**Caution coupling explains linear phase of Covid-19 curves**

John S. McCaskill

European Centre for Living Technology

Chemelion Inc.

Understanding of epidemics through modelling is gained both through highly simplified population models such as the early SIR model [1, 2] (distinguishing Susceptible-Infective-Recovered individuals) and its extensions both to more differentiated models like SEIR [3-6] and SIDARTHE [7, 8], and to include other population structure such as age with a matrix of social mixing [9, 10], stochastic effects [11, 12] and spatial [13-15] or other network structure [16-18]. In addition, in connection with big data [19, 20], understanding of cause and effect can be gained in detailed agent models [21, 22], with differentiated individuals and their interactions characterized by statistically representative properties or behaviours matched to detailed population data. However, certain key features of the Covid-19 pandemic data affecting us all have not been explained simply. In particular, the remarkable global linearity in the cumulative confirmed cases is poorly understood, e.g. potentially arising from a small world effect as a power law [16] (but why with exponent one?). Furthermore, the dominant country response curves show a prolonged near constant growth rate appearing long before the (“herd immunity”) saturation of the population with recovered individuals. In this letter, we show that central features of this societal response complexity can indeed be understood using the S(E)IR family of models by means of a single additional deterministic coupling, one reflecting societal introspection: *caution*. As society reacts to and endeavours to contain the strong effects of the Covid-19 virus on health, social well-being and the economy, it can increasingly appear that in order to capture what is happening every aspect of society must be modelled in detail: from the use of public transport, religious practises and child play patterns to political decision making, the media and legislature[23]. However, the above global linearity in the cumulative number of Corona cases as well as the commonly observed prolonged near linear response in individual populations can be understood as a generic human response to the epidemic in the age of information. This insight may in turn help us to focus societal measures and responses more effectively.

In March 2020, a study in Oxford [24] suggested, using an SIR model, that a much larger portion of society may be infected than normally inferred from the testing data, which was biased to symptom carriers. This was in-line with standard epidemiological modelling that relates the epidemic proliferation peak and subsequent decline to the advent of a significant fraction of the population becoming immune to the disease. Contemplating the linear global data, see Fig. 1, the author was struck by the similarities with bacterial viral proliferation kinetics inside a single cell and in evolution experiments in vitro, which systematically show exponential growth giving way to linear growth in the absence of immunity. The fundamental reason for this is specific resource limitation, for example of the Qß viral replicase enzymes responsible for copying the RNA viral genome. This is, like the nesting site limitation in bird populations, a straightforward thing: when most replicase enzymes are occupied in the copying process with a particular RNA genome, they are not available for proliferation of other RNA, and the throughput of copied RNA becomes a constant, limited by the turnover throughput of such copier enzymes. The author wondered if a somewhat similar mechanism could account for the observed linear growth phase for Covid-19 in societies shown in Fig. 1.

Whereas some countries, with geographic advantages in isolation, by executing radical containment policies, have managed to virtually eliminate the Covid-19 virus, the far more generic growth response is a transition from an exponential (or possibly power law [16]) phase to a relatively constant rate of growth, in some cases after an initial overshoot.

The simplest generic structure of epidemics, captured also by the SIR model, is initial exponential growth tempered by the rise of so-called herd-immunity in the population.

1. Kermack, W.O., McKendrick, A.G., Walker, G.T.: A contribution to the mathematical theory of epidemics. Proceedings of the Royal Society of London. Series A, Containing Papers of a Mathematical and Physical Character 115, 700-721 (1927) doi:10.1098/rspa.1927.0118

2. R.M., A., B., A., R.M., M.: Infectious Diseases of Humans: Dynamics and Control. Oxford University Press, Oxford, UK (1992) 9780198540403

3. Anderson, R., May, R.: Directly transmitted infections diseases: control by vaccination. Science 215, 1053-1060 (1982) 10.1126/science.7063839

4. Hethcote, H.W.: The Mathematics of Infectious Diseases. SIAM Rev. 42, 599–653 (2000) 10.1137/s0036144500371907

5. Wu, Z., McGoogan, J.M.: Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases from the Chinese Center for Disease Control and Prevention. . JAMA 323, 1239–1242 (2020) <https://doi.org/10.1001/jama.2020.2648>

6. Lin, Q., Zhao, S., Gao, D., Lou, Y., Yang, S., Musa, S.S., Wang, M.H., Cai, Y., Wang, W., Yang, L., He, D.: A conceptual model for the coronavirus disease 2019 (COVID-19) outbreak in Wuhan, China with individual reaction and governmental action. Int. J. Infect. Dis. 93, 211-216 (2020) <https://doi.org/10.1016/j.ijid.2020.02.058>

7. Giordano, G., Blanchini, F., Bruno, R., Colaneri, P., Di Filippo, A., Di Matteo, A., Colaneri, M.: Modelling the COVID-19 epidemic and implementation of population-wide interventions in Italy. Nature Medicine (2020) <https://doi.org/10.1038/s41591-020-0883-7>

8. Gumel, A.B., Ruan, S., Day, T., Watmough, J., Brauer, F., van den Driessche, P., Gabrielson, D., Bowman, C., Alexander, M.E., Ardal, S., Wu, J., Sahai, B.M.: Modelling strategies for controlling SARS outbreaks. Proc Biol Sci 271, 2223-2232 (2004) 10.1098/rspb.2004.2800

9. Klepac, P., Kucharski, A.J., Conlan, A.J., Kissler, S., Tang, M., Fry, H., Gog, J.R.: Contacts in context: large-scale setting-specific social mixing matrices from the BBC Pandemic project. medRxiv (2020)

10. Prem, K., Liu, Y., Russell, T.W., Kucharski, A.J., Eggo, R.M., Davies, N., Flasche, S., Clifford, S., Pearson, C.A.B., Munday, J.D., Abbott, S., Gibbs, H., Rosello, A., Quilty, B.J., Jombart, T., Sun, F., Diamond, C., Gimma, A., van Zandvoort, K., Funk, S., Jarvis, C.I., Edmunds, W.J., Bosse, N.I., Hellewell, J., Jit, M., Klepac, P.: The effect of control strategies to reduce social mixing on outcomes of the COVID-19 epidemic in Wuhan, China: a modelling study. The Lancet Public Health 5, e261-e270 (2020) 10.1016/S2468-2667(20)30073-6

11. Hellewell, J., Abbott, S., Gimma, A., Bosse, N.I., Jarvis, C.I., Russell, T.W., Munday, J.D., Kucharski, A.J., Edmunds, W.J., Sun, F., Flasche, S., Quilty, B.J., Davies, N., Liu, Y., Clifford, S., Klepac, P., Jit, M., Diamond, C., Gibbs, H., van Zandvoort, K., Funk, S., Eggo, R.M.: Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. The Lancet Global Health 8, e488-e496 (2020) <https://doi.org/10.1016/S2214-109X(20)30074-7>

12. Kucharski, A.J., Russell, T.W., Diamond, C., Liu, Y., Edmunds, J., Funk, S., Eggo, R.M., Sun, F., Jit, M., Munday, J.D., Davies, N., Gimma, A., van Zandvoort, K., Gibbs, H., Hellewell, J., Jarvis, C.I., Clifford, S., Quilty, B.J., Bosse, N.I., Abbott, S., Klepac, P., Flasche, S.: Early dynamics of transmission and control of COVID-19: a mathematical modelling study. The Lancet Infectious Diseases 20, 553-558 (2020) 10.1016/S1473-3099(20)30144-4

13. Angulo, J., Yu, H.-L., Langousis, A., Kolovos, A., Wang, J., Madrid, A.E., Christakos, G.: Spatiotemporal Infectious Disease Modeling: A BME-SIR Approach. PLOS ONE 8, e72168 (2013) 10.1371/journal.pone.0072168

14. Keeling, M.J.: The effects of local spatial structure on epidemiological invasions. Proc Biol Sci 266, 859-867 (1999) 10.1098/rspb.1999.0716

15. Danon, L., Brooks-Pollock, E., Bailey, M., Keeling, M.J.: A spatial model of CoVID-19 transmission in England and Wales: early spread and peak timing. medRxiv 2020.2002.2012.20022566 (2020) 10.1101/2020.02.12.20022566

16. Ziff, A.L., Ziff, R.M.: Fractal kinetics of COVID-19 pandemic. medRxiv (2020)

17. Simoes, J.M.: Spatial Epidemic Modelling in Social Networks. AIP Conference Proceedings 776, 287-297 (2005) 10.1063/1.1985395

18. Manchein, C., Brugnago, E.L., da Silva, R.M., Mendes, C.F.O., Beims, M.W.: Strong correlations between power-law growth of COVID-19 in four continents and the inefficiency of soft quarantine strategies. Chaos: An Interdisciplinary Journal of Nonlinear Science 30, 041102 (2020) 10.1063/5.0009454

19. Wang, C.J., Ng, C.Y., Brook, R.H.: Response to COVID-19 in Taiwan: Big Data Analytics, New Technology, and Proactive Testing. JAMA 323, 1341-1342 (2020) 10.1001/jama.2020.3151

20. Zhou, C., Su, F., Pei, T., Zhang, A., Du, Y., Luo, B., Cao, Z., Wang, J., Yuan, W., Zhu, Y., Song, C., Chen, J., Xu, J., Li, F., Ma, T., Jiang, L., Yan, F., Yi, J., Hu, Y., Liao, Y., Xiao, H.: COVID-19: Challenges to GIS with Big Data. Geography and Sustainability 1, 77-87 (2020) <https://doi.org/10.1016/j.geosus.2020.03.005>

21. Hunter, E., Mac Namee, B., Kelleher, J.D.: A Taxonomy for Agent-Based Models in Human Infectious Disease Epidemiology. Journal of Artificial Societies and Social Simulation 20, 2 (2017) 10.18564/jasss.3414

22. Chinazzi, M., Davis, J.T., Ajelli, M., Gioannini, C., Litvinova, M., Merler, S., Pastore y Piontti, A., Mu, K., Rossi, L., Sun, K., Viboud, C., Xiong, X., Yu, H., Halloran, M.E., Longini, I.M., Vespignani, A.: The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak. Science 368, 395 (2020) 10.1126/science.aba9757

23. Bruinen de Bruin, Y., Lequarre, A.-S., McCourt, J., Clevestig, P., Pigazzani, F., Zare Jeddi, M., Colosio, C., Goulart, M.: Initial impacts of global risk mitigation measures taken during the combatting of the COVID-19 pandemic. Safety Science 128, 104773 (2020) <https://doi.org/10.1016/j.ssci.2020.104773>

24. Lourenco, J., Paton, R., Ghafari, M., Kraemer, M., Thompson, C., Simmonds, P., Klenerman, P., Gupta, S.: Fundamental principles of epidemic spread highlight the immediate need for large-scale serological surveys to assess the stage of the SARS-CoV-2 epidemic. medRxiv (2020) <https://doi.org/10.1101/2020.03.24.20042291>