A numerical epidemic and pandemic simulation

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SIR models

One well-known way to structure an epidemic model is called SIR (for Susceptible, Infected, Recovered). Starting with an initial small number of infected cases in a fixed-size population, assume that each infected case will, on average, infect R_0 new, susceptible people. The epidemic's progress simulated by tallying the population in pools; initially everyone is susceptible. Assume each infected case has a contagious time span, or cycle time, after which the patient either recovers or dies, but anyway is no longer susceptible. Obviously if R_0 is less than 1.0, the disease will extinguish. Otherwise, the growth of infected cases is exponential until the pool of susceptible people is exhausted.

In this model, R_0 is the "naïve population" average spread rate. That is, it's the transmission rate when almost everyone is susceptible; nobody has yet recovered and become immune. As more and more people recover, the likelihood that an infected person will encounter susceptible people is diminished, so in my model the spread rate gets progressively and proportionately scaled down. This models what epidemiologists call "herd immunity".

Herd immunity effect is a very non-linear effect. Almost everyone is susceptible at first, but there are very few active infectors. As the number of active infectors becomes substantial, say 15% of the population, it will be hard for the remaining susceptible individuals to avoid encountering *someone* who is infected. Then fairly suddenly, the recovered and immune population will begin to dominate transmission behavior.

Designing an outbreak model that accounts for super-spreaders

The SIR model is often explained and written with differential equations, which can be integrated to discover how the model behaves with particular parameters. This makes mathematical sense because the change in infection at each step depends on the current number of infected people. However, that's not the most useful and instructive way to code this model, for three reasons.

- R_0 is not a single, fixed number. Some infected people transmit to many more than R_0 new cases. Why? Mild cases might fail to isolate themselves as very sick people do so. Or the disease might be transmissible for a variable period of time from case to case. Or a sick person might attend a conference. The transmission rate is some kind of probability distribution, not a fixed number. A statistical distribution of transmission rates is a nuisance to represent and solve in differential equations; and if you did that, you'd get a single "average" solution. It is more informative to run multiple, stochastic trials to get a sense of worst vs. best outcomes.
- A pandemic consists of multiple outbreaks over a wide geographic area. I wanted to extend the model to pandemics to understand how they behave differently from an individual outbreak.

- I also wanted to see what happens when an "extinguishing event" occurs, such as isolation policy being imposed, or a vaccine deployed. What does the die-out process look like? And in a multi-center outbreak, the extinguishing event might occur at different stages in different population centers.

I coded the outbreak logic of infection, transmission, and SIR pool counting explicitly as iterated cycles with numeric variables. This approach is nice because if you represent each outbreak as an independent software object, and the execution of one "cycle" step for each outbreak instance is just a method call, then you can easily run any number of simultaneous outbreaks and keep them all in sync as the epidemic progresses.

This design also allows you to explicitly draw from a random distribution of transmission rates (super-spreaders) at each cycle step. In a trivial model with fixed R_0 and *infectedPool* sick individuals on $cycle_k$, then on $cycle_{k+1}$ you would simply have *infectedPool* times R_0 new cases. In my model, in a given cycle and for each individual in the *infectedPool*, we draw a random number of transmissions from an appropriate statistical distribution. Then the total number of transmissions is the sum of all of those. If *infectedPool* has 107,831 cases, we do that 107,831 times and sum them up to get the total number of new cases.

And the design also makes it reasonably easy to model communication between separate outbreaks, e.g. travelers carrying infection to a distant center, or bringing it home.

The transmission distribution

The transmission distribution should produce rates from zero (no transmission) to some large number, with a hump in the middle. In other words it should have a long right tail. Log-normal is a reasonable model distribution for this problem, because it has the correct general shape and transmission is suitable for multiplicative events (the number of infections on the next cycle is some multiple of the number of currently active infections).

Python provides a log-normal distribution generator, to which the programmer provides the mean and standard deviation of the underlying normal distribution. In other words, Python samples from a normal distribution and returns the exponentiated result.

It was already evident that the mean transmission rate in Wuhan was ~2.5 new cases for each infection. We can take 2.5 as the mean of the exponentiated (log-normal) distribution. But since we have to tell Python the mean of the underlying normal distribution and its standard deviation before exponentiation, we can't just drop in the mean 2.5 value. We need to know what mean and sigma will generate the desired (exponentiated) mean and dispersion. Because of the long tail, you can't just use log(2.5) for the mean, although it's reasonably close. There is an equation that gives the right standard deviation for the underlying normal distribution. We can use this to generate a lot of test cases and see the generated result.

```
Desired generated distribution mean R0 = 1.10 with underlying generator dispersion = 0.80
  underlying log-rate for generator = -0.22468982019567513
It's stochastic, but for one generated, log-normal example with 100,000 incidents:
  mean spread rate =    1.1002150
  median spread rate =  0.7992286
  std deviation of spread rate distribution =  1.0357828
  spread rate range = [0.020 .. 28.958]
  80% of transmissions are generated by the top 51.7% of spreaders
```

Single-outbreak simulations

Now we can choose parameters for an outbreak and run it. I created a set of named experiments you can try, described by appropriate parameters. For example, the Wuhan/Hubei outbreak was not recognized until it was too late. In fact, the numbers from there suggest that the outbreak actually started in October or November. Isolation was imposed very late; more or less everyone got infected. We could model this as if no self-isolation had been imposed:

```
# This is probably what happened in Wuhan City / Hubei province: the outbreak ran to burnout.
# While China did impose both isolation and inter-center quarantine, it was too late there.
Wuhan =  \
        {"Experiment": "Wuhan/Hubei run to burnout",
         "population": 10.0E6,        # 10 million ~ population of Wuhan
         "herd": True,                # herd immunity effect?
         "R0": 2.5,                   # mean disease transmission rate for infected individuals
         "dispersion": 0.80,          # dispersion of underlying normal distribution for log-normal R0
         "deathRate": 0.025,          # let's hope not this bad
         "infectiousWeeks": 1,        # 1 week per infectious cycle
         "extinguishOnCycle": -1,      # -1 means no extinguishing event
         "extinguishingR0": 0.70}     # when extinguishing event occurs, spread rate falls to this number
```

```
Wuhan/Hubei run to burnout
  10 million population
  Infection cycle time 1 weeks
  Naive mean spread rate R0 is 2.50 new infections per infected individual
  Standard deviation of the generated log-normal R0 distribution ~ 2.34
  Standard deviation of the underlying Gaussian distribution is 0.80
  Death rate 2.50%
  No extinguishing event will occur
  Herd immunity effect included

Will run 20 trials
Outbreak 1 extinguished
    Week   Active   Active%  Recovered    Died    Total   Uninfected
0   0     201      0.002    98         2       301      9999799
1   1     489      0.005    294        8       791      9999310
2   2     1142     0.011    770        20      1932     9998168
3   3     2836     0.028    1884       48      4768     9995332
4   4     6967     0.070    4649       119     11735    9988365
5   5     17563    0.176    11442      293     29298    9970801
6   6     43862    0.439    28566      732     73160    9926939
7   7     109140   1.091    71332      1829    182301   9817799
8   8     267132   2.671    177744     4558    449434   9550667
9   9     637543   6.375    438197     11236   1086976  8913124
10  10    1420537  14.205   1059801    27174   2507512  7492587
11  11    2661477  26.615   2444825    62688   5168990  4831110
12  12    3210451  32.105   5039765    129225  8379441  1620659
13  13    1301105  13.011   8169955    209486  9680546  319554
14  14    103962   1.040    9438533    242014  9784509  215591
15  15    5591     0.056    9539896    244613  9790100  210001
16  16    295      0.003    9545347    244752  9790394  209706
17  17    14       0.000    9545634    244760  9790408  209692
18  18    1        0.000    9545648    244760  9790409  209691
```

I've only displayed the first of 20 trial runs here. With no intervention the outbreak always burns out, so there is little difference between the best-case and worst-case outcomes:

```
Best trial, per 10 million population:
   2,958,642 was the largest number of concurrent active infections, or 29.59% of population
   9,779,163 cases occurred by end of simulation, or 97.8% of population
     244,479 died, or 2.445% of population

Worst trial, per 10 million population:
```

```
   3,253,002 was the largest number of concurrent active infections, or 32.53% of population
   9,790,109 cases occurred by end of simulation, or 97.9% of population
     244,753 died, or 2.448% of population
```

What if early, stringent isolation had been imposed?

```
# This is what happens if isolation is imposed very early in an outbreak:
EarlyStringentIsolation = \
        {"Experiment": "Early, stringent isolation",
         "population": 10.0E6,       # 10 million ~ population of Wuhan; keep at 100 million or less to avoid long run times
         "herd": True,               # herd immunity effect?
         "R0": 2.5,                  # mean disease transmission rate for infected individuals
         "dispersion": 0.80,         # dispersion of underlying normal distribution for log-normal R0
         "deathRate": 0.025,         # let's hope not this bad
         "infectiousWeeks": 1,       # 1 week per infectious cycle
         "extinguishOnCycle": 3,     # -1 means no extinguishing event
         "extinguishingR0": 0.70}    # when extinguishing event occurs, spread rate falls to this number
```

```
Early, stringent isolation
  10 million population
  Infection cycle time 1 weeks
  Naive mean spread rate R0 is 2.50 new infections per infected individual
  Standard deviation of the generated log-normal R0 distribution ~ 2.39
  Standard deviation of the underlying Gaussian distribution is 0.80
  Death rate 2.50%
  Extinguishing event will begin on cycle 3
  Spread rate 0.70 after extinguishing event
  Herd immunity effect included

Will run 20 trials
Outbreak 1 extinguished
```

	Week	Active	Active%	Recovered	Died	Total	Uninfected
0	0	261	0.003	98	2	361	9999739
1	1	662	0.007	352	9	1023	9999077
2	2	1686	0.017	998	26	2710	9997391
3	3	1133	0.011	2642	68	3843	9996258
4	4	780	0.008	3746	96	4622	9995478
5	5	519	0.005	4506	116	5141	9994959
6	6	363	0.004	5012	129	5504	9994596
7	7	265	0.003	5366	138	5769	9994331
8	8	222	0.002	5625	144	5991	9994109
9	9	149	0.001	5841	150	6140	9993960
10	10	122	0.001	5986	153	6261	9993838
11	11	89	0.001	6105	157	6351	9993749
12	12	65	0.001	6192	159	6416	9993684
13	13	38	0.000	6256	160	6454	9993646
14	14	25	0.000	6293	161	6479	9993621
15	15	15	0.000	6317	162	6494	9993605
16	16	10	0.000	6332	162	6504	9993595
17	17	7	0.000	6342	163	6512	9993588
18	18	6	0.000	6349	163	6518	9993582
19	19	3	0.000	6355	163	6521	9993579
20	20	1	0.000	6358	163	6522	9993578
21	21	1	0.000	6359	163	6523	9993577

```
Best trial, per 10 million population:
       1,196 was the largest number of concurrent active infections, or 0.01% of population
       4,881 cases occurred by end of simulation, or  0.0% of population
         122 died, or 0.001% of population

Worst trial, per 10 million population:
       1,951 was the largest number of concurrent active infections, or 0.02% of population
       7,775 cases occurred by end of simulation, or  0.1% of population
         194 died, or 0.002% of population

Ratio of worst/best cases = 1.59
```

In [31]:

Again, I've displayed only the first trial run, and the summary of 20. This is an excellent result! Early, stringent quarantine can work.

If the dispersion had been set to zero, every trial would produce the same result. But with super-spreaders, the worst simulation trial run produced an outcome 1.6x worse than the best run. This is somewhat sensitive to the dispersion parameter. If the dispersion is 1.5 instead of 0.80, then the worst of 20 trials might be ~2.7 times worse than the best trial (again, it's stochastic).

You might wonder, can the dispersion really vary that much? Dispersion is determined not just by the nature of the virus, but also by the social and cultural environment in which it spreads. Just a few large group gatherings, such as religious gatherings, schools or universities, political rallies, or even staff meetings, can create a catastrophic outbreak.

The Jupyter workbook includes several other informative experiments. For example, you can try EarlySloppyIsolation and LateSloppyIsolation, or see the effect of an extinguishing event such as a useful anti-viral drug. You can also play with parameters yourself.

Key learnings from single-outbreak simulations

- Isolation can really work. Even somewhat sloppy isolation can save a lot of lives, although at the cost of much longer epidemic duration. Delaying isolation is a really bad mistake; even sloppy isolation is very helpful if it happens soon enough.
- Super-spreaders can make a huge difference, both in epidemic growth and extinguishment. But the effect is stochastic and therefore unpredictable. Even a soundly modeled prediction about the number of cases in a single outbreak could easily be wrong by about 2x based on stochastics alone.
- To the extent that super-spreading occurs in large group events, curtailing such exposures by isolation could dramatically improve outcomes and reduce the epidemic peak.
- Even an isolated outbreak with an extinguishing event will run down over many months. It seems unlikely that isolation alone can truly extinguish a large outbreak, because people will get impatient.
- If you see 10 deaths in a region, there might be 1,500 to 3,000 active cases in that region. If you see 100 deaths, there might be 7,000 to 15,000 cases. If you see 1,000 deaths, there might be 70,000 active cases. By the time you see deaths, the epidemic is already into the numbers of the next cycle.

Multi-center outbreaks

What happens if there are multiple outbreaks at separate population centers, when people travel between the population centers? This is a more explicit and formal definition of a pandemic. Are pandemics qualitatively different from non-communicating outbreaks? And what is the effect of a stringent, global travel quarantine?

To explore this, I coded a simulation in which N population centers (e.g. 10 centers each with 10 million people) are randomly placed in a geographic circle around the initial outbreak. I assumed that the probability of individuals traveling between pairs of centers is inverse-exponentially related to the distance between them: P(*distance*) = exp(-1.0 * *distance* / *scalefactor*) where the scale factor can be adjusted experimentally to make the probabilities quite small.

The pandemic model has its own parameters:

```
# geographic parameters for pandemic model
geoParams = {"layout": "circular",        # else it is linear
             "radius": 1000.0,            # centers randomly in a circle around ROOT outbreak
             "numOthers": 10,             # number of centers simulated in addition to the ROOT
             "distanceDecay": 80,         # probability of travel between centers =
                                           # exp(-1.0*distance/distanceDecay)
             "quarantineOnCycle": 10}     # -1 if no global quarantine
```

(If layout is not “circular”, the program creates population centers along a straight line with the distances between them increasing by powers of two. You might prefer that, as the distances between centers are deterministic instead of varying randomly from run to run.)

In the simulation, each outbreak has the same overall parameters. The central outbreak is seeded to start infecting, but the others only get infected by travelers, and the proportion of infected travelers who travel is governed by P(distance).

So what happens?

The outcome obviously depends to some extent on *scalefactor*, which is just an intellectual trick to get a range of travel probabilities. Here’s the thing: you can think of the probability of travel as a fixed, linear factor between any given pair of outbreak centers during the course of the simulation, while the outbreak growth is exponential.

Consequently, while more distant centers may start to show outbreaks later, and might not become very big if an extinguishing event occurs before they become infected, even a little coupling between outbreaks has a profound effect. In an isolated outbreak, the number of new infections (next cycle) depends only on that outbreak’s number of current active infections. But with coupling, it’s as if the infected pool for each outbreak is larger than that outbreak’s own population can generate. The net effect is to somewhat accelerate the progress of the coupled outbreaks. They may grow faster even if the coupling is weak.

Also, the whole pandemic will take longer to extinguish than an isolated outbreak, even when moderated by herd immunity, because travelers continually spread re-infections. The pandemic will grumble along at a low level for a long time. The more communicating centers there are, the longer the pandemic will persist. Depending on circumstances, there may one or more “waves” of infectious activity. And the longer the pandemic persists, the more damage will be done. In the end, almost everyone may be infected.

In contrast, a 3-center pandemic really can be effectively stopped with few total deaths, *provided that an extinguishing event occurs soon enough*.

I had been wondering about the vague definition of “pandemic” as the term is used by epidemiologists and in news articles. One gets the impression from casual language that a pandemic is just an epidemic that pops up in lots of places.

But in fact, a pandemic should be understood as “coupled outbreaks”. In coupled outbreaks, the behavior of individual outbreaks may be qualitatively different and numerically somewhat worse. The degree of coupling matters, but it is dominated by exponential growth within each outbreak center. Even with weak coupling, exponential growth increases the number of travelers very rapidly.

Another important point is that global quarantine can help, particularly in conjunction with stringent self-isolation policies. Even after the initial outbreak becomes pandemic, centers can protect themselves by applying urgent, immediate, stringent isolation. That is the situation we face in the second week of March, 2020.

With 5 or 10 centers, it isn't useful to display an entire pandemic simulation in this document; run it for yourself. Here's a quick overview of a pandemic simulation. First the simulator lays out the other outbreak centers (see embedded printout below).

Here the probability of travel matrix shows the pairwise likelihood of travel that an individual will travel between any two centers during one cycle. Or, you can think of it as the proportion of population that travels between two centers during each cycle. So on a given cycle, a center's active infections times this probability gives the number of infected travelers to another city. Of course in the real world, policy will suppress such travel. But it doesn't take many exceptions to cause a problem.

The Cycle lines give a quick summary of the number of inter-center infected travelers, and the state of each outbreak center. For example `cxxxxxxxxxx` at Cycle 0 shows one continuing outbreak (the initial ROOT infection denoted `c`) and the other centers inactive (denoted `x`). At Cycle 1 there is already a bit of spread to one other center. The symbol `b` if it appears represents an outbreak that has burned itself out, exhausting its uninfected pool. An outbreak that transitions from inactive, to continuing, back to inactive (extinguished, `x`) is a center where the outbreak was extinguished.

You can see that at the peak of the pandemic in cycle 10, there 3,819,497 infected travelers moving between outbreak centers (~3.5% of a total population of 110,000,000 in all centers). This includes infected individuals who leave a center to visit elsewhere, and uninfected travelers who become infected where they go to visit. Travelers return home at the end of each cycle.

```
Locations of other population centers
C001      531 miles from ROOT at (-382.3944693457807, -368.05686432552216)
C002      774 miles from ROOT at (-622.4970759467203, -460.5639606234544)
C003       59 miles from ROOT at (-17.4827685217192, 55.853502087787405)
C004      520 miles from ROOT at (-229.2457882212989, 466.3243142344703)
C005      409 miles from ROOT at (-165.5808838690835, 374.0999171840836)
C006      267 miles from ROOT at (-129.44121135823514, 233.2433088330062)
C007      916 miles from ROOT at (860.2985246472482, 314.95681440059843)
C008      457 miles from ROOT at (206.6390688588547, 407.4650462790592)
C009      515 miles from ROOT at (289.5312820028854, -425.34685265456665)
C010      769 miles from ROOT at (718.0891855267835, -275.46274106759137)
```

Distances between centers

	0	1	2	3	4	5	6	7	8	9	10
0	0	531	774	59	520	409	267	916	457	515	769
1	531	0	257	559	848	773	652	1418	974	674	1104
2	774	257	0	795	1007	952	851	1673	1200	913	1353
3	59	559	795	0	462	351	210	915	417	571	807
4	520	848	1007	462	0	112	254	1100	440	1032	1203
5	409	773	952	351	112	0	145	1028	374	920	1097
6	267	652	851	210	254	145	0	993	379	781	988
7	916	1418	1673	915	1100	1028	993	0	660	935	607
8	457	974	1200	417	440	374	379	660	0	837	853
9	515	674	913	571	1032	920	781	935	837	0	454
10	769	1104	1353	807	1203	1097	988	607	853	454	0

Probability of travel between centers

	0	1	2	3	4	5	6	7	8	9	10
0	1.000000	0.001314	0.000063	0.481152	0.001510	0.006013	0.035635	0.000011	0.003310	0.001610	0.000067
1	0.001314	1.000000	0.040102	0.000919	0.000025	0.000063	0.000288	0.000000	0.000005	0.000218	0.000001
2	0.000063	0.040102	1.000000	0.000048	0.000003	0.000007	0.000024	0.000000	0.000000	0.000011	0.000000
3	0.481152	0.000919	0.000048	1.000000	0.003109	0.012429	0.072652	0.000011	0.005450	0.000797	0.000042
4	0.001510	0.000025	0.000003	0.003109	1.000000	0.246397	0.042030	0.000001	0.004095	0.000003	0.000000
5	0.006013	0.000063	0.000007	0.012429	0.246397	1.000000	0.162393	0.000003	0.009359	0.000010	0.000001
6	0.035635	0.000288	0.000024	0.072652	0.042030	0.162393	1.000000	0.000004	0.008809	0.000058	0.000004
7	0.000011	0.000000	0.000000	0.000011	0.000001	0.000003	0.000004	1.000000	0.000261	0.000008	0.000505
8	0.003310	0.000005	0.000000	0.005450	0.004095	0.009359	0.008809	0.000261	1.000000	0.000029	0.000023
9	0.001610	0.000218	0.000011	0.000797	0.000003	0.000010	0.000058	0.000008	0.000029	1.000000	0.003430
10	0.000067	0.000001	0.000000	0.000042	0.000000	0.000001	0.000004	0.000505	0.000023	0.003430	1.000000

```
Cycle    0          5 travelers  cxxxxxxxxxx
Cycle    1         33 travelers  cxxcxxxxxxx
Cycle    2        136 travelers  cxxcxxcxxxx
Cycle    3        717 travelers  cxxcxccxxxx
Cycle    4       3647 travelers  cxxccccxccx
Cycle    5      17879 travelers  ccxccccxccx
Cycle    6      87768 travelers  cccccccxccx
Cycle    7     435835 travelers  cccccccxccc
Cycle    8    2082860 travelers  ccccccccccc
Cycle    9    2927962 travelers  ccccccccccc
Cycle   10    3621066 travelers  ccccccccccc
Cycle   11    3819497 travelers  ccccccccccc
Cycle   12    3455691 travelers  ccccccccccc
Cycle   13    2811512 travelers  ccccccccccc
Cycle   14    2185346 travelers  ccccccccccc
Cycle   15    1654550 travelers  ccccccccccc
Cycle   16    1210942 travelers  ccccccccccc
Cycle   17     851463 travelers  ccccccccccc
Cycle   18     573774 travelers  ccccccccccc
Cycle   19     371510 travelers  ccccccccccc
Cycle   20     235243 travelers  ccccccccccc
Cycle   21     146694 travelers  ccccccccccc
Cycle   22      90324 travelers  ccccccccccc
Cycle   23      55309 travelers  ccccccccccc
Cycle   24      34196 travelers  ccccccccccc
Cycle   25      20798 travelers  ccccccccccc
Cycle   26      12741 travelers  ccccccccccc
Cycle   27       7955 travelers  ccccccccccc
Cycle   28       4899 travelers  ccccccccccc
Cycle   29       3006 travelers  ccccccccccc
Cycle   30       1919 travelers  ccccccccccc
Cycle   31       1244 travelers  ccccccccccc
```

```
Cycle   32        838 travelers  ccccccccccc
Cycle   33        529 travelers  ccccccccccc
Cycle   34        367 travelers  ccccccccccc
Cycle   35        257 travelers  ccccccccccc
Cycle   36        178 travelers  ccccccccccc
Cycle   37        161 travelers  ccccccccccc
Cycle   38        122 travelers  cccccccxccc
Cycle   39         81 travelers  xccxccccccc
Cycle   40         62 travelers  cccxcccxccc
Cycle   41         48 travelers  cccxcccxccc
Cycle   42         44 travelers  xccxcccxccc
Cycle   43         34 travelers  xccxcccxccc
Cycle   44         26 travelers  xccxccxxccc
Cycle   45         26 travelers  cccxxcxxccc
Cycle   46         28 travelers  cccxxcxxccc
Cycle   47         22 travelers  cccxxxxxccc
Cycle   48         18 travelers  xccxcxxxcxc
Cycle   49         13 travelers  xccxxxxxcxc
Cycle   50         10 travelers  xccxxxxxcxc
Cycle   51          8 travelers  xccxxxxxcxx
Cycle   52          6 travelers  xccxxxxxcxx
Cycle   53          5 travelers  xccxxxxxcxx
Cycle   54          5 travelers  xccxxxxxxxx
Cycle   55          3 travelers  xccxxxxxcxx
Cycle   56          2 travelers  xccxxxxxcxx
Cycle   57          2 travelers  xccxxxxxcxx
Cycle   58          2 travelers  xccxxxxxxxx
Cycle   59          2 travelers  xccxxxxxxxx
Cycle   60          4 travelers  xccxxxxxxxx
Cycle   61          5 travelers  xccxxxxxxxx
Cycle   62          3 travelers  xccxxxxxxxx
Cycle   63          1 travelers  xccxxxxxxxx
Cycle   64          2 travelers  xccxxxxxxxx
Cycle   65          1 travelers  xccxxxxxxxx
Cycle   66          1 travelers  xcxxxxxxxxx
Cycle   67          1 travelers  xcxxxxxxxxx
Cycle   68          0 travelers  xcxxxxxxxxx
Cycle   69          0 travelers  xcxxxxxxxxx
Cycle   70          0 travelers  xcxxxxxxxxx
Cycle   71          0 travelers  xcxxxxxxxxx
```

Key learnings from multi-center pandemic simulations

- When there is travel between outbreak centers, the effect on exponential growth is as if each center had a somewhat larger population of active infections at each cycle. The number of infected cases at the next cycle is some multiple of the active infections in the current cycle, so pandemics can cause accelerated growth in each center, compared to isolated centers. This acceleration can cause an outbreak to run to burnout before an extinguishing policy, vaccine etc. takes effect.

- Even a small degree of coupling can produce significant effects, especially with super-spreader statistics. Each coupling coefficient (travel probability) between outbreak pairs is just a fixed attenuation, which will ultimately be swamped by exponential growth in the outbreaks.

- This emphasizes the importance of reducing or eliminating international links and domestic travel; but for that to work, it needs to be treated as an urgent, persistent, emergency policy action. There isn't a lot of time to think about it. Isolation alone is not enough. Contagion control within each outbreak center is even more important. Stay home. Don't go out.

- In a coupled system, leaks in the isolation barriers matter. Travel restrictions can help, but probably can't eliminate the disease until a substantial degree of "herd immunity" is established, when most people have already been infected and recovered.

- As a pandemic extinguishes, expect sporadic new cases at any population center until all of them are quiescent. Coupling implies that a pandemic will extinguish more slowly than an isolated outbreak.

- The combination of super-spreaders and a range of global government policies and reaction times means that the outcome is genuinely unpredictable, but doesn't have to be catastrophic everywhere.

How valid is this simulation model?

I think this model is qualitatively pretty good, and generally correct structurally. It's obviously possible to create more detailed models, such as agent-based ones, but they would have more parameters and assumptions, making their validity much harder to assess.

The general conclusions and range of outcomes of this model make sense until an exponential flash-fire begins to consume everyone. Initially, the actively infected percentage of the population is quite small; but uncontrolled, it can suddenly explode in just three or four cycles. If the epidemic progresses to the degree 10% - 15 % of a population are currently active, infectious cases, then all bets are off. That is terrifying.

On the other hand, draconian isolation will be imposed long before that. And during the summer, if people stay outside and physically far apart, avoid unnecessary exposure, and pay attention to hygiene, then the spread rate can be much lower.

I have a hunch that real-life herd immunity might prove less suppressive than this model indicates because when the actively infectious population becomes very large, every uninfected person has so many opportunities to become infected.

In what ways could this model be too pessimistic?

It's discouraging that the following ameliorating factors are either relatively small effects, or quite far in the future. Epidemic growth is exponential, so being off even substantially on the simulation parameters will at most make delay the outcome by a few transmission cycles.

First, the death rate might be lower than the assumed 2.5% of the simulation parameters. If many infections are mild, this could be true, and I suspect it is, simply because children don't get very sick from this virus. On the other hand we can't be sure; once you see a death, the epidemic has advanced to the next cycle. Only population-wide antibody sampling can determine the truth here.

Second, while this particular virus is very infectious, behavior matters. We can somewhat reduce the transmission rate behaviorally. That would buy time.

Third, there are already a couple of candidate coronavirus vaccine "platforms". Maybe one of them will work sooner rather than later. The challenge with vaccines is to develop enough immune response to be protective, without that response being too aggressive and therefore harmful. I read a report saying that was a problem with SARS vaccines.

Fourth, the model is stochastic. The worst will not necessarily transpire. The future still offers a substantial range of possibilities.

So what about our current situation?

I am very disturbed by the lack of urgency that I see, particularly at local government levels which seem to be waiting for the states to tell them what to do.

- *First*, it is extremely important to impose isolation within regional outbreaks, and quarantine between them, as soon as effectively as possible. Draconian policies can work. Otherwise the number of cases and deaths could easily be much greater and faster than even pessimists expect.

  Such policies should extend down to regional and municipal governments. Every opportunity to avoid super-spreading is precious.

- *Second, test, test, test!* It is critical to understand where, geographically, things are starting to blow up so that we can try to suppress transmission by isolation and quarantine. I'm reluctant to admit it, but the Chinese have been very intelligent and focused in using apps to track people who have been near other people who have been near active infectors. We might be able to do something similar on a voluntary basis. Even if coverage isn't 100%, the data sampling would be valuable and useful.

- *Third*, no effort and expense should be spared to create an extinguishing event: either an anti-viral drug or a vaccine. Every day counts. Probably some drugs will arrive before any vaccine, but substantial risks are justified to test a promising vaccine candidate. The risk of a dud or dangerous vaccine must be weighed against the exponential certainty of the pandemic.

- *Fourth*, this pandemic seems likely to smolder and persist for much longer than markets and pundits expect. Isolation and quarantine can reduce the total toll and peak health care load, but only by extending the life of the pandemic.

- *Fifth*, the numbers really are big. My simulations are per 10 million population. We are a country of 360 million. There is no way to avoid health care system overload.