International Institute for
Applied Systems Analysis
Schlossplatz 1
A-2361 Laxenburg, Austria

Tel: +43 2236 807 342
Fax: +43 2236 71313
E-mail: publications@iiasa.ac.at
Web: www.iiasa.ac.at

Interim Report **IR-05-080**

Evolution towards Multi-Year Periodicity in Epidemics

Masashi Kamo (kamo@bio-math.biology.kyushu-u.ac.jp)
Akira Sasaki (asasascb@mbox.nc.kyushu-u.ac.jp)

Approved by

Ulf Dieckmann
Program Leader, ADN

December 2005

IIASA STUDIES IN ADAPTIVE DYNAMICS NO. 112

The Adaptive Dynamics Network at IIASA fosters the development of new mathematical and conceptual techniques for understanding the evolution of complex adaptive systems.

Focusing on these long-term implications of adaptive processes in systems of limited growth, the Adaptive Dynamics Network brings together scientists and institutions from around the world with IIASA acting as the central node.

Scientific progress within the network is collected in the IIASA Studies in Adaptive Dynamics series.

No. 1 Metz JAJ, Geritz SAH, Meszéna G, Jacobs FJA, van Heerwaarden JS: *Adaptive Dynamics: A Geometrical Study of the Consequences of Nearly Faithful Reproduction.* IIASA Working Paper WP-95-099 (1995). van Strien SJ, Verduyn Lunel SM (eds): Stochastic and Spatial Structures of Dynamical Systems, Proceedings of the Royal Dutch Academy of Science (KNAW Verhandelingen), North Holland, Amsterdam, pp. 183-231 (1996).

No. 2 Dieckmann U, Law R: *The Dynamical Theory of Coevolution: A Derivation from Stochastic Ecological Processes.* IIASA Working Paper WP-96-001 (1996). Journal of Mathematical Biology 34:579-612 (1996).

No. 3 Dieckmann U, Marrow P, Law R: *Evolutionary Cycling of Predator-Prey Interactions: Population Dynamics and the Red Queen.* IIASA Preprint (1995). Journal of Theoretical Biology 176:91-102 (1995).

No. 4 Marrow P, Dieckmann U, Law R: *Evolutionary Dynamics of Predator-Prey Systems: An Ecological Perspective.* IIASA Working Paper WP-96-002 (1996). Journal of Mathematical Biology 34:556-578 (1996).

No. 5 Law R, Marrow P, Dieckmann U: *On Evolution under Asymmetric Competition.* IIASA Working Paper WP-96-003 (1996). Evolutionary Ecology 11:485-501 (1997).

No. 6 Metz JAJ, Mylius SD, Diekmann O: *When Does Evolution Optimize? On the Relation Between Types of Density Dependence and Evolutionarily Stable Life History Parameters.* IIASA Working Paper WP-96-004 (1996).

No. 7 Ferrière R, Gatto M: *Lyapunov Exponents and the Mathematics of Invasion in Oscillatory or Chaotic Populations.* Theoretical Population Biology 48:126-171 (1995).

No. 8 Ferrière R, Fox GA: *Chaos and Evolution.* IIASA Preprint (1996). Trends in Ecology and Evolution 10:480-485 (1995).

No. 9 Ferrière R, Michod RE: *The Evolution of Cooperation in Spatially Heterogeneous Populations.* IIASA Working Paper WP-96-029 (1996). The American Naturalist 147:692-717 (1996).

No. 10 van Dooren TJM, Metz JAJ: *Delayed Maturation in Temporally Structured Populations with Non-Equilibrium Dynamics.* IIASA Working Paper WP-96-070 (1996). Journal of Evolutionary Biology 11:41-62 (1998).

No. 11 Geritz SAH, Metz JAJ, Kisdi É, Meszéna G: *The Dynamics of Adaptation and Evolutionary Branching.* IIASA Working Paper WP-96-077 (1996). Physical Review Letters 78:2024-2027 (1997).

No. 12 Geritz SAH, Kisdi É, Meszéna G, Metz JAJ: *Evolutionary Singular Strategies and the Adaptive Growth and Branching of the Evolutionary Tree.* IIASA Working Paper WP-96-114 (1996). Evolutionary Ecology 12:35-57 (1998).

No. 13 Heino M, Metz JAJ, Kaitala V: *Evolution of Mixed Maturation Strategies in Semelparous Life-Histories: The Crucial Role of Dimensionality of Feedback Environment.* IIASA Working Paper WP-96-126 (1996). Philosophical Transactions of the Royal Society of London Series B 352:1647-1655 (1997).

No. 14 Dieckmann U: *Can Adaptive Dynamics Invade?* IIASA Working Paper WP-96-152 (1996). Trends in Ecology and Evolution 12:128-131 (1997).

No. 15 Meszéna G, Czibula I, Geritz SAH: *Adaptive Dynamics in a 2-Patch Environment: A Simple Model for Allopatric and Parapatric Speciation.* IIASA Interim Report IR-97-001 (1997). Journal of Biological Systems 5:265-284 (1997).

No. 16 Heino M, Metz JAJ, Kaitala V: *The Enigma of Frequency-Dependent Selection.* IIASA Interim Report IR-97-061 (1997). Trends in Ecology and Evolution 13:367-370 (1998).

No. 17 Heino M: *Management of Evolving Fish Stocks.* IIASA Interim Report IR-97-062 (1997). Canadian Journal of Fisheries and Aquatic Sciences 55:1971-1982 (1998).

No. 18 Heino M: *Evolution of Mixed Reproductive Strategies in Simple Life-History Models.* IIASA Interim Report IR-97-063 (1997).

No. 19 Geritz SAH, van der Meijden E, Metz JAJ: *Evolutionary Dynamics of Seed Size and Seedling Competitive Ability.* IIASA Interim Report IR-97-071 (1997). Theoretical Population Biology 55:324-343 (1999).

No. 20 Galis F, Metz JAJ: *Why Are There So Many Cichlid Species? On the Interplay of Speciation and Adaptive Radiation.* IIASA Interim Report IR-97-072 (1997). Trends in Ecology and Evolution 13:1-2 (1998).

No. 21 Boerlijst MC, Nowak MA, Sigmund K: *Equal Pay for all Prisoners/ The Logic of Contrition.* IIASA Interim Report IR-97-073 (1997). American Mathematical Society Monthly 104:303-307 (1997). Journal of Theoretical Biology 185:281-293 (1997).

No. 22 Law R, Dieckmann U: *Symbiosis Without Mutualism and the Merger of Lineages in Evolution.* IIASA Interim Report IR-97-074 (1997). Proceedings of the Royal Society of London Series B 265:1245-1253 (1998).

No. 23 Klinkhamer PGL, de Jong TJ, Metz JAJ: *Sex and Size in Cosexual Plants.* IIASA Interim Report IR-97-078 (1997). Trends in Ecology and Evolution 12:260-265 (1997).

No. 24 Fontana W, Schuster P: *Shaping Space: The Possible and the Attainable in RNA Genotype-Phenotype Mapping.* IIASA Interim Report IR-98-004 (1998). Journal of Theoretical Biology 194:491-515 (1998).

No. 25 Kisdi É, Geritz SAH: *Adaptive Dynamics in Allele Space: Evolution of Genetic Polymorphism by Small Mutations in a Heterogeneous Environment.* IIASA Interim Report IR-98-038 (1998). Evolution 53:993-1008 (1999).

No. 26 Fontana W, Schuster P: *Continuity in Evolution: On the Nature of Transitions.* IIASA Interim Report IR-98-039 (1998). Science 280:1451-1455 (1998).

No. 27 Nowak MA, Sigmund K: *Evolution of Indirect Reciprocity by Image Scoring/ The Dynamics of Indirect Reciprocity.* IIASA Interim Report IR-98-040 (1998). Nature 393:573-577 (1998). Journal of Theoretical Biology 194:561-574 (1998).

No. 28 Kisdi É: *Evolutionary Branching Under Asymmetric Competition.* IIASA Interim Report IR-98-045 (1998). Journal of Theoretical Biology 197:149-162 (1999).

No. 29 Berger U: *Best Response Adaptation for Role Games.* IIASA Interim Report IR-98-086 (1998).

No. 30 van Dooren TJM: *The Evolutionary Ecology of Dominance-Recessivity.* IIASA Interim Report IR-98-096 (1998). Journal of Theoretical Biology 198:519-532 (1999).

No. 31 Dieckmann U, O'Hara B, Weisser W: *The Evolutionary Ecology of Dispersal.* IIASA Interim Report IR-98-108 (1998). Trends in Ecology and Evolution 14:88-90 (1999).

No. 32 Sigmund K: *Complex Adaptive Systems and the Evolution of Reciprocation.* IIASA Interim Report IR-98-100 (1998). Ecosystems 1:444-448 (1998).

No. 33 Posch M, Pichler A, Sigmund K: *The Efficiency of Adapting Aspiration Levels.* IIASA Interim Report IR-98-103 (1998). Proceedings of the Royal Society London Series B 266:1427-1435 (1999).

No. 34 Mathias A, Kisdi É: *Evolutionary Branching and Coexistence of Germination Strategies.* IIASA Interim Report IR-99-014 (1999).

No. 35 Dieckmann U, Doebeli M: *On the Origin of Species by Sympatric Speciation.* IIASA Interim Report IR-99-013 (1999). Nature 400:354-357 (1999).

No. 36 Metz JAJ, Gyllenberg M: *How Should We Define Fitness in Structured Metapopulation Models? Including an Application to the Calculation of Evolutionarily Stable Dispersal Strategies.* IIASA Interim Report IR-99-019 (1999). Proceedings of the Royal Society of London Series B 268:499-508 (2001).

No. 37 Gyllenberg M, Metz JAJ: *On Fitness in Structured Metapopulations.* IIASA Interim Report IR-99-037 (1999). Journal of Mathematical Biology 43:545-560 (2001).

No. 38 Meszéna G, Metz JAJ: *Species Diversity and Population Regulation: The Importance of Environmental Feedback Dimensionality.* IIASA Interim Report IR-99-045 (1999).

No. 39 Kisdi É, Geritz SAH: *Evolutionary Branching and Sympatric Speciation in Diploid Populations.* IIASA Interim Report IR-99-048 (1999).

No. 40 Ylikarjula J, Heino M, Dieckmann U: *Ecology and Adaptation of Stunted Growth in Fish.* IIASA Interim Report IR-99-050 (1999). Evolutionary Ecology 13:433-453 (1999).

No. 41 Nowak MA, Sigmund K: *Games on Grids.* IIASA Interim Report IR-99-038 (1999). Dieckmann U, Law R, Metz JAJ (eds): The Geometry of Ecological Interactions: Simplifying Spatial Complexity, Cambridge University Press, Cambridge, UK, pp. 135-150 (2000).

No. 42 Ferrière R, Michod RE: *Wave Patterns in Spatial Games and the Evolution of Cooperation.* IIASA Interim Report IR-99-041 (1999). Dieckmann U, Law R, Metz JAJ (eds): The Geometry of Ecological Interactions: Simplifying Spatial Complexity, Cambridge University Press, Cambridge, UK, pp. 318-332 (2000).

No. 43 Kisdi É, Jacobs FJA, Geritz SAH: *Red Queen Evolution by Cycles of Evolutionary Branching and Extinction.* IIASA Interim Report IR-00-030 (2000). Selection 2:161-176 (2001).

No. 44 Meszéna G, Kisdi É, Dieckmann U, Geritz SAH, Metz JAJ: *Evolutionary Optimisation Models and Matrix Games in the Unified Perspective of Adaptive Dynamics.* IIASA Interim Report IR-00-039 (2000). Selection 2:193-210 (2001).

No. 45 Parvinen K, Dieckmann U, Gyllenberg M, Metz JAJ: *Evolution of Dispersal in Metapopulations with Local Density Dependence and Demographic Stochasticity.* IIASA Interim Report IR-00-035 (2000). Journal of Evolutionary Biology 16:143-153 (2003).

No. 46 Doebeli M, Dieckmann U: *Evolutionary Branching and Sympatric Speciation Caused by Different Types of Ecological Interactions.* IIASA Interim Report IR-00-040 (2000). The American Naturalist 156:S77-S101 (2000).

No. 47 Heino M, Hanski I: *Evolution of Migration Rate in a Spatially Realistic Metapopulation Model.* IIASA Interim Report IR-00-044 (2000). The American Naturalist 157:495-511 (2001).

No. 48 Gyllenberg M, Parvinen K, Dieckmann U: *Evolutionary Suicide and Evolution of Dispersal in Structured Metapopulations.* IIASA Interim Report IR-00-056 (2000). Journal of Mathematical Biology 45:79-105 (2002).

No. 49 van Dooren TJM: *The Evolutionary Dynamics of Direct Phenotypic Overdominance: Emergence Possible, Loss Probable.* IIASA Interim Report IR-00-048 (2000). Evolution 54:1899-1914 (2000).

No. 50 Nowak MA, Page KM, Sigmund K: *Fairness Versus Reason in the Ultimatum Game.* IIASA Interim Report IR-00-57 (2000). Science 289:1773-1775 (2000).

No. 51 de Feo O, Ferrière R: *Bifurcation Analysis of Population Invasion: On-Off Intermittency and Basin Riddling.* IIASA Interim Report IR-00-074 (2000). International Journal of Bifurcation and Chaos 10:443-452 (2000).

No. 52 Heino M, Laaka-Lindberg S: *Clonal Dynamics and Evolution of Dormancy in the Leafy Hepatic Lophozia Silvicola.* IIASA Interim Report IR-01-018 (2001). Oikos 94:525-532 (2001).

No. 53 Sigmund K, Hauert C, Nowak MA: *Reward and Punishment in Minigames.* IIASA Interim Report IR-01-031 (2001). Proceedings of the National Academy of Sciences of the USA 98:10757-10762 (2001).

No. 54 Hauert C, De Monte S, Sigmund K, Hofbauer J: *Oscillations in Optional Public Good Games.* IIASA Interim Report IR-01-036 (2001).

No. 55 Ferrière R, Le Galliard J: *Invasion Fitness and Adaptive Dynamics in Spatial Population Models.* IIASA Interim Report IR-01-043 (2001). Clobert J, Dhondt A, Danchin E, Nichols J (eds): Dispersal, Oxford University Press, pp. 57-79 (2001).

No. 56 de Mazancourt C, Loreau M, Dieckmann U: *Can the Evolution of Plant Defense Lead to Plant-Herbivore Mutualism.* IIASA Interim Report IR-01-053 (2001). The American Naturalist 158:109-123 (2001).

No. 57 Claessen D, Dieckmann U: *Ontogenetic Niche Shifts and Evolutionary Branching in Size-Structured Populations.* IIASA Interim Report IR-01-056 (2001). Evolutionary Ecology Research 4:189-217 (2002).

No. 58 Brandt H: *Correlation Analysis of Fitness Landscapes.* IIASA Interim Report IR-01-058 (2001).

No. 59 Dieckmann U: *Adaptive Dynamics of Pathogen-Host Interacations.* IIASA Interim Report IR-02-007 (2002). Dieckmann U, Metz JAJ, Sabelis MW, Sigmund K (eds): Adaptive Dynamics of Infectious Diseases: In Pursuit of Virulence Management, Cambridge University Press, Cambridge, UK, pp. 39-59 (2002).

No. 60 Nowak MA, Sigmund K: *Super- and Coinfection: The Two Extremes.* IIASA Interim Report IR-02-008 (2002). Dieckmann U, Metz JAJ, Sabelis MW, Sigmund K (eds): Adaptive Dynamics of Infectious Diseases: In Pursuit of Virulence Management, Cambridge University Press, Cambridge, UK, pp. 124-137 (2002).

No. 61 Sabelis MW, Metz JAJ: *Taking Stock: Relating Theory to Experiment.* IIASA Interim Report IR-02-009 (2002). Dieckmann U, Metz JAJ, Sabelis MW, Sigmund K (eds): Adaptive Dynamics of Infectious Diseases: In Pursuit of Virulence Management, Cambridge University Press, Cambridge, UK, pp. 379-398 (2002).

No. 62 Cheptou P, Dieckmann U: *The Evolution of Self-Fertilization in Density-Regulated Populations* . IIASA Interim Report IR-02-024 (2002). Proceedings of the Royal Society of London Series B 269:1177-1186 (2002).

No. 63 Bürger R: *Additive Genetic Variation Under Intraspecific Competition and Stabilizing Selection: A Two-Locus Study.* IIASA Interim Report IR-02-013 (2002). Theoretical Population Biology 61:197-213 (2002).

No. 64 Hauert C, De Monte S, Hofbauer J, Sigmund K: *Volunteering as Red Queen Mechanism for Co-operation in Public Goods Games.* IIASA Interim Report IR-02-041 (2002). Science 296:1129-1132 (2002).

No. 65 Dercole F, Ferrière R, Rinaldi S: *Ecological Bistability and Evolutionary Reversals under Asymmetrical Competition.* IIASA Interim Report IR-02-053 (2002). Evolution 56:1081-1090 (2002).

No. 66 Dercole F, Rinaldi S: *Evolution of Cannibalistic Traits: Scenarios Derived from Adaptive Dynamics.* IIASA Interim Report IR-02-054 (2002). Theoretical Population Biology 62:365-374 (2002).

No. 67 Bürger R, Gimelfarb A: *Fluctuating Environments and the Role of Mutation in Maintaining Quantitative Genetic Variation.* IIASA Interim Report IR-02-058 (2002). Genetical Research 80:31-46 (2002).

No. 68 Bürger R: *On a Genetic Model of Intraspecific Competition and Stabilizing Selection.* IIASA Interim Report IR-02-062 (2002). Amer. Natur. 160:661-682 (2002).

No. 69 Doebeli M, Dieckmann U: *Speciation Along Environmental Gradients.* IIASA Interim Report IR-02-079 (2002). Nature 421:259-264 (2003).

No. 70 Dercole F, Irisson J, Rinaldi S: *Bifurcation Analysis of a Prey-Predator Coevolution Model.* IIASA Interim Report IR-02-078 (2002). SIAM Journal on Applied Mathematics 63:1378-1391 (2003).

No. 71 Le Galliard J, Ferrière R, Dieckmann U: *The Adaptive Dynamics of Altruism in Spatially Heterogeneous Populations.* IIASA Interim Report IR-03-006 (2003). Evolution 57:1-17 (2003).

No. 72 Taborsky B, Dieckmann U, Heino M: *Unexpected Discontinuities in Life-History Evolution under Size-Dependent Mortality.* IIASA Interim Report IR-03-004 (2003). Proceedings of the Royal Society of London Series B 270:713-721 (2003).

No. 73 Gardmark A, Dieckmann U, Lundberg P: *Life-History Evolution in Harvested Populations: The Role of Natural Predation.* IIASA Interim Report IR-03-008 (2003). Evolutionary Ecology Research 5:239-257 (2003).

No. 74 Mizera F, Meszéna G: *Spatial Niche Packing, Character Displacement and Adaptive Speciation Along an Environmental Gradient.* IIASA Interim Report IR-03-062 (2003). Evolutionary Ecology Research 5:363-382 (2003).

No. 75 Dercole F: *Remarks on Branching-Extinction Evolutionary Cycles.* IIASA Interim Report IR-03-077 (2003). Journal of Mathematical Biology 47:569-580 (2003).

No. 76 Hofbauer J, Sigmund K: *Evolutionary Game Dynamics.* IIASA Interim Report IR-03-078 (2003). Bulletin of the American Mathematical Society 40:479-519 (2003).

No. 77 Ernande B, Dieckmann U, Heino M: *Adaptive Changes in Harvested Populations: Plasticity and Evolution of Age and Size at Maturation.* IIASA Interim Report IR-03-058 (2003). Proceedings of the Royal Society of London Series B-Biological Sciences 271:415-423 (2004).

No. 78 Hanski I, Heino M: *Metapopulation-Level Adaptation of Insect Host Plant Preference and Extinction-Colonization Dynamics in Heterogeneous Landscapes.* IIASA Interim Report IR-03-028 (2003). Theoretical Population Biology 63:309-338 (2003).

No. 79 van Doorn G, Dieckmann U, Weissing FJ: *Sympatric Speciation by Sexual Selection: A Critical Re-Evaluation.* IIASA Interim Report IR-04-003 (2004). American Naturalist 163:709-725 (2004).

No. 80 Egas M, Dieckmann U, Sabelis MW: *Evolution Restricts the Coexistence of Specialists and Generalists - the Role of Trade-off Structure.* IIASA Interim Report IR-04-004 (2004). American Naturalist 163:518-531 (2004).

No. 81 Ernande B, Dieckmann U: *The Evolution of Phenotypic Plasticity in Spatially Structured Environments: Implications of Intraspecific Competition, Plasticity Costs, and Environmental Characteristics.* IIASA Interim Report IR-04-006 (2004). Journal of Evolutionary Biology 17:613-628 (2004).

No. 82 Cressman R, Hofbauer J: *Measure Dynamics on a One-Dimensional Continuous Trait Space: Theoretical Foundations for Adaptive Dynamics.* IIASA Interim Report IR-04-016 (2004).

No. 83 Cressman R: *Dynamic Stability of the Replicator Equation with Continuous Strategy Space.* IIASA Interim Report IR-04-017 (2004).

No. 84 Ravigné V, Olivieri I, Dieckmann U: *Implications of Habitat Choice for Protected Polymorphisms.* IIASA Interim Report IR-04-005 (2004). Evolutionary Ecology Research 6:125-145 (2004).

No. 85 Nowak MA, Sigmund K: *Evolutionary Dynamics of Biological Games.* IIASA Interim Report IR-04-013 (2004). Science 303:793-799 (2004).

No. 86 Vukics A, Asbóth J, Meszéna G: *Speciation in Multidimensional Evolutionary Space.* IIASA Interim Report IR-04-028 (2004). Physical Review 68:041-903 (2003).

No. 87 de Mazancourt C, Dieckmann U: *Trade-off Geometries and Frequency-dependent Selection.* IIASA Interim Report IR-04-039 (2004). American Naturalist 164:765-778 (2004).

No. 88 Cadet CR, Metz JAJ, Klinkhamer PGL: *Size and the Not-So-Single Sex: disentangling the effects of size on sex allocation.* IIASA Interim Report IR-04-084 (2004). American Naturalist 164:779-792 (2004).

No. 89 Rueffler C, van Dooren TJM, Metz JAJ: *Adaptive Walks on Changing Landscapes: Levins' Approach Extended.* IIASA Interim Report IR-04-083 (2004). Theoretical Population Biology 65:165-178 (2004).

No. 90 de Mazancourt C, Loreau M, Dieckmann U: *Understanding Mutualism When There is Adaptation to the Partner.* IIASA Interim Report IR-05-016 (2005). Journal of Ecology 93:305-314 (2005).

No. 91 Dieckmann U, Doebeli M: *Pluralism in Evolutionary Theory.* IIASA Interim Report IR-05-017 (2005). Journal of Evolutionary Biology 18:1209-1213 (2005).

No. 92 Doebeli M, Dieckmann U, Metz JAJ, Tautz D: *What We Have Also Learned.* IIASA Interim Report IR-05-018 (2005). Evolution 59:691-695 (2005).

No. 93 Egas M, Sabelis MW, Dieckmann U: *Evolution of Specialization and Ecological Character Displacement of Herbivores Along a Gradient of Plant Quality.* IIASA Interim Report IR-05-019 (2005). Evolution 59:507-520 (2005).

No. 94 Le Galliard J, Ferrière R, Dieckmann U: *Adaptive Evolution of Social Traits: Origin, Trajectories, and Correlations of Altruism and Mobility.* IIASA Interim Report IR-05-020 (2005). American Naturalist 165:206-224 (2005).

No. 95 Doebeli M, Dieckmann U: *Adaptive Dynamics as a Mathematical Tool for Studying the Ecology of Speciation Processes.* IIASA Interim Report IR-05-022 (2005). Journal of Evolutionary Biology 18:1194-1200 (2005).

No. 96 Brandt H, Sigmund K: *The Logic of Reprobation: Assessment and Action Rules for Indirect Reciprocity.* IIASA Interim Report IR-04-085 (2004). Journal of Theoretical Biology 231:475-486 (2004).

No. 97 Hauert C, Haiden N, Sigmund K: *The Dynamics of Public Goods.* IIASA Interim Report IR-04-086 (2004). Discrete and Continuous Dynamical Systems - Series B 4:575-587 (2004).

No. 98 Meszéna G, Gyllenberg M, Jacobs FJA, Metz JAJ: *Link Between Population Dynamics and Dynamics of Darwinian Evolution.* IIASA Interim Report IR-05-026 (2005). Physical Review Letters 95:Article 078105 (2005).

No. 99 Meszéna G: *Adaptive Dynamics: The Continuity Argument.* IIASA Interim Report IR-05-032 (2005). Journal of Evolutionary Biology 18:1182-1185 (2005).

No. 100 Brännström NA, Dieckmann U: *Evolutionary Dynamics of Altruism and Cheating Among Social Amoebas.* IIASA Interim Report IR-05-039 (2005). Proceedings of the Royal Society London Series B 272:1609-1616 (2005).

No. 101 Meszéna G, Gyllenberg M, Pasztor L, Metz JAJ: *Competitive Exclusion and Limiting Similarity: A Unified Theory.* IIASA Interim Report IR-05-040 (2005).

No. 102 Szabo P, Meszéna G: *Limiting Similarity Revisited.* IIASA Interim Report IR-05-050 (2005).

No. 103 Krakauer DC, Sasaki A: *The Greater than Two-Fold Cost of Integration for Retroviruses.* IIASA Interim Report IR-05-069 (2005).

No. 104 Metz JAJ: *Eight Personal Rules for Doing Science.* IIASA Interim Report IR-05-069 (2005). Journal of Evolutionary Biology 18:1178-1181 (2005).

No. 105 Beltman JB, Metz JAJ: *Speciation: More Likely Through a Genetic or Through a Learned Habitat Preference?* IIASA Interim Report IR-05-072 (2005). Proceedings of the Royal Society of London Series B 272:1455-1463 (2005).

No. 106 Durinx M, Metz JAJ: *Multi-type Branching Processes and Adaptive Dynamics of Structured Populations.* IIASA Interim Report IR-05-065 (2005). Haccou P, Jager P, Vatutin V (eds): Branching Processes: Variation, Growth and Extinction of Populations, Cambridge University Press, Cambridge, UK, pp. 266-278 (2005).

No. 107 Brandt H, Sigmund K: *The Good, the Bad and the Discriminator - Errors in Direct and Indirect Reciprocity.* IIASA Interim Report IR-05-070 (2005).

No. 108 Brandt H, Sigmund K: *Punishing and Abstaining for Public Goods.* IIASA Interim Report IR-05-071 (2005).

No. 109 Ohtsuki A, Sasaki A: *Epidemiology and Disease-Control Under Gene-for-Gene Plant-Pathogen Interaction.* IIASA Interim Report IR-05-068 (2005).

No. 110 Brandt H, Sigmund K: *Indirect Reciprocity, Image-Scoring, and Moral Hazard.* IIASA Interim Report IR-05-078 (2005). Proceedings of the National Academy of Sciences of the United States of America 102:2666-2670 (2005).

No. 111 Nowak MA, Sigmund K: *Evolution of Indirect Reciprocity.* IIASA Interim Report IR-05-079 (2005). Nature 437:1292-1298 (2005).

No. 112 Kamo M, Sasaki A: *Evolution Towards Multi-Year Periodicity in Epidemics.* IIASA Interim Report IR-05-080 (2005). Ecology Letters 8:378-385 (2005).

Issues of the IIASA Studies in Adaptive Dynamics series can be obtained at www.iiasa.ac.at/Research/ADN/Series.html or by writing to adn@iiasa.ac.at.

Contents

Evolution towards multi-year periodicity in epidemics

Masashi Kamo* & Akira Sasaki

Department of Biology, Graduate School of Sciences, Kyushu University, Higashi-ku, Hakozaki 6-10-1, Fukuoka, Japan

***Corresponding Author:** Masashi Kamo

E-mails: kamo@bio-math10.biology.kyushu-u.ac.jp (Masashi Kamo)

asasascb@mbox.nc.kyushu-u.ac.jp (Akira Sasaki)

tel: +81-92-642-2642

fax: +81-92-642-2645

Number of words: 87 words in an abstract and approximately 4500 words in total.

Number of references: 30

Keywords: compartment model, seasonality, basic reproductive rate, evolution in a fluctuating environment

Abstract

We studied why many diseases has multi-year period in their epidemiological dynamics, whereas a main source of the fluctuation is a seasonality with period of one year. Previous studies using a compartment model succeeded to generate a multi-year epidemics when they have a large seasonal difference in a transmission rate. However, those studies have focused on the dynamical consequence of seasonal forcing in epidemiological dynamics and an adaptation of pathogens in the seasonal environment has been neglected. In this paper, we describe our study of the evolution of pathogen's sensitivity to seasonality and show that a larger fluctuation in the transmission rate can be favored in the life history evolution of pathogens, suggesting that multi-year periodicity may evolve by natural selection. Our result proposes a new aspect of the evolution of multi-year epidemics.

1 INTRODUCTION

Oscillations in demography and epidemiology have been a challenging issue in ecology for decades (Nisbet & Gurney 1982; Grenfell *et al.* 1995). Seasonal forcing and entrainment in nonlinear oscillatory dynamics is thought to play a key role in the multi-year periodicity in epidemics (Hethcote & York 1984; Rand & Wilson 1991; Bolker & Grenfell 1993; Kamo & Sasaki 2002; Greenman *et al.* 2004). Seasonal forcing is also thought to be important in resetting phases in ecological oscillations. For example, a common environmental fluctuation can synchronize chaotic nonlinear dynamics of isolated wild sheep populations (Grenfell *et al.* 1998).

Various factors bring seasonality into epidemiological dynamics, and different strains of pathogens may respond differently to seasonality. Cholera epidemics in a large geographical scale synchronize with El Niño event (Pascual *et al.* 2000), and at a smaller geographical scale synchronize with monsoon season at each locality (Pascual *et al.* 2002). When the classical biotype of *Vibrio cholerae* is replaced by the El Tor biotype in Bengal (Colwell 1996), seasonal patterns in cholera epidemic have been changed as well (Pascual *et al.* 2002), suggesting that the two strains had different characteristics related to seasonality. Among two malaria strains, *Plasmodium vivax* and

P. falcipaum, P. falcipaum is known to show less seasonality in epidemics than *P. vivax* (Abeku *et al.* 2002). Meningococcal infection to the mucous membranes occurs more easily in dry air condition, and the meningococcal epidemics in Sub-Saharan Africa starts with the dry season and ends with the beginning of the wet season. However, in Oregon, the number of meningococcal disease cases is peaked in the middle of rainy season, suggesting that meningococcus in Africa and Oregon has adapted differently to dry/wet climatic cycles (see a review article by Dowell (2001) and the papers therein).

These studies suggest that there would be pathogen strains that adapt differently to seasonality by changing their response to environmental fluctuation. In this paper, we deal with the adaptive evolution of pathogen trait that affects the sensitivity of pathogen's transmission rate to seasonal fluctuation of environment. We theoretically derive the conditions for a seasonal specialist which has a large fluctuation in its transmission process to be selected for over a seasonal generalist which has less fluctuation in the transmission rate (and *vice versa*). As the sensitivity to seasonal environment in transmission rate greatly affects the dynamical behavior (and multiyear periodicity, in particular) of epidemics, our model also explores an evolutionary reason why many epidemiological dynamics have multiyear periodicity (Anderson & May 1983 1991).

To study the effect of seasonal forcing in epidemiological dynamics, an external seasonal fluctuation in transmission rate has been introduced in the conventional compartment model with susceptible, (exposed), infected, and recovered (S(E)IR) classes in a host population (Hethcote & York 1984; Rand & Wilson 1991; Bolker & Grenfell 1993; Kamo & Sasaki 2002). Studies of a seasonally forced S(E)IR model have revealed how the annual cycle in the number of infected hosts for weak enough seasonal forcing shows a cascade of bifurcations towards subharmonics (cycles with multi-year periods) and finally towards chaos as the seasonality becomes large (Schwartz & Smith 1983; Aron & Schwartz 1984; Schwartz 1985; Keeling & Grenfell 1997; Keeling *et al.* 2001; Rohani *et al.* 2002; Greenman *et al.* 2004). Most studies of seasonally forced epidemiological models have focused on how their dynamical behaviors depend on parameters (e.g., Sugihara *et al.* 1990). However, little attention has been paid to how the life history evolution of pathogen affects the periodicity, which is the focus in this paper.

Multi-year periodicity in childhood diseases is widely observed in many cities of greatly different climatic and demographic conditions (e.g., temperature, humidity and birth/death rates) (Anderson & May 1983; Earn *et al.* 2000). In this paper, we explore a hypothesis that a longer period in epidemiological oscillation might be realized as a consequence of life history evolution in pathogens. More specifically, we deal with the evolution of sensitivity (or tolerance) to seasonally fluctuating environment and examine how the evolution of epidemiological parameters changes dynamical behavior. This is an attempt to extend previous studies on the interplay between evolution of life history parameters and its consequence in dynamical behavior (e.g., Rand *et al.* 1995; Haraguchi & Sasaki 2000; Doebeli & Koella 1995; Ferrière & Gatto 1993) into seasonal fluctuating environments.

According to bifurcation analysis (Schwartz & Smith 1983), a longer period in epidemics is associated with a larger seasonal fluctuation in transmission rate. We consider two strains of pathogens that have seasonally varying transmission rates with the same mean but different variance. One of the strains has a larger amplitude in transmission rate, hence it is more likely to cause a longer epidemic period. The difference in transmission rates is implemented by introducing a different sensitivity to seasonal fluctuation. The strain having a larger sensitivity has a higher transmission rate than that of the other in an epidemic season, but it has a lower transmission rate in the off season. If there is a tendency for a larger sensitivity (i.e., a larger amplitude in transmission rate) to be preferred in pathogen evolution, multi-year epidemic period appears as a consequence. In this paper, we ask which amount of sensitivity is evolutionarily stable, and where does the sensitivity parameter fall in the bifurcation diagram.

2 MODEL

We consider a simple epidemiological model called the SIS model with a seasonally varying transmission rate, in which there is no acquired immunity. Extensions to the SIR model with acquired immunity are discussed later. In the SIS model, a susceptible host (S) may be infected (I) at transmission rate β. The infected host suffers an additional mortality α and may recover and become

susceptible again at rate γ. Denoting the birth rate of host by r and its natural mortality by μ, the densities of susceptible and infected hosts change in time as

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI + \gamma I - \mu S + rS, \\ \frac{dI}{dt} &= \beta SI - (\gamma + \mu + \alpha)I. \end{aligned} \tag{1}$$

We assume an infinite population and the following arguments are free from population extinction and fade-out. We assume that the transmission rate varies seasonally as

$$\beta = \beta_0(1 + \delta P(t)), \tag{2}$$

where β_0 is the base infection rate, and $P(t)$ denotes the environmental fluctuation with mean 0 and a period of one year (i.e., seasonality). Note that δ represents the sensitivity to the seasonal fluctuation ($P(t)$). Though seasonal fluctuation is common to all the strains, pathogen strains would have different amplitudes of fluctuation in transmission rate by having different sensitivities (δ) to the seasonal environment. Throughout this paper, we assume that the sensitivity δ is a trait of the pathogen not rather than of the host. This is simply because we focus on the evolution of the pathogen. In reality, seasonal fluctuation in transmission rate is largely affected by host density varying by school/holiday terms; however, these factors are embedded in $P(t)$ in our model.

When there is no seasonal variation in transmission rate ($\delta = 0$), there are two equilibria (trivial and endemic) of Eq. (1). With the assumption that the birth rate of host is greater than its natural mortality ($r > \mu$) and with a nonzero recovery rate ($\gamma > 0$), the trivial equilibrium ($S = I = 0$) is always unstable and the endemic equilibrium

$$(S^*, I^*) = \left(\frac{\mu + \alpha + \gamma}{\beta}, \frac{(r - \mu)(\mu + \alpha + \gamma)}{(\mu + \alpha)\beta} \right)$$

is stable.

As reported previously (Schwartz & Smith 1983; Rand & Wilson 1991; Kamo & Sasaki 2002; Greenman *et al.* 2004), such seasonally forced epidemiological models show a cascade of bifurcations

as δ is increased. Figure 1 illustrates a bifurcation diagram.

2.1 Invasion in a seasonally fluctuating environment

We first examine the condition for the invasibility of a mutant pathogen strain in a host population where a resident strain circulates and is stably maintained in a seasonally fluctuating environment. We denote by $\bar{\beta}_i$, δ_i, γ_i, and α_i the base transmission rate, the sensitivity in transmission rate, the recovery rates, and the virulence of strain i, respectively. Let us assume that the density I_1 of the resident strain is on a stable periodic attractor. When the density I_2 of a mutant strain is rare, it follows that

$$\frac{dI_2}{dt} = I_2 \left[\hat{S}^1(t)\beta_2(t) - (\gamma_2 + \alpha_2 + \mu) \right],$$

where $\beta_2(t) \left(= \bar{\beta}_2(1 + \delta_2 P(t))\right), \gamma_2$ and α_2 are the transmission rate, the recovery rate and the virulence of the mutant strain, respectively. $\hat{S}^1(t)$ denotes the density of susceptible hosts on the stable periodic attractor with the resident strain.

The mutant strain can invade if its marginal logarithmic growth rate, $\rho(2|1)$, is positive(Chesson & Ellner 1989), as follows

$$\rho(2|1) = \left\langle \frac{d}{dt} \log I_2 \right\rangle = \left\langle \hat{S}^1(t)\beta_2(t) \right\rangle - (\gamma_2 + \alpha_2 + \mu) > 0, \tag{3}$$

where $\langle x \rangle$ denotes the long-term average of x. We note that from the stationarity condition,

$$\rho(1|1) = \langle \frac{d}{dt} \log I_1 \rangle = \left\langle \hat{S}^1(t)\beta_1(t) \right\rangle - (\gamma_1 + \alpha_1 + \mu) = 0 \tag{4}$$

must be satisfied. Then, we have,

$$\left\langle \hat{S}^1(t)(1 + \delta_1 P(t)) \right\rangle = \frac{(\gamma_1 + \alpha_1 + \mu)}{\bar{\beta}_1} = \frac{1}{B^{(1)}}, \tag{5}$$

where $B^{(1)} = \bar{\beta}_1/(\gamma_1 + \alpha_1 + \mu)$ is a per-host transmission factor (van Baalen & Sabelis 1995) and is equal to the basic reproductive ratio,R_0 (Anderson & May 1991), when the host densities are

scaled by total host density.

In the same way, Eq. (3) can be rewritten as

$$\left\langle \hat{S}^1(t)(1+\delta_2 P(t)) \right\rangle > \frac{1}{B^{(2)}}, \tag{6}$$

where $B^{(2)}$ is the basic reproductive ratio of strain 2, defined in the same way as $B^{(1)}$. If we combine Eqs. (4) and (6), we have an invasion condition in the general form,

$$\rho(2|1) = (\delta_2 - \delta_1)\left\langle \hat{S}^1(t)P(t) \right\rangle - \left(\frac{1}{B^{(2)}} - \frac{1}{B^{(1)}} \right) > 0. \tag{7}$$

This condition gives us two important pieces of information. One is that the difference in seasonality affects the invasibility of a mutant strain. More precisely, the sign of $\langle \hat{S}^1(t)P(t) \rangle$ determines whether a mutant strain with a greater degree of sensitivity can invade and replace the resident. The other is that if two strains have the same sensitivities ($\delta_1 = \delta_2$) or if there is no seasonal variation ($P(t) \equiv 0$), the conventional wisdom of evolutionary maximization of basic reproductive ratio remains true.

3 RESULT

3.1 Evolutionarily stable sensitivity

As shown in Eq. (7), the difference in δ, the sensitivity to seasonal environment, affects the invasibility of a mutant and hence affects the evolutionary outcome as well. In examining the effect of sensitivity on the evolution, we focus on the simplest case in which the strains differ only in their sensitivities, by assuming that the per-host transmission factor, are the same among strains. In other words, we concentrate only on the difference in the response of pathogens to a seasonally changing environment, by assuming that other life history parameters are equal.

If the strains differ only in sensitivity, the invasion condition (Eq. (7)) is simplified to be

$$\rho(2|1) = (\delta_2 - \delta_1) \left\langle \hat{S}^1(t) P(t) \right\rangle > 0. \tag{8}$$

If $\rho(2|1)$ is positive, the second strain can invade the population that is endemic with strain 1. Thus the sign of $\langle \hat{S}^1(t) P(t) \rangle$, the correlation between seasonal variation in transmission rate ($P(t)$) and the density of susceptible hosts ($\hat{S}^1(t)$), determines the invasibility of a mutant. This result is summarized as follows:

(i) if the susceptible host density and the transmission rate are positively correlated in the resident population, the strain showing more seasonal difference in transmission rate (i.e., larger δ) can invade the population;

(ii) conversely, if there is negative correlation, the strain showing a smaller seasonal difference can invade;

(iii) thus an evolutionarily stable sensitivity δ^* is the one at which the correlation between $S(t)$ and $P(t)$ vanishes.

Thus natural selection favors a pathogen with a greater seasonal specificity when the fluctuations in transmission rate and susceptible host density are, on average, in phase (positively correlated). In contrast, if they are out of phase on average (negatively correlated), a pathogen with a greater tolerance to seasonality is favored.

3.2 Numerical simulations for evolutionary dynamics

To confirm whether the sensitivity to seasonal variation evolves towards the predicted ESS in which the correlation between transmission rate and susceptible density vanishes, we conducted numerical simulations which allow many strains of pathogen, with their sensitivity parameters ($\delta_i' s$) equally divided between 0 and 1, to compete with each other in a given seasonal environment. We assume a sinusoidal form of seasonal environmental fluctuation: $P(t) = \sin 2\pi t$, where time is measured in

units of year. Figure 2a shows how the correlation $\langle \hat{S}^1(t) \sin 2\pi t \rangle$ between susceptible density and transmission rate varies as the sensitivity δ to seasonality of pathogen varies. In calculating the correlation as a function of δ, we assume that the pathogen is monomorphic in the δ.

We found that when the mean sensitivity is less than about 0.7, the epidemiological dynamics falls in the region of a one-year period attractor (see Fig. 1). In this region, the correlation between $P(t)$ and $S(t)$ is positive. When the sensitivity passes through the threshold for period-doubling bifurcation, the correlation suddenly drops and becomes negative. Since the evolutionarily stable sensitivity is the one when the correlation vanishes, evolution comes to a halt with the sensitivity at which the correlation changes its sign. Thus the evolution in δ brought the population to the region of a two-year period epidemic. The time change in the mean sensitivity in the pathogen population is plotted in Figure 2b, which shows that the sensitivity evolves, with temporal overshooting, towards the threshold at which the correlation between $P(t)$ and $S(t)$ vanishes (Fig. 2b).

3.3 Trade-off between sensitivity δ and mean transmissibility $\bar{\beta}$

To confirm the robustness of the result, we introduce a trade-off between the sensitivity parameter and the base transmission rate. We assume that the pathogen has to increase the specificity to seasonal variation at a cost of lower mean transmission rate. Specifically, we assume that $\beta(t)$ obeys

$$\beta(t) = \begin{cases} \beta_0(1 + \delta \sin 2\pi t) & \text{when } \sin 2\pi t \leq 0 \\ \beta_0(1 + \delta\Omega \sin 2\pi t) & \text{when } \sin 2\pi t > 0 \end{cases} \tag{9}$$

where Ω is a positive number smaller than 1. This modulation of the shape of fluctuation in β gives rise to a negative trade-off between the mean transmission rate $\bar{\beta}$ and sensitivity δ:

$$\bar{\beta}(\delta) = \beta_0 \left[1 - \delta \frac{(1 - \Omega)}{\pi} \right]. \tag{10}$$

Figure 3a shows the correlation between $\hat{S}(t)$ and $\beta(t)$ as a function of δ when there is a negative trade-off (Eq. (10)), and Fig. 3b shows the time change in the mean sensitivity when many strains with slightly different sensitivities compete with each other.

With this negative trade-off, the correlation between $S(t)$ and $P(t)$ is negative for both small and large δ, and positive for an intermediate range, thereby generating an evolutionary bistability. That is, there are two locally stable ES sensitivities (closed circles in Fig. 3a), and locally unstable one (open circle). The evolutionary outcome then depends on the initial condition.

If we switch the condition in Eq. 9, we have a positive trade-off. The result with the trade-off is almost the same as in Figure 2.

3.4 When does selection prefer a larger sensitivity?

We have so far shown that whenever there is a positive correlation between susceptible host density ($S(t)$) and seasonal variation ($P(t)$) in transmission rate, there is a selection for a larger sensitivity to seasonality in pathogen evolution. In this section, we ask under what condition the correlation becomes positive, by applying standard linear analysis of a weakly forced system (i.e., a system with a small δ). We also extend our analysis to include a broader range of compartment models: SIS models when infected hosts can also give birth, and SIS and SIR models with a fixed total population. The correlations between S and P for these models obtained by linear perturbation are listed in Table 1 (also see Appendix for a description of the models).

The analysis reveals that an adaptive evolution of sensitivity from zero to a larger value is impossible in the SIS model with a fixed total population. However, in the other models, there is a broad range of parameters in which the selection favors a positive sensitivity. In particular, in the SIR model with a fixed total population size, as long as we assume that the natural death rate (μ) of the host is much smaller than other parameters (as is the case in most human infectious diseases), the leading term of the correlation between $S(t)$ and $P(t)$ for small δ, when we denote

the transmission rate as $\beta(1+\delta P(t)) = \beta(1+\delta \sin 2\pi t)$, is

$$\langle S(t)P(t)\rangle = \frac{\mu\delta(\alpha+\gamma)(\beta-(\alpha+\gamma))}{8\beta\pi^2} + O(\mu^2). \tag{11}$$

Since we assume that $B = \beta/(\mu+\alpha+\gamma) \approx \beta/(\alpha+\gamma) > 1$, the leading term is always positive. This implies that, if the host is long lived and can have acquired immunity against a focal disease, there is always a selection for a larger sensitivity to seasonality, and hence selection favors a longer period in epidemics.

4 DISCUSSION

Fluctuations in epidemiological dynamics and the role of seasonality on the fluctuations have been widely studied both theoretically and empirically. The authors of previous studies have focused on drawing the bifurcation diagram and finding the parameter range within which the observed periodicity in the dynamics can be reproduced. By virtue of these studies, we know that a simple compartment model (SEIR or SIR) with a seasonally forced transmission rate can successfully explain the multi-year periodicity in childhood diseases (Earn *et al.* 2000). However, authors previously have discussed the evolution of pathogens' life history parameters and dynamical behavior of epidemics separately. In this paper, we intended to combine these two topics and derive a new evolutionary principle.

We showed that a greater sensitivity to seasonality is favored when the density of susceptible hosts, $S(t)$, and the seasonal variation in transmission rate, $P(t)$, are positively correlated. As this positive correlation is expected when the epidemic shows an annual cycle, there is a selection towards a larger sensitivity (a greater seasonal specificity), resulting in a longer period in epidemics. As shown in Fig. 2a, an evolutionary end point is the sensitivity at which the correlation changes its sign, which often brings a biennial cycle into the system. Of course, the biennial cycle is not always the evolutionary consequence; however, the most important result of our analysis is that the evolution towards a larger temporal variation in transmissibility occurs as long as the correlation is

positive, and hence there is a tendency to push the population towards period-doubling. We used the simple sinusoidal function for the seasonally varying transmission rate in this study. However, as is obvious from our formula for invasibility, even if we use a more general function form for seasonality including term-timing transmission rate, the sign of the correlation still determines the direction of the evolution.

In the literature about life history evolution in a changing environment (Levins 1968; Segar & Brockmann 1987), it is well known that a trait that causes a larger temporal fluctuation in fitness is selected against because it reduces the geometric mean fitness (the evolution of bet-hedging). This principle is derived from single species genetic dynamics with frequency-independent selection, and it has no guarantee for multi-species dynamics or with frequency dependence in selection. A literal application of this principle to the evolution of a pathogen's life history parameter in a seasonal environment suggests the evolution towards a reduced seasonality. However, as we have shown in this paper, the selection can favor a greater fluctuation in transmissibility in a seasonally changing environment, depending on the sign of the correlation mentioned above.

Our analysis here is largely based on a simple SIS model. To verify the reality of our invasion criteria, we adopt the SIR models. The bifurcation diagram of the SIR model becomes much more complex than that of the SIS (see, for example, Greenman *et al.* 2004). However, we can derive the same invasion criteria also in the SIR model very easily, indicating that the sign of a correlation between density of a susceptible host and seasonal variation in the transmission rate determines the direction of evolution. Figure 4 shows our preliminary analysis of the evolution of the sensitivity using the SIR model with a constant total population size (model 4 in the Appendix) with measles parameters. The bifurcation diagram is more complicated (Fig. 4a). Some attractors coexist with the same level of sensitivity (for example, period 1, 3 and 4 exist at δ=0.1) and each period has period-doubling bifurcation. However, if we know the correlation for each period (Fig. 4b), we can know the direction of evolution. With the measles parameters, evolution comes to a halt at $\delta = 1$ (Fig. 4c) and the period of host dynamics is 2 years (Fig. 4d).

To conclude, we have found a new agent for evolution of multi-year periodicity by introduc-

ing a new parameter: the sensitivity to the seasonally fluctuating environment. It is interesting to ask if the same logic may also provide an evolutionary explanation for the periodic demographic fluctuations in other biological systems like prey-predator and host-parasitoid dynamics.

5 ACKNOWLEDGMENT

We thank Drs. Jon Greenman, Yoh Iwasa and Hans Metz. MK has been supported by the Japan Society for the Promotion of Science.

APPENDIX

The full descriptions for models are in Table 1. $\dot{S}$ and $\dot{I}$ represent a time derivative of susceptible and infected hosts, respectively. Only endemic equilibria, (S^*, I^*), are shown.

(1) SIS model we used in this paper. See Eq. 1

(2) SIS model with reproduction both by infected and susceptible hosts.

$$\begin{aligned} \text{Dynamics:} \qquad \dot{S} &= r(S+I) - \beta SI + \gamma I - \mu S, \\ \dot{I} &= \beta SI - (\alpha + \gamma + \mu) I. \end{aligned}$$

$$\text{Equilibrium:} \qquad (S^*, I^*) = \left(\frac{\alpha + \gamma + \mu}{\beta}, \frac{(r-\mu)(\alpha + \gamma + \mu)}{\beta(\alpha + \mu - r)} \right).$$

(3) SIS model with constant population size.

$$\begin{aligned} \text{Dynamics:} \qquad \dot{S} &= \mu - \beta SI + (\gamma + \alpha) I - \mu S, \\ \dot{I} &= \beta SI - (\alpha + \gamma + \mu) I. \end{aligned}$$

$$\text{Equilibrium:} \qquad (S^*, I^*) = \left(\frac{\alpha + \gamma + \mu}{\beta}, \frac{\alpha + \gamma + \mu - \beta}{\beta} \right).$$

(4) SIR model with constant population size.

$$\text{Dynamics:} \qquad \begin{aligned} \dot{S} &= \mu - \beta SI + \alpha I - \mu S, \\ \dot{I} &= \beta SI - (\alpha + \gamma + \mu) I. \end{aligned}$$

$$\text{Equilibrium:} \qquad (S^*, I^*) = \left(\frac{\alpha + \gamma + \mu}{\beta}, \frac{\mu(\alpha + \gamma + \mu - \beta)}{\beta(\gamma + \mu)} \right).$$

6 References

Abeku, T. A., de Vlas, S. J., Borsboom, G., Teklehaimanot, A., Kebede, A., Olana, D., van Oortmarssen, G. J. & Habbema, J. D. F. (2002). Forecasting malaria incidence from historical morbidity patterns in epidemic-prone areas of ethiopia: a simple seasonal adjustment method performs best. *Tropical Medicine and International Health,* **7**, 851–857.

Anderson, R. M. & May, R. M. (1983). Vaccination and herd immunity to infectious diseases. *Nature,* **318** (28), 323–329.

Anderson, R. M. & May, R. M. (1991). *Infectious diseases of humans – dynamics and control.* Oxford University, Oxford.

Aron, J. L. & Schwartz, I. B. (1984). Seasonality and period-doubling bifurcations in an epidemic model. *Journal of Theoretical Biology,* **110**, 665–679.

Bolker, B. M. & Grenfell, B. T. (1993). Chaos and biological complexity in measles dynamics. *Proceedings of the Royal Society of London, B,* **251**, 75–81.

Chesson, P. L. & Ellner, S. (1989). Invasibility and stochastic boundedness in monotonic competition models. *Journal of Mathematical Biology,* **27**, 117–138.

Colwell, R. R. (1996). Global climate and infectious disease: the cholera paradigm. *Science,* **274**, 2025–2031.

Doebeli, M. & Koella, J. C. (1995). Evolution of simple population dynamics. *Proceedings of the Royal Society of London, B,* **260**, 119–125.

Dowell, S. F. (2001). Seasonal variation in host susceptibility and cycles of certain infectious diseases. *Emerging Infectious Diseases,* **7**, 369–374.

Earn, D. J., Rohani, P., Bolker, B. M. & Grenfell, B. T. (2000). A simple model for complex dynamical transitions in epidemics. *Science,* **287**, 667–670.

Ferrière, R. H. & Gatto, M. (1993). Chaotic population dynamics can result from natural selection. *Proceedings of the Royal Society of London, B,* **251**, 33–38.

Greenman, J., Kamo, M. & Boots, M. (2004). External forcing of ecological and epidemiological systems: a resonance approach. *Physica D,* **190**, 136–151.

Grenfell, B. T., Bolker, B. M. & Kleczkowski, A. (1995). Seasonality and extinction in chaotic metapopulations. *Proceedings of the Royal Society of London, B,* **259**, 97–103.

Grenfell, B. T., Wilson, K., Finkenstädt, B. F., Coulson, T. N., Murry, S., Albon, S. D., Pemberton, J. M., Clutton-Brock, T. H. & Crawley, M. J. (1998). Noise and determinism in synchronized sheep dynamics. *Nature,* **394**, 674–677.

Haraguchi, Y. & Sasaki, A. (2000). The evolution of parasite virulence and transmission rate in a spatially structured population. *Journal of Theoretical Biology,* **203**, 85–96.

Hethcote, H. W. & York, J. A. (1984). *Gonorrhea Transmission Dynamics and Control*. Springer-Verlag, Berlin.

Kamo, M. & Sasaki, A. (2002). The effect of cross-immunity and seasonal forcing in multi-strain epidemic model. *Physica D,* **165**, 228–241.

Keeling, M. J. & Grenfell, B. T. (1997). Disease extinction and community size: modeling the persistence of measles. *Science,* **275** (3), 65–67.

Keeling, M. J., Rohani, P. & Grenfell, B. T. (2001). Seasonally forced disease dynamics explored as switching between attractors. *Physica D,* **148**, 347–335.

Levins, R. (1968). *Evolution in Changing Environments*. Princeton University Press, Princeton.

Nisbet, R. & Gurney, W. (1982). *Modelling Fluctuating Populations*. John Wiley & Sons, New York.

Pascual, M., Bouma, M. J. & Dobson, A. P. (2002). Cholera and climate: revisiting the quantitative evidence. *Microbes and Infection,* **4**, 237–245.

Pascual, M., Rodó, X., Ellner, S. P., Colwell, R. & Bouma, M. J. (2000). Cholera dynamics and El Niño-southern oscillation. *Science,* **289**, 1766–1769.

Rand, D. A., Keeling, M. & Wilson, H. B. (1995). Invasion, stability and evolution to criticality in spatially extended, artificial host-pathogen ecology. *Proceedings of the Royal Society of London, B,* **259**, 55–63.

Rand, D. A. & Wilson, H. B. (1991). Chaotic stochasticity: a ubiquitous source of unpredictability in epidemics. *Proceedings of the Royal Society of London, B,* **246**, 179–184.

Rohani, P., Keeling, M. J. & Grenfell, B. T. (2002). The interplay between determinism and stochasticity in childhood diseases. *The American Naturalist,* **159** (5), 469–481.

Schwartz, I. B. (1985). Multiple stable recurrent outbreaks and predictability in seasonally forced nonlinear epidemic model. *Journal of Mathematical Biology,* **21**, 347–361.

Schwartz, I. B. & Smith, H. L. (1983). Infinite subharmonic bifurcation in an seir epidemic model. *Journal of Mathematical Biology,* **18**, 233–253.

Segar, J. & Brockmann, H. J. (1987). What is bet-hedging? *Oxford Surveys in Evolutionary Biology,* **4**, 182–211.

Sugihara, G., Grenfell, B. & May, R. M. (1990). Distinguishing error from chaos in ecological time series. *Philosophical Transactions of the Royal Society London: B,* **330**, 235–251.

van Baalen, M. & Sabelis, M. W. (1995). The dynamics of multiple infection and the evolution of virulence. *American Naturalist,* **146**, 881–910.

Model	Correlation when δ is small
SIS (Eq. 1 in the text)	$\frac{I^*\delta(\alpha+\gamma+\mu)(-I^*\beta(\alpha+\mu)^2+(r+\alpha-I^*\beta)\omega^2)}{2((r-\mu)^2(\alpha+\gamma+\mu)^2+(I^*\beta(-2(r+\alpha)+I^*\beta)+(r-\mu)^2)\omega^2+\omega^4)}$
SIS with reproduction by both hosts	$\frac{S^*I^*\beta\delta(-2I^*\beta(-r+\alpha+\mu)^2+2(\alpha-I^*\beta)\omega^2)}{4(I^{*2}\beta^2(-r+\alpha+\mu)^2+(I^*\beta(-2\alpha+I^*\beta)+(r-\mu)^2)\omega^2+\omega^4)}$
SIS with fixed population size	$-\frac{S^*I^{*2}\beta^2\delta}{2I^{*2}\beta^2+2\omega^2}$
SIR with fixed population size	$\frac{S^*I^*\beta\delta(-I^*\beta(\gamma+\mu)^2+(-I^*\beta+\gamma)\omega^2)}{2(I^{*2}\beta^2(\gamma+\mu)^2+(I^{*2}\beta^2-2I^*\beta\gamma+\mu^2)\omega^2+\omega^4)}$

Table 1: Correlation between $S(t)$ and $P(t)(=\sin 2\pi t)$ when δ is small. S^* and I^*, represent the densities of susceptible and infected hosts at an equilibria in the absence of seasonality, respectively (see Appendix). $\omega = 2\pi$ is the angular frequency of seasonal forcing.

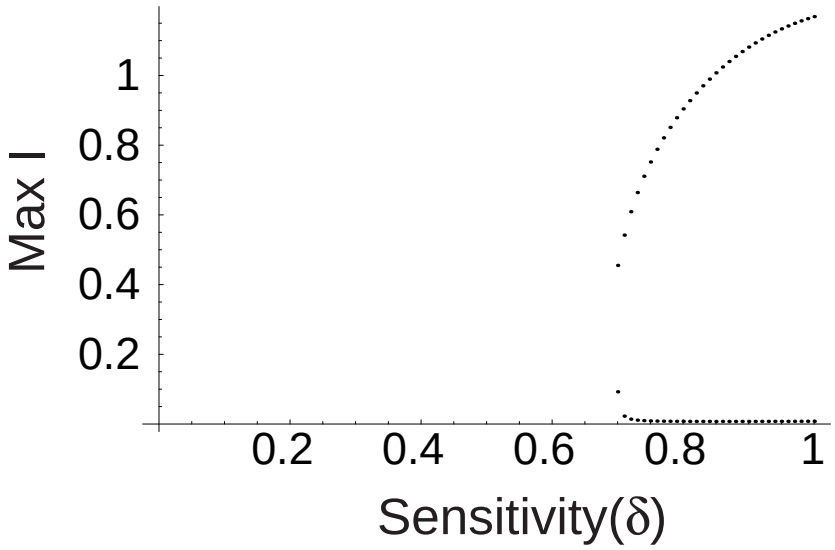
Figure Captions

Figure 1. Bifurcation diagram of SIS model with seasonally varying transmission rate. The maximum density of infected hosts in each year, after the epidemiological dynamics reached stationarity, is plotted against the sensitivity, δ, to seasonality in the transmission rate. The population converges to annual cycles when δ is below about 0.7, and to biennial cycles when it is larger than this value. The transmission rate $\beta(t)$ varies with time t as $\beta(t) = \beta_0(1 + \delta \sin 2\pi t)$. Parameters: $\mu = 1$, $\alpha = 5$, $\beta_0 = 20$, $r = 4$,$\gamma = 1$.

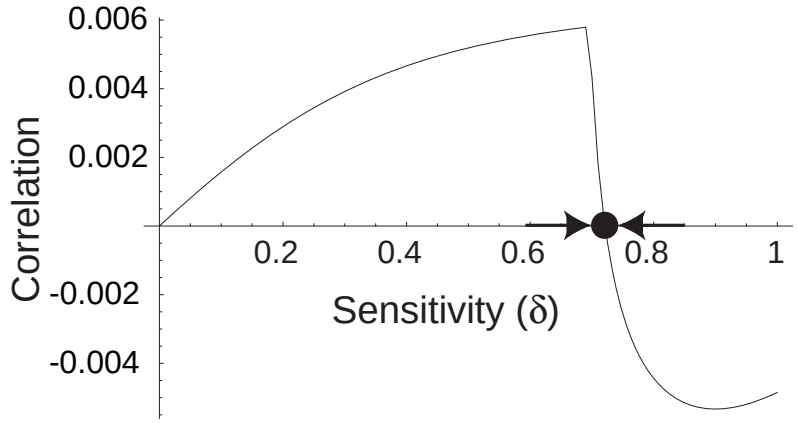
Figure 2. The correlation between the density of susceptible host and the transmission rate, $\langle \hat{S}^1(t) \sin 2\pi t \rangle$, as a function of sensitivity δ (a), and the time change in the mean sensitivity of the pathogen population, when many strains with different sensitivities compete (b). In the evolutionary simulation, we used a multi-strain SIS model given by a set of equations, $\dot{S} = -S \sum_{i=1}^{n} I_i \beta_i + \gamma \sum_{i=1}^{n} I_i - \mu S + rS$ and $\dot{I}_i = S\beta_i I_i - (\gamma + \mu + \alpha) I_i$, where I_i is the density of the i-th strain infected hosts. $\dot{x}$ represents the time derivative of x. Each strain has a different value of sensitivity, assigned one of the equally divided values between 0 and 1. A small amount of mutation is introduced between the strains having neighboring values of sensitivity. Parameters are $\mu = 1$, $\alpha = 5$, $\beta_0 = 20$, $r = 4$, $\gamma = 1$.

Figure 3. The correlation between S and $P(t)$ plotted against the sensitivity parameter δ (a), and the evolutionary trajectory for mean sensitivity (b), when there is a negative trade-off between the mean transmissibility and the sensitivity. There are two evolutionary end points for δ – two closed circles at 0 and right are a stable equilibrium in evolutionary dynamics, while the open circle in the middle is unstable. The evolutionary trajectory converges at either of two end points depending on the initial condition. The numbers on the trajectories in (b) indicate the initial amount of sensitivity in the population. Parameters: $\mu = 1$, $\alpha = 5$, $\beta_0 = 20$, $r = 4$, $\gamma = 1$, $\Omega = 0.9$.

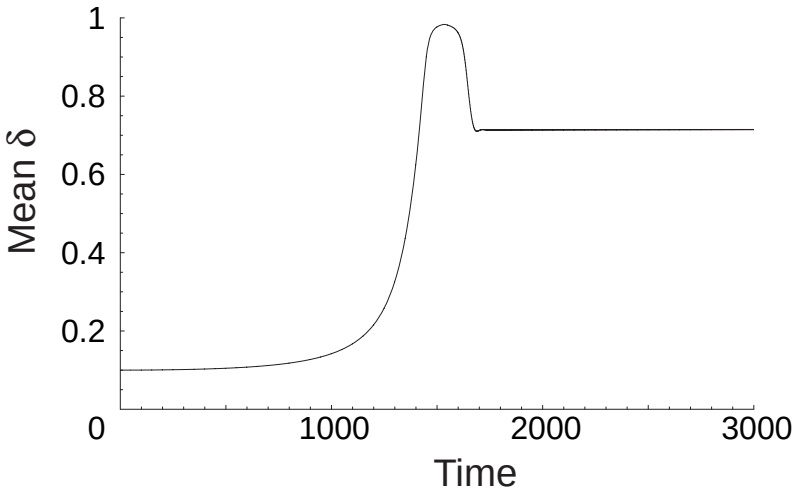
Figure 4. Evolution of the sensitivity parameter with the SIR model. Bifurcation diagram (a), correlation between $S(t)$ and $P(t)$, evolutionary trajectory of a mean δ (c), and dynamics after evolution comes to a halt (d) . Numbers beside branches in (a) and (b) indicate periods in years. In (a), a few attractors coexist with the same sensitivity (e.g., around δ= 0.1 attractors for 1-, 3- and 4-years periods exist). Each attractor is followed by period-doubling bifurcation and the period is doubled when we increase δ. Attractors for a period of 1 year (and 2 years derived by a bifurcation) exist for all the range of δ, whereas the others exist for limited ranges. Circles in (b) indicate unstable evolutionary end points (as described in Figure 2). If we start our evolutionary simulation for small δ (less than 0.05), the dynamics becomes period of 1 year because there are no other attractors. The correlation is always positive on the attractor, so that the evolution increases δ along the branch. Evolution comes to a halt eventually when δ hits 1 (c), and the dynamics at the final δ is a period of 2 years (d). In the simulation, we use measles parameters (β=476, γ=28, α=0; Greenman *et al.* (2004)) and assume that the mean life time of hosts is 80 years (μ= 0.0125).


Max I
1
0.8
0.6
0.4
0.2
0.2
0.4
0.6
0.8
1
Sensitivity(δ)

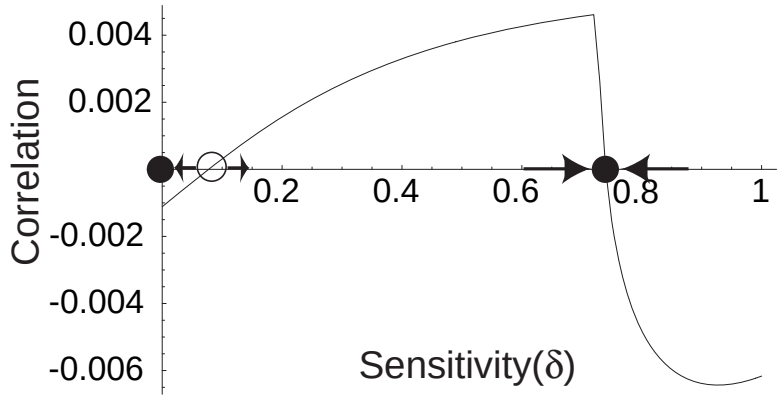
(a)


0.006
0.004
0.002
-0.002
-0.004
Correlation
0.2
0.4
0.6
0.8
1
Sensitivity (δ)

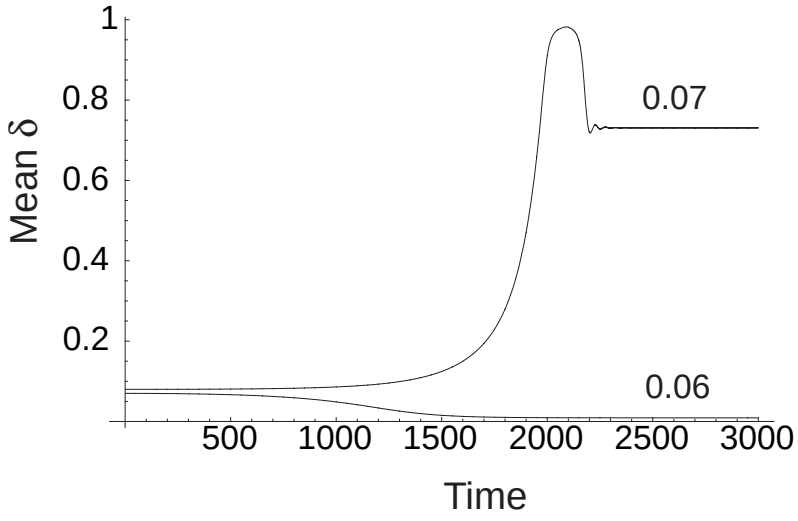
(b)


1
0.8
0.6
0.4
0.2
0
Mean δ
1000
2000
3000
Time

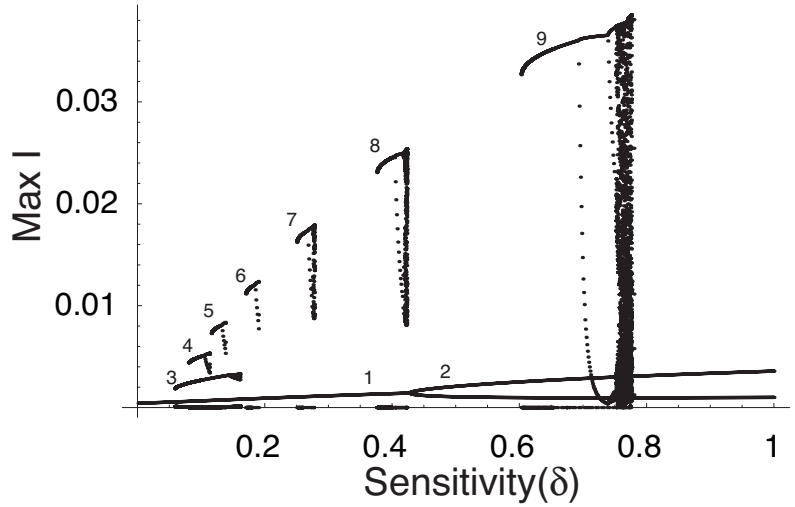
(a)


0.004
0.002
-0.002
-0.004
-0.006
Correlation
0.2
0.4
0.6
0.8
1
Sensitivity(δ)

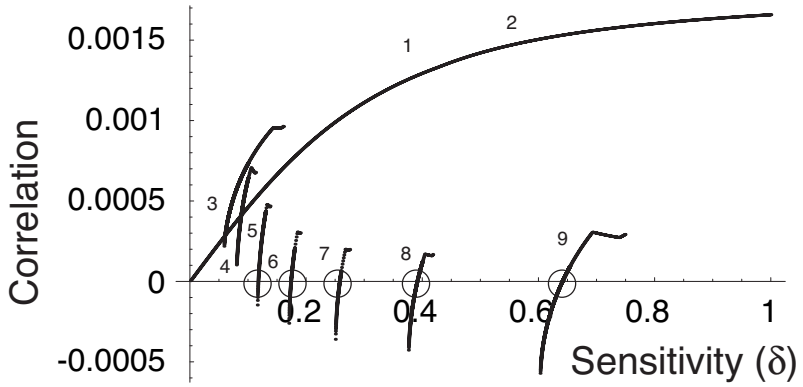
(b)


1
0.8
0.6
0.4
0.2
Mean δ
0.07
0.06
500
1000
1500
2000
2500
3000
Time

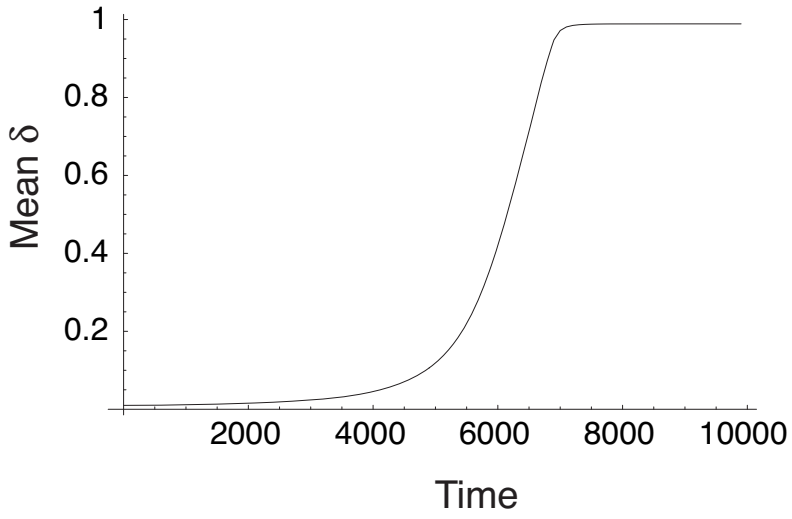
(a)


Max I
0.03
0.02
0.01
0.2
0.4
0.6
0.8
1
Sensitivity(δ)
1
2
3
4
5
6
7
8
9

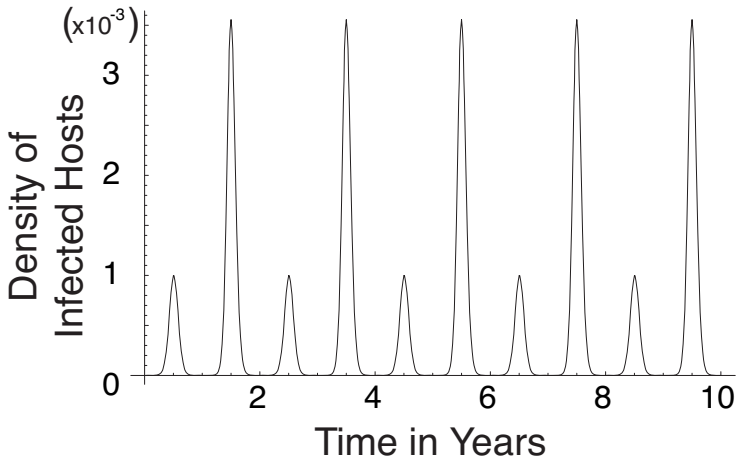
(b)


Correlation
0.0015
0.001
0.0005
0
-0.0005
0.2
0.4
0.6
0.8
1
Sensitivity (δ)
1
2
3
4
5
6
7
8
9

(c)


1
0.8
0.6
0.4
0.2
Mean δ
2000
4000
6000
8000
10000
Time

(d)


(x10-3)
3
2
1
0
Density of
Infected Hosts
2
4
6
8
10
Time in Years