A brief theory of epidemic kinetics

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In the context of the COVID-19 epidemic, and on the basis of the Theory of Dynamical Systems, we propose a simple model for the expansion of contagious diseases, with a particular focus on viral respiratory tracts. The infection develops through contacts between contagious and exposed people, with a rate proportional to contact duration and turnover, inversely proportional to the efficiency of protection measures, and balanced by the average immunological response. The obvious initial exponential increase is readily hindered by the size reduction of the exposed population. The system converges towards a stable attractor whose value is expressed in terms of the ratio C/D of contamination vs decay factors. Decreasing this ratio below a critical value leads to a tipping point beyond which the epidemic is over. By contrast, significant values of C/D may bring the system through a bifurcating hierarchy of stable cycles up to a chaotic behaviour.

Keywords: epidemic; COVID-19; contamination kinetics; immunological response; dynamical systems; reproduction rate; critical state; attractor; stable cycle; chaos.

1. Introduction

In the beginning of 2020, we started experiencing the so-called COVID-19, an unprecedented epidemic, at least since the "Spanish Flu" in 1918-1919. In spite of considerable scientific and medical advances since then, most countries seem to be overtaken by the epidemic development, and unable to predict, even qualitatively, when and in which way it may recede and possibly disappear.

Understanding the kinetic evolution of infectious diseases is a long lasting challenge. As soon as in the beginning of the XXth century [1,2], a basis for theoretical modeling was established, particularly in terms of population groups experiencing the different infectious stages of the epidemic.

Such approaches were subsequently extended and refined, incorporating for instance host demography and migrations, as well as diffusion and mutation of infectious agents [3].

Another and quite recent example [4] is a detailed analysis of the COVID-19 outbreak in Wuhan. A set of differential equations describe the evolution of the traditional four types of populations, Healthy, Exposed, Infected and Recovered (HEIR). The equations are parametrized using reported cases, and solved numerically in order to estimate the number of unreported cases and to predict the epidemic evolution.

On the other hand, it is well known that a fundamental characteristic of the evolution of complex non-linear systems is the extreme sensitivity to initial conditions, as first discovered by Henri Poincaré [5]. In the case of epidemic dynamics, this sensitivity makes difficult long term predictions and standard system stability analysis [6].

However, due to the highly non-linear nature of the dynamics, even simple models may reveal the possible occurrence of complex behaviours, which standard local stability analyses may not be able to detect. Simple models are also useful to understand and validate basic control parameters of epidemic expansion.

In this spirit and on the basis of the Theory of Dynamical Systems, we propose here a simple and general model for expansion and possible recession of contagious epidemics. Using assumptions fairly similar to (but simpler than) HEIR ones, we look for the possible attractor(s) of the system, the influence of its finite size on their position, the necessary conditions to bring the reproduction factor below 1, and the possible occurrence of multi-stable cycles and chaotic behaviour.

2. Contamination kinetics:

We study an epidemic starting at a given time and place, from a contamination of a human being, following for instance a mutation of an animal virus. The infection is gradually transmitted to other people around, resulting in a contaminated area (cluster).

By contrast for instance with condensation of water vapour into droplets, the "energy" of the interface that separates the cluster from the remainder of the population is zero. There is no physical restriction against cluster growth, which is only governed by exchange kinetics of infectious agents. The critical size in the sense of nucleation-growth processes is therefore also zero, which means that a cluster made of only two individuals is already unstable and may grow spontaneously. The interfacial energy being zero, the cluster is also likely to expand in space with a fractal structure (e.g. romanesco structure), that favours exchange mechanisms between contagious and exposed people by an optimization of the exchange interface.

Let us consider at a given time a total population of N individuals, a number N_C of them being contagious. The remainder (N-N_C) is made of healthy people (i.e. still not contaminated), but also of those who were contaminated, have recovered, and are or are not protected any more by a possible long-term immunization. Neglecting the number of fatalities (about 2% in the case of COVID-19), the number of exposed people (i.e. liable to infection) may therefore be written $N - \theta N_C$, where the coefficient $\theta \leq 1$ is taken equal to one in the case of total long-term immunization.

We therefore assume that the contamination rate $(dN_C/dt)^+$ is proportional to the product $N_C(N - \theta N_C)$ of the number of contagious individuals by that of those liable to infection in close contact with them at a given time. It is also taken proportional to the duration δt of the contact, to the turnover rate ν of exposed / contagious pairs, and inversely proportional to protection efficiency p (e.g. mask wearing, lockdown measures, and so forth).

The contamination rate is also controlled by the activity of the infectious agent. In the case of viral respiratory tract diseases, it is sometimes stated that viruses develop in winter season, and get asleep, or at least less active, in summer. This might be due to enhanced UV radiation and air dryness in summer, but this point is still debated. In this state of uncertainty, we shall introduce this supposed influence through a seasonal virus activity factor S taken equal to 1 for "season-insensitive" epidemics, and otherwise proportional to a "season parameter" S varying sinusoidally with time:

$$S = \frac{1}{2}\left[1 + \cos\left[2\pi(t/12)\right]\right] = \frac{1}{2}\left[1 + \cos\left[\pi t/6\right]\right] \tag{1}$$

where t is the time in months, starting in December in the northern hemisphere. Thus, the season parameter S would decrease from 1 in December down to 0 in July, and start increasing again in autumn, and is kept equal to 1 if virus activity is constant throughout the year.

The <u>contamination</u> evolution equation can be written:

$$\left(\frac{dN_c}{dt}\right)^+ = (\nu\,\delta t/p)S\,N_c(N - \theta N_c)$$
$$= C\,N_c(N - \theta N_c) \tag{2}$$

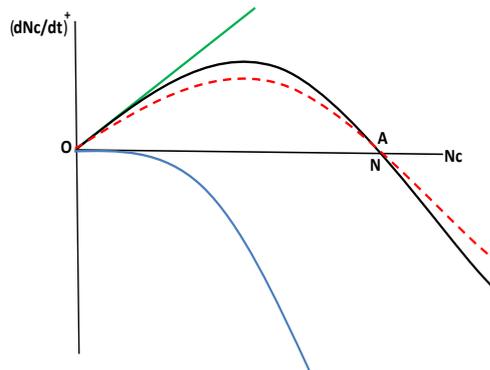as illustrated by the black solid curve in Figure 1.

Figure 1: Contamination kinetics $(dN_C/dt)^+$ vs N_C. *The green line represents the linear term of equation (2), and the blue curve the negative quadratic term. The black solid curve $(dN_C/dt)^+$ is the sum of these two terms. It intersects the horizontal axis at an attractor A and a repulsor O (see text). Starting from any N_C value, the system always converges to A, corresponding to $N_C = N$ where all people are contaminated. Reducing the contamination factor C flattens the curve (dashed red parabola), decreasing the average contamination rate, but not the final number of contaminated people.*

In this situation where no decay factor (negative feed-back) is introduced, as soon as the first individual has been contaminated, the system enters the positive $(dN_C/dt)^+$ (growth) zone (usually called attraction basin of A), that inexorably brings it to A where all people are contaminated.

The run from O to A may take some time. An indicator for the epidemic growth rate is the <u>instantaneous</u> value of $(dN_C/dt)^+$, which goes through a maximum at $N_C = N/2$, before decreasing down to zero at A. The decrease obviously results from the fact that, as the epidemic propagates, the reservoir of exposed people goes down.

Reducing the contamination factor C of equation (2) flattens the solid black parabola into the dashed red one in Figure 1, decreasing the average contamination rate. In this case, the system is still expected to converge at $N_C=N$, but the average epidemic growth rate being lower, the progress toward the attractor would take a longer time. Among the contamination factors considered, S may have a periodic evolution in time (equation 1). In htiscase, the red dashed curve in Figure 1 would oscillate from the solid red curve in winter to zero in summer.

3. Decay kinetics and global evolution:

We have now to introduce an infection decay term. The contamination decay rate is taken proportional to the number N_C of contaminated individuals, and is controlled by the strength of the "short term" immunological answer D, that may be understood as the average reciprocal lifetime $(1/\tau)$ of viruses hosted by individuals (or alternatively the average lifetime of the infected patient!).

$$\left(\frac{dN_c}{dt}\right)^- = DN_c \tag{3}$$

The global evolution equation is thus obtained combining equations (2) and (3), and schematized in Figure 2:

$$\frac{dN_c}{dt} = \left(\frac{dN_c}{dt}\right)^+ - \left(\frac{dN_c}{dt}\right)^-$$
$$= C N_c (N - \theta N_c) - DN_c \tag{4}$$
$$= (CN - D)N_c - C\theta N_c^2$$

As compared to Figure 1, due to the introduction of the decay term, the attractor now corresponds to a N_C value N* lower than N (red curve). The N* value is easily found from equation (4), solving the equation:

$$\frac{dN_c}{dt} = (CN - D)N_c - C\theta N_c^2 = 0$$

whose non-zero solution is:
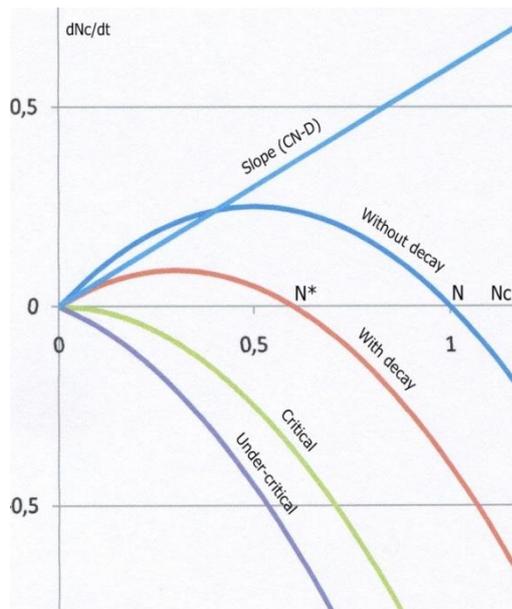
$$N* = \frac{CN - D}{C\theta} \tag{5}$$

Figure 2: Epidemic growth kinetics. *(dN/dt) is shown without infection decay (blue parabola) and with infection decay (red parabola). Incorporating the decay term D makes the attractor shift to a lower stable number N*. Increasing D further, the attractor at N* and the repulsor O may merge, resulting in the green parabola for which O becomes an attractor with a number of infected people equal to zero (critical point). A further increase of D would result in a parabola with a negative slope from the start (under-critical case). In early epidemic stages, the red curve may be approximated by the blue tangent at the origin, of slope CN-D, corresponding to an exponential increase with time of the number of infected people (see paragraph 5).*

As compared to Figure 1, a lower proportion of people would be contaminated in the new attractor equilibrium. N* decreases for higher immunological response D and long-term immunity θ, as intuitively expected. An important point is that this stable number of contaminated people is a "dynamical" steady state in which recovering people are continuously replaced by new contaminated ones, a fraction of them being always vulnerable to death. Reducing N* would therefore decrease the occupancy rate of hospital beds.

The green parabola in Figure 2 illustrates the limiting case where the decay factor is strong enough to bring the attractor to the origin O. For a precise value of D indeed, the attractor of the red curve merges with the repulsor O, reducing to zero the epidemic development. This situation occurs for N*=0, or, using equation (5):

$$\frac{D}{C} = N \tag{6}$$

Remarkably, this condition is independent of the long-term immunity factor θ.

In this case dN_C/dt is negative everywhere. The new attractor O corresponds to a number of contaminated people equal to zero from the very first attempt of the epidemic development. This situation where D/C=N is equivalent to the critical transition in a nuclear reaction, at which the neutron reproduction rate, usually named R_O, is equal to 1. In this critical state, only one of the two neutrons produced by every fission of a Uranium nucleus is able (in average) to trigger the fission of another Uranium nucleus, and so forth. For $R_O<1$

(undercritical situation), the system remains under control, whereas for $R_O>1$ (overcritical situation), it diverges and the nuclear explosion takes place.

In our case, using equation (6), we have:

$$R_0 = \frac{NC}{D} \qquad\qquad (7)$$

For $R_O>1$ (large contamination, low immunological response), the number of infected people starts increasing exponentially with time, but its growth ("explosion") is gradually hindered by the decreasing available amount of exposed individuals. In a same way, $R_O<1$ corresponds to the undercritical case: every chain reaction gradually slows down and eventually vanishes; the epidemic is over, at least as long as R_O is kept low enough. If not, a new epidemic would be liable to start again somewhere and develop, unless long-term immunity has developed, or efficient vaccines have been produced meanwhile.

It is worth noting, from equation (7), that an epidemic propagating in a larger population N would require a more stringent limitation of C/D (in particular stronger protection measures) to be controlled, as intuitively expected from the non-linear nature of contamination kinetics. In other words, provisional confinement of people in smaller areas would help controlling the epidemic.

4. Early epidemic stages and corresponding mitigation measures

At the very beginning of the epidemics, the reservoir of exposed people ($N-\theta N_C$) is large as compared to N_C. The term ($N-\theta N_C$) in equation (4) may be approximated by N, and equation (4) writes:

$$\frac{dN_c}{dt} = (CN - D)N_c \qquad\qquad (8)$$

corresponding to the blue straight line of Figure 2 with a slope CN-D. As expected, the long-term immunity factor θ does not appear in this early stage of contamination .

Integration of equation (8) shows that such a linear dependence of the derivative dN_C/dt vs N_C corresponds to an exponential increase of N_C with time as mentioned above, at least as long as (CN-D) is positive (i.e. $R_O>1$). This is observed <u>in early stages</u> of COVID-19 epidemic in most countries, as shown in [7], and represented by straight lines if the number of infected people is plotted vs time in a semi-logarithmic scale.

Reducing the contamination term C (for instance by containment measures) and increasing the immunological response D brings the reproduction factor R_O below 1, stopping the epidemic propagation, as already found in the general case (equations (6) and (7)), and shown for instance in [8].

5. Convergence towards the attractor, a possible route to chaos?

We shall now investigate the different possible types of convergence to the attractor N* shown in Figure 2. The system might indeed converge either monotonically to the attractor, or to a limit cycle, or even possibly experience a transition to a chaotic behavior [9-11]. For

this purpose, we shall use so-called "logistic maps", a simple and quite efficient technique to solve this type of problem.

We start from the global evolution equation (equation 4), written for the sake of simplicity:

$$dx/dt = \alpha\, x - \beta\, x^2 \tag{9}$$

with α=CN-D and β=Cθ. We discretize this equation into a recursive relation considering finite time steps δt=1 corresponding to steps δx for x. Starting from an initial value x_0, the evolution of x with time can be obtained by the recursive relation:

$$
\begin{aligned}
x_{n+1} &= x_n + \delta\, x_n \\
&= x_n + \left(\alpha\, x_n - \beta\, x_n^{\,2}\right) \\
&= (1+\alpha)x_n - \beta\, x_n^{\,2}
\end{aligned}
\tag{10}
$$

associated with a "functional relation":

$$f(x) = (1+\alpha)x - \beta\, x^2 \tag{11}$$

The fixed points of the system are obtained setting $x_{n+1}=x_n$, or equivalently:

$$f(x) = x = (1+\alpha)x - \beta\, x^2 \tag{12}$$

giving:

x=0 and x=x*=α/β   (13)

It is obvious from equation (12) that fixed points can be represented in a f(x) vs x graph by the intersections of the f(x) curve with the diagonal line with unit slope, as shown for instance in Figure 3.

From equation (11), the slope f'(x) of f(x) is:

$$f'(x) = (1+\alpha) - 2\beta\, x \tag{14}$$

Using equations (13) and (14), we obtain the slope at the fixed points:

f'(0)=1+α, and f'(x*)=1-α   (15)

We shall now use the recursive relation (equation 10) to determine the various behaviours of the system as it approaches the fixed points.

The first example corresponds to α=-0.5 and β=0.2. On the logistic map of Figure 3, x_n values are represented on the horizontal axis, and x_{n+1} ones on the vertical axis. We start the iteration from $x_n=x_0=1.4$ from which we draw a vertical line. It intersects the red parabola giving $x_1=0.32$. A horizontal line drawn from this intersection to the blue diagonal with unit slope transfers x_1 back to the horizontal axis, from which a second iteration is performed, and so forth. The successive x_n values obtained by such iterations are represented by the thin staircase line, that eventually converges to the origin O which is (in this example) the unique fixed point. This is the undercritical case, corresponding to $R_o<1$.
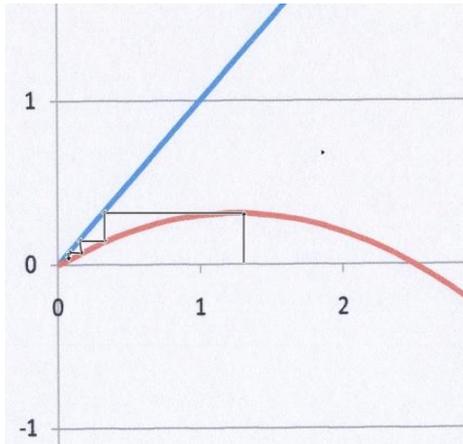
Figure 3: Logistic map for α=-0.5 and β=0.2. *The origin O is the only fixed point, towards which the system converges.*

The second example (Figure 4) corresponds to α=1.2, β=0.6. In this case, there are two fixed points as shown by equation (13). Starting from x_0=0.5, the iteration converges to the fixed point at x* = α/β = 1.2/0.6 = 2.0, which is an attractor, whereas O is clearly a repulsor. In addition, the trajectory to x* is monotonic as in Figure 3.
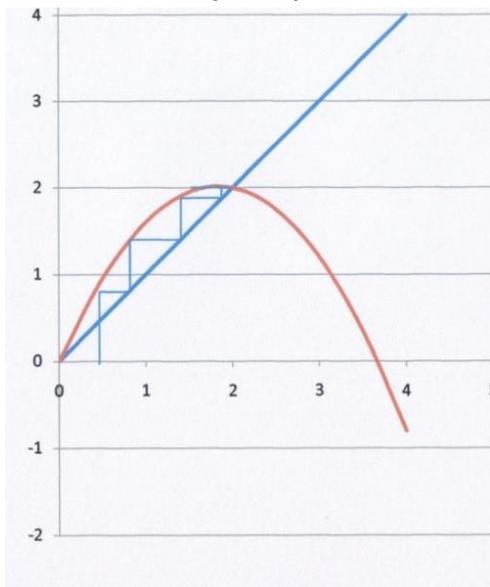

Figure 4: Logistic map for α=1.2, β=0.6. *O is now a repulsor, and the system converges monotonically towards the attractor at* x=2*.*

The third example (Figure 5) corresponds to α=2.1, β=1. Starting from x_0=0.3 (black lines), the system does not converge to x*, but instead to a so-called "limit cycle" for which *x* oscillates between two different values on both sides of the attractor (bi-stable state). Starting from x_0=2.8 (green lines) the system also converges to the same limit cycle, though after a larger number of iterations. This kind of result is geometrically obvious as soon as the slope of the parabola at *x** becomes lower than (-1). In Figure 5, the slope at *x** is indeed (-1.1 < -1). It can be shown [9-11] that decreasing further *f'(x*)* (as α goes up) may drive the system through a bifurcating hierarchy of multi-stable cycles, that eventually leads to a tipping point and a chaotic behaviour.
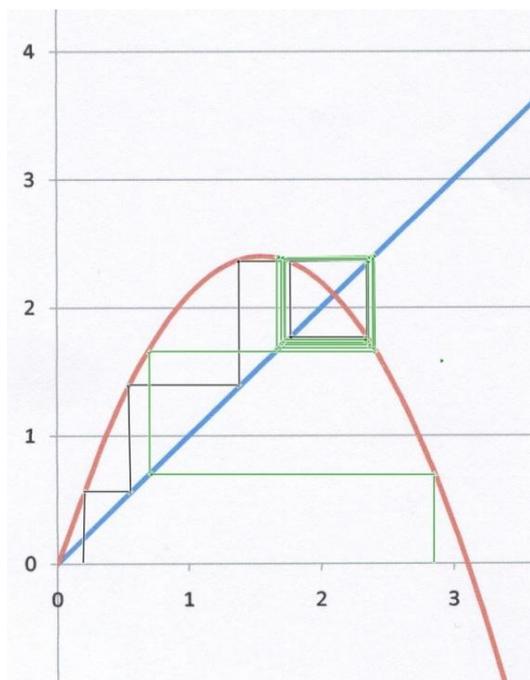
Figure 5: Logistic map for α=2.1, β=1. *The slope of the parabola at x=x* (which is still an attractor) is now less than -1, leading to a bi-stable limit cycle, whatever the starting point (black or green lines).*

Since α=CN-D, such a trajectory toward deterministic chaos is favoured by a high contamination factor C, and a low decay rate D. As already mentioned in paragraph 3, a larger population N would worsen the situation.

A possible consequence of this result is that a sudden decrease of protection factors, as for instance during a rapid release of containment measures that would bring R_o to a value well above 0, is liable to trigger strong instabilities that might be difficult to control, since needs for emergency hospital beds may suffer large periodic or, even worse, chaotic variations. In this case, a subdivision of infected areas into smaller isolated ones may bring the system back to a more stable and manageable situation. In any case, the post-crisis release of protection policies should be conducted in a gradual and controlled manner. Other possible consequences of such a route to chaos are worth being studied.

6. Conclusion

We applied standard methods used in the theory of dynamical systems to investigate kinetics of epidemics propagation.

As infection extends through exchanges of infectious agents between contagious and exposed people, the net increase rate dN_C/dt of contaminated people results from a competition between two terms: i) a contamination factor proportional to both the number of contagious individuals and the number of those still liable to infection, and ii) a decay factor related to recovery kinetics of contaminated individuals.

The contamination factor involves the duration and turnover frequency of pair contacts, the protection efficiency (e.g. lockdown measures, mask wearing), a long-term immunity factor, and the possible seasonal variations of virulence of infectious agents. The decay factor is controlled by the strength of the short-term immunological answer.

The system converges to a steady state attractor at which contamination and decay factors balance each other. The larger are the contamination factor C and the smaller the short-term immunological response D and the long-term immunity factor θ, the higher would be the steady state number of contaminated people, as intuitively expected. However, this would not be the end of contamination events, since in this stage recovering people are continuously replaced by new contaminated ones. A decrease of the number of such people would help manage the occupancy of hospital beds.

Decreasing drastically the difference between contamination and decay factors (CN-D=α) may lead to a tipping point beyond which the epidemic is actually over, at least as long as such measures are applicable, or as long as the long-term immunity of the population (possibly helped by vaccination) has increased enough to be able to take over the lack of protection measures. On the opposite, a sudden increase of α, for instance through a too rapid release of confinement measures, may bring the system through a bifurcating hierarchy of stable cycles to a chaotic behaviour, whose management would result problematic. In both cases, the α factor varies linearly with the involved population N, pointing out the fact that small isolated areas (everything equal otherwise) remain safer than larger ones.

Acknowledgements:

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