Intervention Serology and Interaction Substitution: Exploring the Role of 'Immune Shielding' in Reducing COVID-19 Epidemic Spread

Joshua S. Weitz[1,2,*]

[1] *School of Biological Sciences, Georgia Institute of Technology, Atlanta, GA, USA*
[2] *School of Physics, Georgia Institute of Technology, Atlanta, GA, USA*

(Dated: March 21, 2020)

The Premise: Serology and Virus Testing to Enable Interventions via Immune Shielding

The COVID-19 pandemic has precipitated a global crisis. At present, two central public health control strategies have emerged: (i) mitigation; (ii) suppression (e.g, [1]). Mitigation uses a combination of social distancing (including school and university closures), case testing, and infection isolation to reduce epidemic spread and burden on hospitals. Suppression imposes complete shut-downs of the bulk of non-essential services in society for extended periods (e.g., sheltering in place). Both strategies focus on reducing new infections by reducing interactions (and both raise questions of sustainability and long-term tactics). Complementary to those approaches, here we propose ways to leverage the combined used of serological and virus shedding tests to identify and deploy recovered individuals as focal points for sustaining safer interactions, i.e., as 'immune shields'. Recovered individuals, in the present context, denote *individuals who have developed protective antibodies to SARS-CoV-2 and are no longer shedding virus*. The objective of this approach is to help sustain the number of total interactions necessary for the functioning of essential goods and services (including but not limited to tending to the elderly, hospital care, schools, and food supply) while decreasing the probability of transmission during such essential interactions. The present model builds upon calls for increased serological testing (e.g.,[2] towards intervention serology (see Figure 1). We examine the potential for such an approach using a conventional SIR model and a model with age-structured risk adapted to the COVID-19 epidemic.

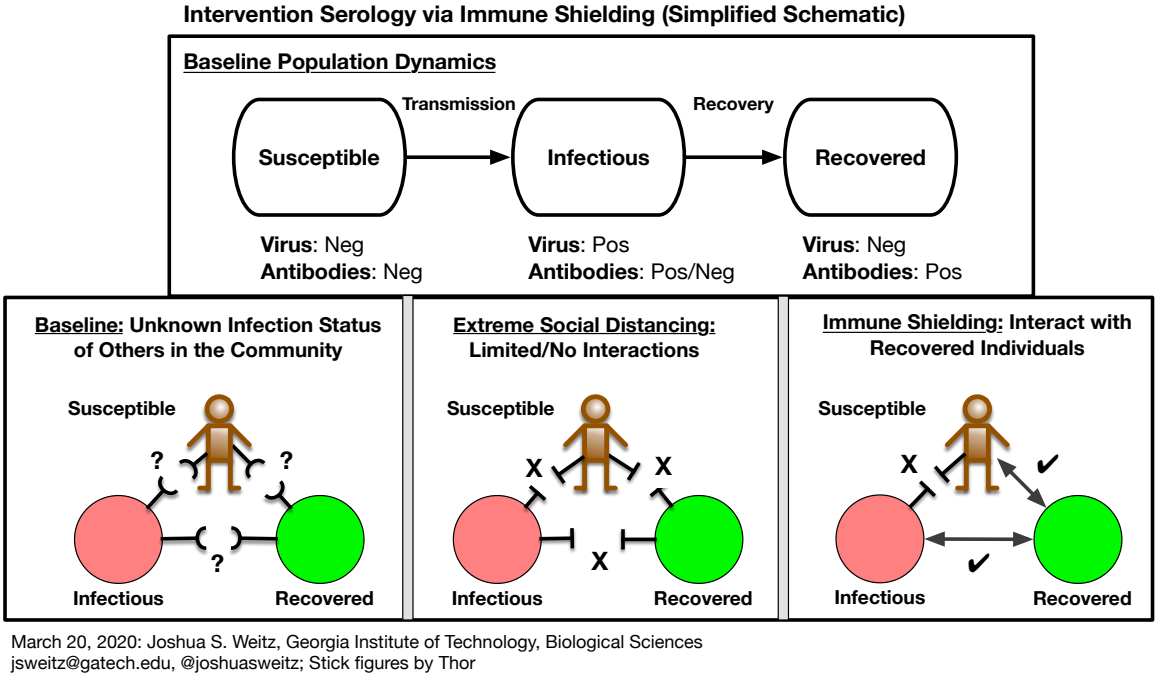

FIG. 1: Simplified schematic of intervention serology via immune shielding. Recovered individuals (virus negative and antibody positive) interact more frequently than do infectious individuals, thereby diluting interactions. This interaction substitution forms the basis for using shielding as a means to reduce epidemic size before conventional herd immunity sets in.

*Electronic address: jsweitz@gatech.edu; URL: http://ecotheory.biology.gatech.edu

I. IMMUNE SHIELDING IN SIR-LIKE EPIDEMICS

Consider a SIR model in which individuals substitute their interactions with identified (or strategically located) recovered individuals. Hence, rather than mixing at random, we consider that there is a relative preference of $1+\alpha$ that an individual will interact with a R individual:

$$\dot{S} = -\beta \frac{SI}{1+\alpha R} \tag{1}$$

$$\dot{I} = \beta \frac{SI}{1+\alpha R} - \gamma I \tag{2}$$

$$\dot{R} = \gamma I \tag{3}$$

such that when $\alpha = 0$ we recover the usual SIR model. Note that the denominator of $1+\alpha R$ can be thought of as $S+I+R+\alpha R$. Given that $S+I+R = 1$, this is equivalent to the term $1+\alpha R$. Detailed mixing and substitution models could lead to alternative terms. Figure 2 illustrates the impact of shielding on an SIR epidemic with $\mathcal{R}_0 = 2$. As is evident, shielding can have a protective effect by interaction substitution reducing the peak and duration of epidemics. In effect, shielding acts as a negative feedback loop on the epidemic, i.e., given that $\mathcal{R}_{eff}(t)/\mathcal{R}_0 = S(t)/(1+\alpha R(t))$.

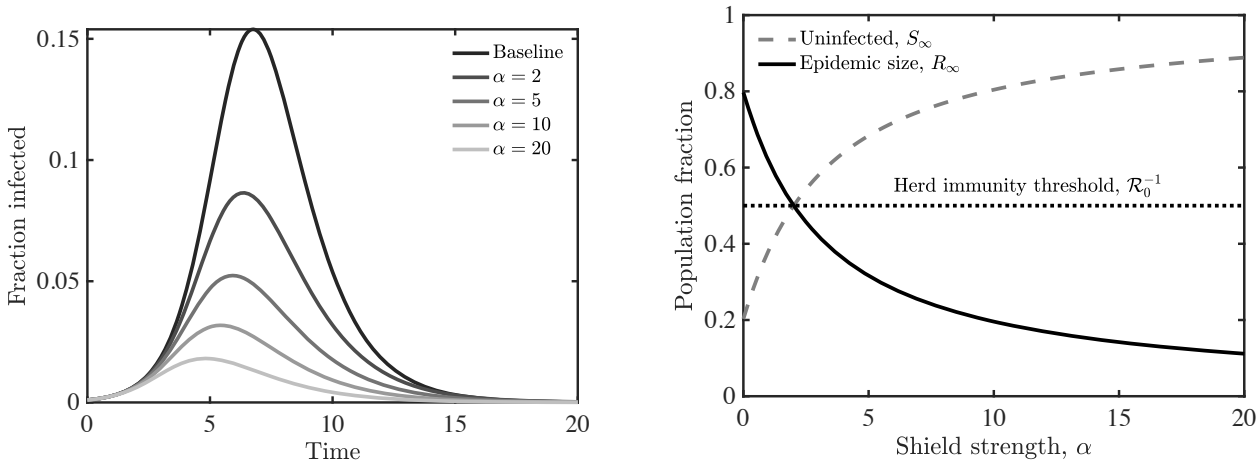

FIG. 2: Serology intervention dynamics. (Left) Infection dynamics in a SIR model with different levels of shielding, α. (Right) Final state of the system as a function of α. In both panels, $\beta = 2$ and $\gamma = 1$.

II. MATHEMATICAL MODEL OF COVID-19 – BASELINE CASE AND INTERVENTIONS

Consider a population of susceptible S, exposed E, infectious asymptomatically I_a, infectious symptomatically I_s, and recovered R who are free to move, without restrictions in a 'business as usual' scenario. A subset of symptomatic cases will require hospital care, which we further divide into subacute I_{hsub}, and critical/acute (i.e., requiring ICU intervention) I_{hcri} cases. We assume that a substantial fraction of critical cases will die. The following model considers these 8 classes of individuals, further stratified by age a, in 10 categories, from 0-9; 10-19; 20-19, and so on, until 90-99, and avoids the inclusion of birth and death processes (for simplicity). The total number of asymptomatic and symptomatic infected cases are $I_{tot,a}$ and $I_{tot,s}$ respectively. The equations retain age structure for all categories – an

important point when moving from this baseline scenario to the intervention scenario.

$$\dot{S}(a) = -\beta_a \frac{S(a)I_{tot,a}}{N_{tot}+\alpha R_{shields}} - \beta_s \frac{S(a)I_{tot,s}}{N_{tot}+\alpha R_{shields}} \quad (4)$$

$$\dot{E}(a) = \beta_a \frac{S(a)I_{tot,a}}{N_{tot}+\alpha R_{shields}} + \beta_s \frac{S(a)I_{tot,s}}{N_{tot}+\alpha R_{shields}} - \gamma_e E(a) \quad (5)$$

$$\dot{I}_a(a) = p\gamma_e E(a) - \gamma_a I_a(a) \quad (6)$$

$$\dot{I}_s(a) = (1-p)\gamma_e E(a) - \gamma_s I_s(a) \quad (7)$$

$$\dot{I}_{hsub}(a) = h(1-\xi)\gamma_s I_s(a) - \gamma_h I_{hsub}(a) \quad (8)$$

$$\dot{I}_{hcri}(a) = h\xi\gamma_s I_s(a) - \gamma_h I_{hcri}(a) \quad (9)$$

$$\dot{R}(a) = \gamma_a I_a(a) + (1-h)\gamma_s I_s(a) + \gamma_h I_{hsub}(a) + (1-\mu)\gamma_h I_{hcri}(a) \quad (10)$$

$$\dot{D}(a) = \mu\gamma_h I_{hcri}(a) \quad (11)$$

where $N_{tot} = S_{tot} + E_{tot} + I_{tot,a} + I_{tot,s} + R_{tot}$ denotes the fraction of the population in the 'circulating baseline', and $R_{shields}$ denotes the total number of identified recovered individuals operating as immune shields. In these simulations, only recovered individuals between the ages of 20-60 are included as potential shields. The model assumes hospital infection control for now, which must be relaxed in developing combination scenarios. The basic reproduction number of this model is

$$\mathcal{R}_0 = p\mathcal{R}_a + (1-p)\mathcal{R}_s \quad (12)$$

where $\mathcal{R}_a = \beta_a/\gamma_a$ and $\mathcal{R}_s = \beta_a/\gamma_s$. Technically this model has 80 ODE-s (all code available via github; of note, the code itself is modifiable to include age-structured asymptomatic fraction, as suggested by Leung and colleagues, Nature Medicine, 2020). The baseline epidemiological parameters, age stratified risk, and population structure are listed in tables at the end of this manuscript (adapted from [3–6]).

We use the baseline epidemiological parameters and start all outbreaks with 0.1% total prevalence, e.g., akin to 500 symptomatic and 9500 asymptomatic individuals out of a population of 10,000,000. We consider outbreak scenarios that differ in transmission rates, such that for the low scenario, $\beta_a = 2.5$ and $\beta_s = 5$ with $\mathcal{R}_0 = 1.85$ and for the high scenario $\beta_a = 3.5$ and $\beta_s = 7$ with $\mathcal{R}_0 = 2.59$; in both cases $p = 0.9$. Figure 3 shows the results of comparing interventions to the baseline case (assuming infected individuals are in the 20-29 age range, for purposes of exploration). As in the simple SIR model, shielding (on its own) could potentially decrease epidemic burden across multiple metrics, decreasing both the total impact and shortening the peak event. In a population of size 10,000,000 for the high scenario, the final epidemic predictions are 11,400 deaths in the baseline case vs. 9,700 deaths given intermediate shielding. 3,600 deaths given aggressive shielding and In a population of size 10,000,000 for the low scenario, the final epidemic predictions are 9,500 deaths in the baseline case vs. 7,000 deaths given intermediate shielding. 2,000 deaths given aggressive shielding. The baseline results are broadly consistent with the more complex Imperial College London Model, with the majority of deaths centered around those ages 60 and above, despite the lower fraction of individuals in those ranges (see Figure 3). However, we assume higher asymptomatic rates consistent with recent detailed studies from Wuhan. Note that these results consider impacts based on shielding alone; whereas ongoing restrictions will reduce interaction rates. It is also important to point out that even in the optimistic cases, a significant fraction of the population will get sick. In the present model, the effectiveness of shielding depends on the product of the number of potential shields identified and their effective substitutability, i.e, αR. Operationally, we only consider a subset of the population as potential shields, focusing on those between 20-60 years of age.

III. DISCUSSION

Serology testing is needed now, at scale, for many reasons. Here, we have shown a rationale for serology testing as a means to facilitate interventions beyond those of mitigation and suppression. We have shown that identifying and deploying recovered individuals could represent more than just a metric of the state of the COVID-19 epidemic, but an opportunity to slow it. Many logistical, social, and dynamical challenges remain if such an idea were to move from theory to feasibility. First, we need more serological tests – both targeted and large-scale surveys. Second, such tests need to be fast, accurate, and readily available. Yet, even if such tests were available, who should get them? Public health authorities and governmental agencies should consider how to prioritize those in critical roles, those with experience in disaster response, as well as prior individuals who have tested positive for COVID-19 (and could then return for both serology-based and viral shedding assays). Positive confirmation of immunity and cessation of

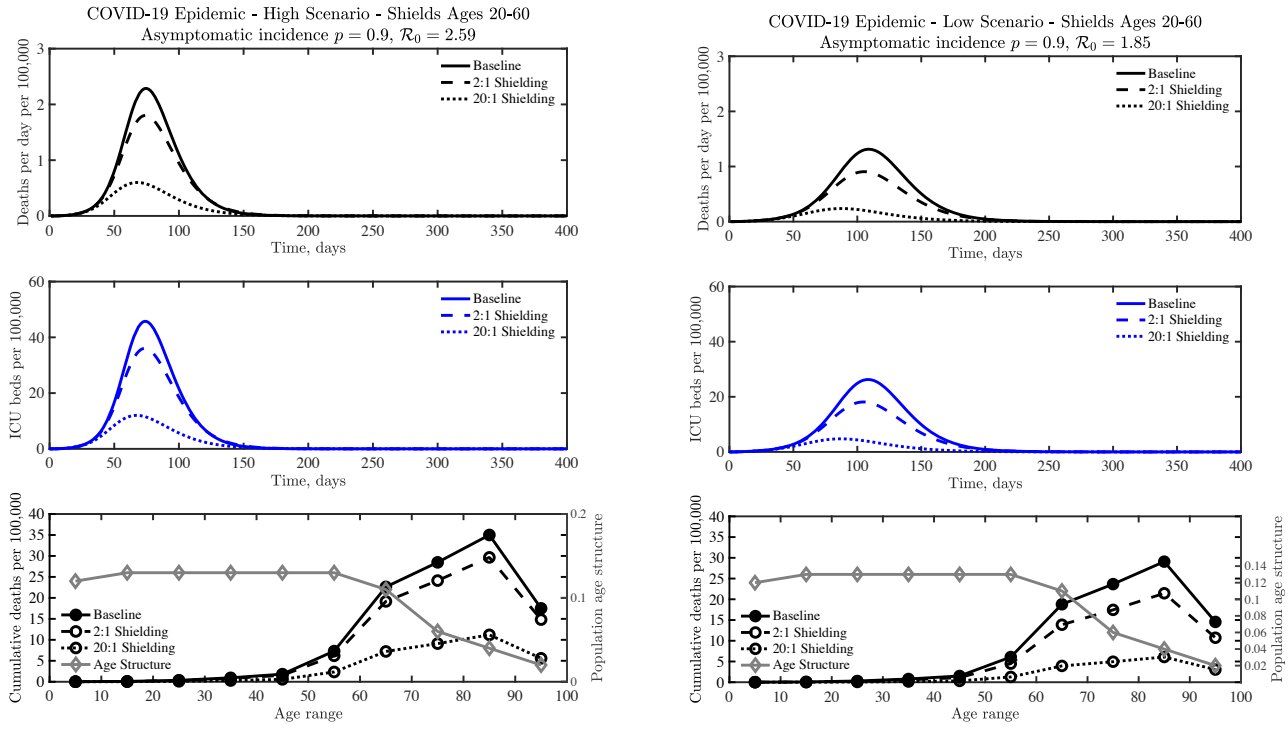

FIG. 3: COVID-19 dynamics in a baseline case without interventions compared to two shielding scenarios. Left and right correspond to different epidemic potential. Irrespective, total deaths and hospital ICU beds peak together – suggesting further failures in the baseline case. Critically, total deaths are centered largely on older individuals (bottom) panel, whereas age structured populations with sufficient younger individuals are relatively less at risk.

viral shedding could help identify and deploy (tens of) thousands of individuals as serological shields; with the greatest concentration of such shields likely co-located with areas in greatest need of intervention.

We recognize there are also challenges. First, the testing would need to be of high accuracy and repeated. In contrast, inaccurate testing could endanger susceptible individuals (and inadvertently enhance epidemic spread). Next, the long-term duration of immunity to SARS-CoV-2 is unknown, and the impact of waning immunity would need to be included - as a means to evaluate the suitability and availability of shields. In addition, availability of shields will be demographic and context dependent, e.g., here we assumed that shields would need to be drawn from a 20-60 age range. The duration of immune memory is also relevant if one were to extend the present model to multi-year time frames and include demographic dynamics (and strain evolution, e.g., via Nextstrain.org [7]). In addition, the present model neglects spatial and network structure. In a network, well-connected individuals have a disproportionate effect on the spread of disease. Perhaps such network structure is an opportunity, e.g., would it be possible to position immune shields at focal points of 'essential' services, or to prioritize the focus of population-scale serological prevalence assays based on the physical connectivity of individuals? With tens of thousands of confirmed cases and likely many more asymptomatic cases who have recovered (or will soon recover), it is time for collective action to ascertain more information on prevalence and to consider strategic use of serology as the basis for intervention.

Acknowledgements and Code: JSW thanks M. Lipsitch, K. Levy, P. Dodds, D. Muratore, A. Coenen, C.Y. Leung, D. Demory, S. Beckett, S.W. Park, J. Dushoff, J. Shaman, and B. Lopman for comments and feedback. Mistakes are the fault of the author solely. Tweet threads by T. Bedford (`https://twitter.com/trvrb/status/1240444821593944064?s=20`) and N. Christakis (`https://twitter.com/NAChristakis/status/1240689935557865472?s=20`) were influential in refining initial ideas into the current form. All code is available at: `https://github.com/jsweitz/covid_immune_shields`.

1 Ferguson N, et al. (2020) Impact of non-pharmaceutical interventions (npis) to reduce covid19 mortality and healthcare demand.

2 Danzig R, Lipsitch M (2020) Prepare Now for the Long War Against Covid-19.
3 Park SW, Cornforth DM, Dushoff J, Weitz JS (2020) The time scale of asymptomatic transmission affects estimates of epidemic potential in the covid-19 outbreak. *medRxiv*.
4 Wu JT, Leung K, Leung GM (2020) Nowcasting and forecasting the potential domestic and international spread of the 2019-ncov outbreak originating in wuhan, china: a modelling study. *The Lancet* 395:689–697.
5 Li R, et al. (2020) Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (sars-cov2). *Science*.
6 Wu J, Leung K, Bushman M, et al. (2020) Estimating clinical severity of covid-19 from the transmission dynamics in wuhan, china. *Nature Medicine*.
7 Hadfield J, et al. (2018) Nextstrain: real-time tracking of pathogen evolution. *Bioinformatics* 34:4121–4123.

Assumptions for Age-Structured COVID-19 Model

Parameter	Meaning	Value
β_a	Asymp transmission	0.25/day (low) and 0.35/day (high)
β_s	Symp transmission	0.5/day (low) and 0.7/day (high)
$1/\gamma_e$	Mean exposed period	4 days
$1/\gamma_a$	Mean asymp period	6 days
$1/\gamma_s$	Mean symp period	10 days
$1/\gamma_h$	Mean hospital period	10 days
p	Fraction asymptomatic	0.9
$\mathcal{R}_0$	Basic reproduction number	1.85 (low) and 2.59 (high)

TABLE I: Epidemiological characteristics.

Age	Hospital Fraction	ICU (given hospitalization) Fraction
0-9	0.001	0.05
10-19	0.003	0.05
20-29	0.012	0.05
30-39	0.032	0.05
40-49	0.049	0.063
50-59	0.102	0.122
60-69	0.166	0.274
70-79	0.243	0.432
80-89	0.273	0.709
90-99	0.273	0.709

TABLE II: Age-stratified risk for COVID-19. Of note, the model assumes that 50% of ICU cases die.

Age	Fraction of Population
0-9	0.12
10-19	0.13
20-29	0.13
30-39	0.13
40-49	0.13
50-59	0.13
60-69	0.11
70-79	0.06
80-89	0.04
90-99	0.02

TABLE III: Assumed age structure of the population.