

The global stability of a epidemiological model with n strain "all coronavirus mutations"

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Abstract

In this work, we have constructed a new system of differential equations which mathematically models infectious diseases with several mutations. (such as covid 19 disease and their mutations). Therefore, we are interested in studying the asymptotic stability of our new system.

1 Introduction

After the appearance of the disease Covid 19 and after a small period of time, several mutations of the disease it appeared because of a change on the ADN of the virus. Most mutations have little or no effect on the properties of the virus, see [1]. However, some mutations can affect the properties of the virus and influence, for example, the ease with which it spreads, the severity of the disease it causes, or the effectiveness of vaccines, drugs, diagnostic tools or other social and public health measures.

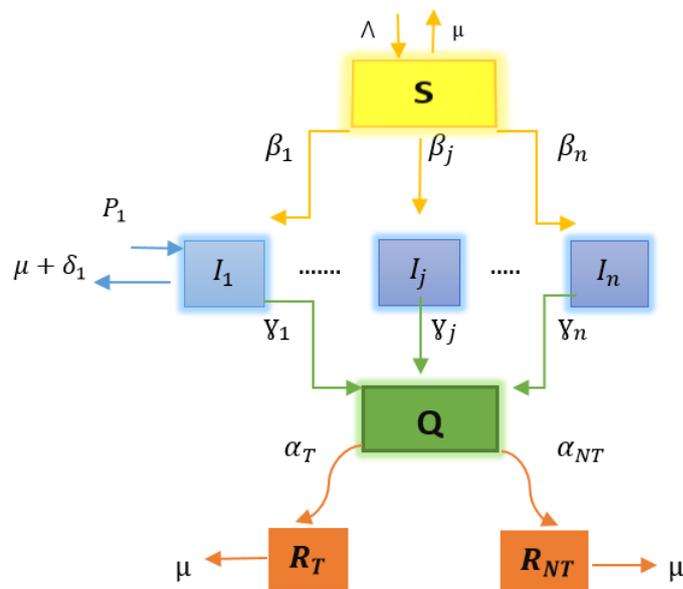
The latest variants of concern have largely supplanted other SARS-CoV-2 variants that were circulating at the same time. The Delta variant accounted for nearly 90% of all viral sequences submitted in October 2021, and Omicron is currently the dominant variant worldwide, accounting for > **98%** of viral sequences after February 2022. As transmission of these variants of concern has persisted, there has been significant internal evolution. Since being designated as a variant of concern by WHO on November 26, 2021, viruses within the Omicron complex have continued to evolve and their descendant lineages exhibit different constellations of genetic mutations. The constellations may or may not differ in terms of the risk they pose to public health, and further research on each lineage with substitutions at key sites may be needed to determine whether or not its characteristics differ from those that define the variant of concern from which it originated.

We are interested in clustering all Covid 19 mutations in an epidemiological model so that at the end we study the asymptotic stability (our approach

is based on a functional Lyapunov) and give a threshold condition for the disease that disappears or spreads for the epidemic model as a function of the base reproduction rate R_0 .

2 Diagram transmission of all mutation Covid-19 between humans :

Some of the emergence of Corona disease and the infection of many people in the whole world with it and for a short time, then a mutated appearance of this disease called ‘British Variant, omecron, delta,...’. Moreover, the new idea in our article is to divide the people who are exposed to the disease into alot of categories, a category that has previously contracted the omicron anoder mutation like delta .



Description of biological parameters :

- S : The susceptible individuals of covid-19.
- I_i : The individuals infected by covid 19 mutations each strain i for one mutation (omecron delta,...).
- R : The individuals withdrawn (healed or dead).

- β_i The rate of individuals who become infected by the mutation of covid-19.
- γ_i : Infection rate of Q class.
- α_T, α_{NT} : Recovery rate.
- μ : Natural mortality rate .
- Λ_N : Birth rate.

This diagram can translated mathematically by the following system of differential equations :

$$(1) \left\{ \begin{array}{l} \dot{S} = \Lambda - \sum_{i=1}^n \beta_i S I_i + \sum_{i=1}^n \psi_i I_i - \mu S \\ \dot{I}_i = \beta_i S I_i - \gamma_i I_i - \mu I_i - \delta_i I_i + P_i I_i \\ \dot{Q} = \sum_{i=1}^n \gamma_i I_i Q - (\alpha_1 + \alpha_2) Q - \mu Q \\ \dot{R}_T = \alpha_1 Q - \mu R_T \\ \dot{R}_{NT} = \alpha_2 Q - \mu R_{NT} \end{array} \right.$$

The system (1) is provided with the initial conditions :

$$S(0) = S_0 > 0, \quad I(0) = I_0 > 0, \quad Q(0) = Q_0 > 0, \quad R_T(0) = R_{T_0} > 0, \quad R_{NT}(0) = R_{NT_0} > 0.$$

And,

$$N = S_0 + I_0 + Q_0 + R_{T_0} + R_{NT_0}$$

3 Global existence, positivity and limitation of the solution :

Proposition :

Given $(S_0, I_0, Q_0, R_{T_0}, R_{NT_0}) \in \mathbb{R}^5$, there is a unique solution to the problem (1) defined on $[0, +\infty)$ and this solution rest non négative and bounded $\forall t \geq 0$.

Proof :

We put,

$$X(t) = \begin{pmatrix} S(t) \\ I(t) \\ Q(t) \\ R_T(t) \\ R_{NT}(t) \end{pmatrix}$$

and,

$$F : \mathbb{R}^5 \longrightarrow \mathbb{R}^5$$

$$F \begin{pmatrix} S(t) \\ I(t) \\ Q(t) \\ R_T(t) \\ R_{NT}(t) \end{pmatrix} = \begin{pmatrix} \Lambda - \sum_{i=1}^n \beta_i S I_i + \sum_{i=1}^n \psi_i I - \mu S \\ \beta_i S I_i - \gamma_i I_i - \mu I_i - \delta_i I_i + P_i I_i \\ \sum_{i=1}^n \sigma_i I_i Q - (\alpha_1 + \alpha_2) Q - \mu Q \\ \alpha_1 Q - \mu R_T \\ \alpha_2 Q - \mu R_{NT} \end{pmatrix}$$

The system is in the following form :

$$X'(t) = F(X(t)), \quad \forall t \geq 0$$

with,

$$X(0) = X_0 = \begin{pmatrix} S_0 \\ I_0 \\ Q_0 \\ R_{T_0} \\ R_{NT_0} \end{pmatrix}$$

We observe that F is a vector polynomial function. Then, it is class C^∞ . So, it locally lipschitzian. We deduce that there is a unique local solution defined on $[0, T_{max})$, where T_{max} is the maximum existence time.

Now, we show the positivity of the solution, we have :

$$\begin{aligned}\frac{dS(t)}{dt}\Big|_{S=0} &= \Lambda + \sum_{i=1}^n \psi_i I \geq 0 \\ \frac{dI(t)}{dt}\Big|_{I=0} &= 0 \geq 0 \\ \frac{dQ(t)}{dt}\Big|_{Q=0} &= 0 \geq 0 \\ \frac{dR_T(t)}{dt}\Big|_{R_T=0} &= \alpha_1 Q \geq 0 \\ \frac{dR_{NT}(t)}{dt}\Big|_{R=0} &= \alpha_2 Q \geq 0\end{aligned}$$

and since the initials conditions are positives, then we deduce the positivity of the local solution.

Finally, we establish the boundary of the solution.
the set

$$\Omega = \{(S, Q, I, R_T, R_{NT}) \in \mathbb{R}^5, S + Q + I + R_T + R_{NT} \leq \frac{\Lambda_N}{\mu}\}$$

is compact and positively invariant by the system (1).

Proof :

Let $(S_0, I_0, Q_0, R_{T0}, R_{NT0}) \in \Omega$ and let $(S, I, Q, R_T, R_{NT}) \in \mathbb{R}_+^5$ then the differential equation of the total population is given by :

$$\frac{dN(t)}{dt} = \frac{d}{dt} (S(t) + I(t) + Q(t) + R_{NT}(t) + R_T(t)) = \Lambda_N - \mu N(t).$$

Using the formula for the variation of the constant, the solution of the equation is given by

$$N(t) = \exp(-\mu t) \left(N_0 - \frac{\Lambda_N}{\mu} \right) + \frac{\Lambda_N}{\mu}, \quad \forall t \in [0, T_{max}]$$

With,

$$N_0 = N(0) = S_0 + I_0 + Q_0 + R_{T0} + R_{NT0} \leq \frac{\Lambda}{\mu}.$$

Consequently, $N(t) \leq \frac{\Lambda}{\mu}$, that is to say, $S(t) + I(t) + Q(t) + R_T(t) + R_{NT}(t) \leq \frac{\Lambda_N}{\mu}$.

Hence, Ω is positively invariant.

Mereover, $S(t), Q(t), I(t), R_T(t), R_{NT} \in [0, \frac{\Lambda N}{\mu}]$, $\forall t \in [0, T_{max}]$.

We conclude that $T_{max} = +\infty$

4 Equilibrium :

4.1 Disease free equilibrium (DFE) :

We search $\bar{S} \geq 0$, $\bar{I} \geq 0$, $\bar{Q} \geq 0$, $\bar{R}_T \geq 0$ et $\bar{R}_{NT} \geq 0$ satisfying :

$$\begin{cases} 0 = \Lambda - \sum_{i=1}^n \beta_i \bar{S} \bar{I}_i + \sum_{i=1}^n \psi_i \bar{I}_i - \mu \bar{S} \\ 0 = \beta_i \bar{S} \bar{I}_i - \gamma_i \bar{I}_i - \mu \bar{I}_i - \delta_i \bar{I}_i + P_i \bar{I}_i \\ 0 = \sum_{i=1}^n \gamma_i \bar{I}_i \bar{Q} - (\alpha_1 + \alpha_2) \bar{Q} - \mu \bar{Q} \\ 0 = \alpha_1 \bar{Q} - \mu \bar{R}_T \\ 0 = \alpha_2 \bar{Q} - \mu \bar{R}_{NT} \end{cases}$$

With, $\bar{I} = 0$ We obtain : $\bar{S} = \frac{\Lambda}{\mu}$, $\bar{Q} = 0$, $\bar{R}_T = 0$ et $\bar{R}_{NT} = 0$.

Therefore,

$$E_0 = \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0 \right)$$

4.2 Calcul of R_0 : (Method of van den Driessche watmough) :

We denote by :

- $\mathcal{F}_j(S, I, Q, R_{NT}, R_T)$ the rate of newly infected in the compartment j.
- $\mathcal{V}_j(S, I, Q, R_{NT}, R_T)$ the transfer rate of an individual from one compartment to another everywhere average.

The matrices \mathcal{F} and \mathcal{V} are represented by :

$$\mathcal{F} = \begin{pmatrix} 0 \\ \beta_i S I_i + P_i I_i \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

And,

$$\mathcal{V} = \begin{pmatrix} \Lambda - \beta_i S I_i + \psi_i I_i - \mu S \\ -(\gamma_i + \mu + \delta_i) I_i \\ \gamma_i I_i Q - (\alpha_1 + \alpha_2) Q - \mu Q \\ \alpha_1 Q - \mu R_T \\ \alpha_2 Q - \mu R_{NT} \end{pmatrix}$$

The calculation of their respective Jacobian at the disease free equilibrium

point $\mathbf{E}_0 = (\frac{\Lambda}{\mu}, 0, 0, 0, 0)$ given :

$$\mathcal{F}(\mathbf{E}_0) = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\beta_i \Lambda}{\mu} + P_i & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

$$\mathcal{V}(\mathbf{E}_0) = \begin{pmatrix} -\mu & -\frac{\beta_i \Lambda}{\mu} + \psi_i & 0 & 0 & 0 \\ 0 & -(\gamma_i + \mu + \delta_i) I_i & 0 & 0 & 0 \\ 0 & 0 & -(\alpha_1 + \alpha_2 - \mu) & 0 & 0 \\ 0 & 0 & \alpha_1 & -\mu & 0 \\ 0 & 0 & \alpha_2 & 0 & -\mu \end{pmatrix}$$

The basic reproduction rate is the spectral radius of the matrix $-\mathcal{F}\mathcal{V}^{-1}$ the calculation given :

$$R_0 = \frac{\beta_i \Lambda + P_i \mu}{\mu(\alpha_1 + \alpha_2 + \mu)}$$

4.3 Endemic equilibrium (EE) :

The system (1) has n endemic equilibrium.

Be $(S, I_1, \dots, Q, R_T, R_{NT}), \dots, (S, \dots, I_n, Q, R_T, R_{NT})$

For $\bar{I} > 0$. Using the second equation of the system we get :

$$\bar{S} = \frac{\gamma_i + \mu + \delta_i - P_i}{\beta_i}$$

By considering the first equation of the system we obtain :

$$\bar{I} = \frac{\mu(\gamma_i + \mu + \delta_i - P_i) - \Lambda\beta_i}{\beta_i(\mu_i - \gamma_i - \mu - \delta_i + P_i)}$$

Using the third equation of the system we get :

$$\bar{Q} = 0$$

According to the fourth equations we obtain :

$$\bar{R}_T = 0$$

According to the 6 equation of the system we obtain :

$$\bar{R}_{NT} = 0$$

Therefore, the endemic equilibrium point given by :

$$E = \left(\frac{\gamma_i + \mu + \delta_i - P_i}{\beta_i}, \frac{\mu(\gamma_i + \mu + \delta_i - P_i) - \Lambda\beta_i}{\beta_i(\mu_i - \gamma_i - \mu - \delta_i + P_i)}, 0, 0, 0 \right)$$

6 Global stability of the disease free equilibrium :

We know that, the basic reproduction rate is a dimensionless quantity which measures the ability of an infectious agent to spread infection through a given population immediately after without introductions, In addition, from a mathematical point of view it allows under certain conditions to establish the stability either local or global of a point of equilibrium of a dynamic system.

the basic reproduction number for the complete system is the maximum of all the basic reproduction numbers taken individually

$$R_0 = \max_{i=0,\dots,n} R_{0,i}$$

In our epidemiological model we have n strain so it is difficult to control the disease by the basic reproduction rate, and it is not the basic reproduction rate that determines the destion of a strain,this is why we associate with

each strain i which models such a mutation of covid 19 a threshold which depends on the personal parameter for strain i , which helps us to properly control the spread of each strain i . Moreover, the strain that maximizes its threshold wins the competition.

Thus, we can speak of a maximization of a single but not of a maximization of basic reproduction rate

Border balance $(\bar{S}_i, \mathbf{0}, \dots, \bar{I}_i, \mathbf{0} \dots \mathbf{0})$ is in Ω if and only if

$$\xi_{0,i} = \frac{\mu(\gamma_i + \mu + \delta_i - P_i)}{\beta_i \Lambda}$$

is it clear that

$$\xi_{0,i} > 1 \Leftrightarrow R_{0,i} > 1$$

Therefore, $\xi_{0,i}$ is a threshold, and we have

$$\bar{S}_i = \frac{S^*}{\xi_{0,i}} \text{ and } \bar{I} = \frac{\mu(\gamma_i + \mu + \delta_i - P_i)}{-\beta_i(\gamma_i + \mu + \delta_i - P_i) + \gamma_i \beta_i - P_i \gamma_i} \left(1 - \frac{1}{\xi_{0,i}}\right),$$

$$\bar{Q} = 0$$

Without loss of generality, let's remember that, $R_0 = \max_{i=0, \dots, n} R_{0,i}$ and $\xi_0 = \max_{i=0, \dots, n} \xi_{0,i}$, moreover, we have seen that, $\xi_0 \Leftrightarrow R_0$

since each strain in our system has its own threshold which depends on the rate concerned, it is preferable to use the threshold of each strain ξ_0 , to properly study the overall stability of our system.

Theorem :

If $\xi_0 \leq 1$, the DFE is globally asymptotically stable in the positive orthant. if $\xi_0 > 1$, the DFE est instable.

Proof :

Consider the following Lyapunov function :

$$V = \sum_{i=0}^n I_i$$

To prove the asymptotic stability, we will use the Lasalle invariance principle. We have,

$$\dot{V} = (\gamma_i + \mu + \delta_i - P_i)(\xi_{0,i} - 1) \leq 0$$

consider the set contained in Ω where $\dot{V} = 0$, moreover we associate to each subset \mathcal{I} . A point defined by if $j \notin \mathcal{I}$ so $I_j = 0$ and if $i \in \mathcal{I}$ so $S = \bar{S}_i$

Consider the largest invariant set contained in Ω

We affirm than for any solution in Ω . We have $\dot{I}_i = 0$. By invariance $\dot{S} = 0$, thus

$$\Lambda - \mu \frac{S^*}{\xi_{0,i}} = \sum_{i \in I} \left(\beta_i \frac{S^*}{\xi_{0,i}} - (\gamma_i - P_i) \right) I_i = \sum_{i \in I} (\mu + \delta_i) I_i$$

If, $\xi_{0,i} < 1$ cannot be satisfied in the positive orthant, we see that \mathcal{I} is such that, $\xi_{0,i} = 1$ this still implies $I_i = 0$ by invariance.

6 Global stability of the endemic equilibrium (EE) :

We assume that $R_0 > 1$ or equivalently $\xi_0 > 1$

Theorem :

Under the assumption $\xi_{0,1} > \xi_{0,i}$ for $i = 2, \dots, n$ the endemic equilibrium is globally asymptotically stable on the intersection of the positive orthant with the two open half-spaces defined by the inequalities $S > 0$ and $I_1 > 0$

Proof :

Consider the following Lyapunov function :

$$\begin{aligned} V(S, I, Q) = & S - \bar{S} \log S + \frac{\mu + \delta_1}{\mu + \delta_1 + \gamma_1 - P_1} (I_1 - \bar{I}_1 \log I_1) \\ & + \sum_{i=2}^n \left(1 - \frac{\gamma_i - P_i}{\beta_i S} \left(\frac{\xi_{0,i}}{\xi_{0,1}} \right)^2 \right) I_i + Q + K \end{aligned}$$

with

$$K = -\bar{S} + \bar{S} \log \bar{S} - \frac{\mu + \delta_1}{\mu + \delta_1 + \gamma_1 - P_1} (\bar{I}_1 - \bar{I}_1 \log \bar{I}_1)$$

The derivative of V along the trajectories of system (1) is given by :

$$\begin{aligned} \dot{V} = & (Q - \bar{Q})(\gamma_i I_i - (\alpha_1 + \alpha_2) - \mu) \\ & (\mu \bar{S} + (\mu + \delta_1) \bar{I}_1 + (\gamma_1 - P_1) I_1) \left(2 - \frac{S}{\bar{s}} - \frac{\bar{S}}{S} \right) \\ & + \sum_{i=2}^n (\gamma_i - P_i - \beta_i S - \frac{\bar{S}}{S} (\gamma_i - P_i - \beta_i S)) I_i + C \end{aligned}$$

with,

$$C = \sum_{i=2}^n \left(1 - \frac{\gamma_i - P_i}{\beta_i S} \left(\frac{\xi_{0,i}}{\xi_{0,1}} \right)^2 \right) (\beta_i S I_i - (\gamma_i + \mu + \delta_i - P_i)) I_i$$

Note B the sum of the last two terms in \dot{V} and using the relation we find :

$$B = \sum_{i=2}^n (\gamma_i - P_i) + \beta_i \bar{S} - \frac{\bar{S}}{S} (\gamma_i - P_i) - \frac{(\beta_i \bar{S})^2 \xi_{0,1}}{\gamma_i - P_i \xi_{0,i}} - (\gamma_i - P_i) \left(\frac{\xi_{0,i}}{\xi_{0,1}} \right)^2 + (\gamma_i - P_i) \left(\frac{\xi_{0,i}}{\xi_{0,1}} \right)^3$$

since $\gamma_i - P_i \leq \gamma_i - P_i + \mu + \delta_i = \beta_i \bar{S} \frac{\xi_{0,1}}{\xi_{0,i}}$ for $i = 2, \dots, n$ we prove that $B \leq 0$ using the inequalities between the arithmetic and geometric means, we get $\dot{V} \leq 0$

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