and comparison of models with data.

This course is intended for graduate students in public health or other related disciplines (e.g. ecology, veterinary medicine) wishing to learn about infectious disease models, for example for incorporating mathematical models into their own research. The course is also intended for mathematics students wishing to learn about infectious disease modeling, including both upper level undergraduates and graduate students (in particular, MMS Bio students interested in mathematical epidemiology).

Summary of Mathematical Content: Dynamical systems, linear algebra (e.g. Perron-Frobenius), branching processes, elements of probability. Model construction, working with empirical data. Fitting dynamic models to data.

Credits: 3. Cross-listed in public health (graduate) and mathematics (MMS; open to upper level undergraduates).

Prerequisites: 1 year of calculus, or instructor permission. Additional mathematical topics will be developed in the course as needed.

Textbook: None required; suggested reference is [4]. Notes and additional readings will be supplied.

Assignments / Exams / Project: Problem sets (≈ 6), midterm exam. Final project (small group, pairing public health and mathematics students together).

Topics:

1. Basic deterministic modeling frameworks. (5 weeks)
    - Basic SIR model. Introduction to compartmental differential equation models. Fixed points, linearization, stability. Basic reproduction number $\mathcal{R}_0$: biological and mathematical definitions. Next generation matrix. Initial epidemic growth rate, serial interval, and $\mathcal{R}_0$. Incidence functions. Herd immunity and critical vaccination threshold. Final outbreak size relation.
    - Case studies: rotavirus in the U.S. [13], measles in the U.K. pre- and post-vaccination [3], global smallpox eradication [1, 5, 15].
2. Age-structured models (1 week)
    - Who acquires infection from whom (WAIFW) matrices; age profile for endemic vs. invading diseases with disease-induced immunity. Age-specific interventions.

- Case study: Age-based vaccination strategies and flu policy in the U.S. [11].

3. Stochastic models (2 weeks)
   - Branching process basics; probability of extinction and $\mathcal{R}_0$; demographic fade-out; critical community size. Gillespie simulations.
   - Case studies: contact tracing and SARS [10]. Measles in Iceland [2].
4. Heterogeneity (1 week)
   - Mixing patterns: mean, variance and $\mathcal{R}_0$. Multigroup models. Core groups; disease hot spots.
   - Case study: Gonorrhea in the U.S. [8].
5. Spatial models (2 weeks)
   - Patch models; metapopulations; gravity models.
   - Case studies: measles in the U.K. [7, 14].
6. Disease on networks (1 week)
   - Basic network terminology. Degree distribution and probability of disease outbreak. Social networks.
   - Case studies: SARS [12]. HIV (relevant portions of [6, 9]).
7. Parameter estimation (2 weeks)
   - Optimization: basic concepts, software (Matlab and R). Sampling models. Maximum likelihood.

References

[1] J. G. Breman and I. Arita. The confirmation and maintenance of smallpox eradication. *New England Journal of Medicine*, 303(22):1263–1273, 1980.

[2] A. D. Cliff, P. Haggett, J. K. Ord, and G. R. Versey. *Spatial diffusion: an historical geography of epidemics in an island community.* Cambridge University Press, 1981.

[3] David J.D. Earn, P. Rohani, B. M. Bolker, and B. T. Grenfell. A simple model for complex dynamical transitions in epidemics. *Science*, 287:667–670, 2000.

[4] O. Diekmann, H. Heesterbeek, and T. Britton. *Mathematical tools for understanding infectious disease dynamics.* Princeton University Press, 2012.

[5] N. M. Ferguson, M. J. Keeling, W. J. Edmunds, R. Gani, B. T. Grenfell, R. M. Anderson, and S. Leach. Planning for smallpox outbreaks. *Nature*, 425:681–685, 2003.

[6] N. C. Grassly and C. Fraser. Mathematical models of infectious disease transmission. *Nature Reviews Microbiology*, 6(6):477–487, 2008.

[7] B. T. Grenfell, O. N. Bjørnstad, and J. Kappey. Travelling waves and spatial hierarchies in measles epidemics. *Nature*, 414(6865):716–723, 2001.

[8] H. W. Hethcote and J. A. Yorke. *Gonorrhea transmission dynamics and control*, volume 56 of *Lecture Notes in Biomathematics.* Springer-Verlag, 1984.

[9] J. Koopman. Modeling infection transmission. *Annual Review of Public Health*, 25:303–326, 2004.

[10] J. O. Lloyd-Smith, S. J. Schreiber, P. E. Kopp, and W. M. Getz. Superspreading and the effect of individual variation on disease emergence. *Nature*, 438:355–359, 2005.

[11] J. Medlock and A. P. Galvani. Optimizing influenza vaccine distribution. *Science*, 325(5948):1705–1708, 2009.

[12] L. A. Meyers, B. Pourbohloul, M. E. Newman, D. M. Skowronski, and R. C. Brunham. Network theory and SARS: predicting outbreak diversity. *Journal of Theoretical Biology*, 232:71–81, 2005.

[13] V. Pitzer, C. Viboud, L. Simonsen, C. Steiner, C. Panozzo, W. Alonso, M. Miller, R. Glass, J. Glasser, U. Parashar, and B. Grenfell. Demographic variability, vaccination, and the spatiotemporal dynamics of rotavirus epidemics. *Science*, 325(5938):290–294, 2009.

[14] Y. Xia, O. N. Bjornstad, and B. T. Grenfell. Measles metapopulation dynamics: a gravity model for pre-vaccination epidemiological coupling and dynamics. *American Naturalist*, 164:267–281, 2004.

[15] J. A. Yorke, N. Nathanson, G. Pianigiani, and J. Martin. Seasonality and the requirements for perpetuation and eradication of viruses in populations. *American Journal of Epidemiology*, 109(2):103–123, 1979.