PARADOXICAL PHENOMENA AND CHAOTIC DYNAMICS IN EPIDEMIC MODELS SUBJECT TO VACCINATION

ALFONSO RUIZ HERRERA
Departamento de Matemáticas, Universidad de Oviedo
Oviedo, Spain

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ABSTRACT. An alternative to the constant vaccination strategy could be the administration of a large number of doses on “immunization days” with the aim of maintaining the basic reproduction number to be below one. This strategy, known as pulse vaccination, has been successfully applied for the control of many diseases especially in low-income countries. In this paper, we analytically prove (without being computer-aided) the existence of chaotic dynamics in the classical SIR model with pulse vaccination. To the best of our knowledge, this is the first time in which a theoretical proof of chaotic dynamics is given for an epidemic model subject to pulse vaccination. In a realistic public health context, our analysis suggests that the combination of an insufficient vaccination coverage and high birth rates could produce chaotic dynamics and an increment of the number of infectious individuals.

1. Introduction. The complete eradication of some diseases, such as malaria, rubella, or measles, is one of the main challenges of the World Health Organization (WHO) in the 21st century [1, 28, 11, 3, 13]. All countries have difficulties in the eradication of these epidemics despite the availability of adequate vaccination programs. The main obstacle in industrialized countries is the presence of regions with higher levels of susceptibility, that is poor neighbourhoods with reduced access to health programs [1]. In developing countries, the main difficulties are the limited health infrastructure and the high birth rates [11, 3, 13]. The common control of these diseases is to immunize infants before they reach a specific age cohort which is normally less than three years [15, 1]. These programs require a rather high vaccination coverage for complete eradication which is a non-viable effort in developing countries [11, 3, 13]. A possible alternative for this goal could be the administration of a large number of vaccination doses on “immunization days” with the aim of maintaining the basic reproduction number below one [26, 29]. This strategy is known as pulse vaccination and it has been successfully applied for the control of poliomyelitis and measles in Central America, poliomyelitis in India, measles in UK, etc [1, 26, 5, 21, 22, 25]. The main advantage of the pulse vaccination is its relative low cost. More importantly, under the pulse vaccination, a complete eradication of the disease is possible and the whole population need not receive a second dose.
This is in contrast to the current strategy of two doses (1 and 3 years) for measles in the industrialized countries.

Many scientific papers have studied the dynamics of a population subject to pulse vaccination from theoretical and applied perspectives [26, 9, 17, 8, 6, 23, 30, 4]. A paradigm with practical implications is the presence of chaotic dynamics in many epidemics [6, 23]. Although there have been many advances, the biological mechanisms that generate these erratic patterns are not understood well yet. To fill this gap, the aim of this paper is to derive sufficient conditions for the existence of chaotic dynamics in the classical SIR model with pulse vaccination. It is well-known that in the absence of vaccination, the model presents a “threshold dynamics” [15, 16]: the basic reproduction number (that depends on the relevant parameters of the model) determines whether the epidemic persists or there is global eradication of the disease. Our results suggest that this dynamic is not maintained under the strategy of pulse vaccination. We stress that our results are based on mathematical theorems and rigorous proofs (without being computer-aided). In fact, we propose a new geometrical construction to prove chaotic dynamics that could be applied to other biological situations.

The motivation for this paper comes from the optimum design of vaccination programs [10, 12]. Adding a pulse campaign, or even replacing cohort immunization with a pulse program, requires a previous analysis on the expected risks and costs. In addition, it is crucial to find the weakest pulse vaccination design that would still succeed with the minimum number of interventions. In a realistic public health context, our results indicate that the combination of an insufficient vaccination coverage and the presence high birth rates could produce erratic patterns and an increase in the number of infectious individuals. In other words, when the vaccination coverage is not enough to eradicate the disease, the periodic nature of the pulses becomes an external force which could have negative effects on the population. These erratic outbreak dynamics have been broadly tested in the treatment of some diseases in low-income countries [11, 3]. Another recommendation from our results is the design of vaccination campaigns with the intervention time being as short as possible. This recommendation is in agreement with the one provided by WHO in the eradication of the polio [14].

The structure of this paper is as follows. Initially, in Section 2, we collect some well-known properties of the classical SIR model with pulse vaccination. Then, in Section 3, we analyze the role of the intervention time on the eradication of the epidemic. Some of these results have been already deduced by Agur et al., Stone and collaborators, and Donofrio in [8, 29, 26]. In Sections 4 and 5, we state and prove the main theorems of the paper. The mathematical construction to detect chaotic dynamics that have been employed here could also be applied to other biological contexts. Finally, in the last section, we discuss the implications of our results.

### 2. The classical SIR model with pulse vaccination

We analyze the dynamic behavior of a population which consists of susceptible, infected, and recovered individuals. The dynamics of this population is modelled by

\[
\begin{align*}
S' &= \lambda - \mu S - \beta SI \\
I' &= \beta SI - (\gamma + \mu)I \\
R' &= \gamma I - \mu R.
\end{align*}
\]

(1)
where, $\lambda$ is the birth rate, $\mu$ denotes the death rate of the susceptible individuals, $\beta$ represents the contact rate, and $\gamma$ is the recovery rate \cite{16, 15}. The analysis of (1) can be reduced to the study of the following:

\[
\begin{align*}
S' &= \lambda - \mu S - \beta SI \\
I' &= \beta SI - (\gamma + \mu)I.
\end{align*}
\]

(2)

It is well-known that the basic reproduction number

\[ R_0 = \frac{\beta \lambda}{\mu(\gamma + \mu)} \]  

(3)

determines the dynamical behavior of (2): The endemic equilibrium

\[ \left( \frac{\lambda}{\mu}, 0 \right) \]  

(4)

is a global attractor provided $R_0 > 1$ whereas there is global attraction to the disease free equilibrium

\[ \left( \frac{\lambda}{\mu}, 0 \right) \]  

(5)

when $R_0 < 1$ \cite{16, 15}.

The pulse vaccination control consists of the periodic vaccination of a fraction $q \in (0, 1)$ of the susceptible population each of $T$ years \cite{9, 26, 29, 1}. A susceptible individual, after vaccination, enters into the recovered group. Following these considerations, model (1) is transformed into the following:

\[
\begin{align*}
S' &= \lambda - \mu S - \beta SI \\
I' &= \beta SI - (\gamma + \mu)I \\
R' &= \gamma I - \mu R
\end{align*}
\]

(4)

with

\[
\begin{align*}
S(nT^+) &= (1-q)S(nT^-) \\
R(nT^+) &= qS(nT^-) + R(nT^-).
\end{align*}
\]

(5)

As usual, $S(nT^-)$ and $S(nT^+)$ are the proportions of susceptible individuals at the moment immediately before and after the $n$th vaccination pulse has been administered \cite{26, 9, 17, 8, 6}. In more mathematical terms,

\[
S(nT^-) = \lim_{\varepsilon \to 0^+} S(nT - \varepsilon) \quad \text{and} \quad S(nT^+) = \lim_{\varepsilon \to 0^+} S(nT + \varepsilon).
\]

A solution of model (4)-(5) with initial condition $(S_0, I_0, R_0) \in [0, \infty)^3$ is function $(S(t), I(t), R(t)) : [0, \infty) \to \mathbb{R}_{+}^3$ that has the following properties:

- $(S(0), I(0), R(0)) = (S_0, I_0, R_0)$.
- $(S(t), I(t), R(t))$ is a solution of the system of differential equations (4) for all $t \in (nT, (n+1)T)$ with $n \in \mathbb{N}$.
- $\lim_{t \to nT^+} S(t) = \lim_{t \to nT^-} (1-q)S(t)$, $\lim_{t \to nT^+} R(t) = \lim_{t \to nT^-} qS(t) + R(t)$.

We observe that $I(t)$ is a continuous function and $S(t), R(t)$ are continuous except for $t = nT$ with $n \in \mathbb{N}$. More importantly,

\[
\begin{align*}
S' &= \lambda - \mu S - \beta SI \\
I' &= \beta SI - (\gamma + \mu)I
\end{align*}
\]

(6)

with

\[ S(nT^+) = (1-q)S(nT^-) \]  

(7)

suffice to describe the dynamical behavior of model (4)-(5).
In this paper, we work with the map
\[ A : [0, \infty)^2 \rightarrow [0, \infty)^2 \]  
\[ A(S_0, I_0) = (A_1(S_0, I_0), A_2(S_0, I_0)) = ((1 - q)S(T; (S_0, I_0)), I(T; (S_0, I_0))) \]  
where, \( (S(t; (S_0, I_0)), I(t; (S_0, I_0))) \) is the unique solution of (6) with initial condition \((S_0, I_0)\). This map represents the population densities of susceptible and infectious individuals at the moment immediately after the first administration of the pulse vaccination. An important point to be noted is that \( A \) can be written as follows:
\[ A(S_0, I_0) = ((1 - q)S(T; (S_0, I_0)), I_0 e^{\int_0^T \beta S(t; (S_0, I_0)) dt - (\gamma + \mu)T}). \]  
An analogous map that also determines the dynamical behaviour of (6)-(7) is
\[ B : [0, \infty)^2 \rightarrow [0, \infty)^2 \]  
\[ B(S_0, I_0) = (B_1(S_0, I_0), B_2(S_0, I_0)) = (S(T; ((1 - q)S_0, I_0)), I(T; ((1 - q)S_0, I_0))) \]  
In this case, \( B(S_0, I_0) \) represents the population densities of susceptible and infectious individuals at the moment immediately before the second vaccination pulse is administered. The main difference between the maps \( A \) and \( B \) is the time in which we count the number of individuals of each group of population. For the map \( A \), we apply system (6), then the vaccination and finally we count the population. However, for the map \( B \), we apply the vaccination, followed by the system (6), and finally we count the population. Evidently, the dynamic behavior of both maps is the same because they are topologically conjugated. For further detail,
\[ H^{-1} \circ A \circ H = B \]  
with \( H(x, y) = ((1 - q)x, y) \). To see this property, we simply realize that \( A = H \circ \phi \) and \( B = \phi \circ H \) where \( \phi : [0, \infty)^2 \rightarrow [0, \infty)^2 \) denotes the Poincaré map of system (6) at time \( T \), that is
\[ \phi(S_0, I_0) = (S(T; (S_0, I_0)), I(T; (S_0, I_0))). \]  
The reader can consult [18] for some properties related to impulsive differential equations.

3. Some basic properties of the model. From this section onward, we focus our attention on the dynamic behavior of the discrete system
\[ \begin{align*}
S_{n+1} &= A_1(S_n, I_n) \\
I_{n+1} &= A_2(S_n, I_n)
\end{align*} \]  
with initial condition \((S_0, I_0) \in (0, \infty)^2 \) (see (8) for the definition of \( A = (A_1, A_2) \)). The equation
\[ S'(t) = \lambda - \mu S(t) \]  
can be explicitly solved and so we obtain that
\[ A_1(S_0, 0) = (1 - q)[e^{-\mu T}(S_0 - \lambda_\mu) + \lambda_\mu]. \]  
The non-trivial fixed point of \( A \) on the axis \( \{(S_0, I_0) : I_0 = 0\} \) is \((\tilde{S}, 0)\) with
\[ \tilde{S} = \frac{\lambda(1 - q)(1 - e^{-\mu T})}{\mu(1 - (1 - q)e^{-\mu T})}. \]
By a simple analysis, we can prove that $\tilde{S} > 0$ is a global attractor in $(0, \infty)$ for the discrete equation

$$S_{n+1} = A_1(S_n, 0).$$

The eigenvalues of the Jacobian matrix of $A$ at $(\tilde{S}, 0)$ are $(1 - q)e^{-\mu T}$ and

$$\Upsilon = \exp\left(\int_0^T \beta S(t; (\tilde{S}, 0)) - (\gamma + \mu) dt\right),$$

$S(t; (\tilde{S}, 0)) = e^{-\mu t}(\tilde{S} - \frac{\lambda}{\mu}) + \frac{\lambda}{\mu}$ (see Expression (9)). It is important to note that the eigenvectors associated with $\Upsilon$ are the sub-space spanned by a vector $(v_1, v_2)$ with $v_2 \neq 0$. Thus, if $\Upsilon < 1$, $(\tilde{S}, 0)$ is a local attractor and $\Upsilon > 1$, $(\tilde{S}, 0)$ is a local saddle point. In fact, by using the results obtained in [8], we can conclude that $(\tilde{S}, 0)$ is a global attractor of (11) if and only if $\Upsilon < 1$.

In a practical situation, it is desirable to have the value of $\Upsilon$ as small as possible (especially less than 1) with the minimum number of interventions. We note that $\Upsilon$ indicates the velocity of attraction to the disease free equilibrium when $\Upsilon < 1$.

After simple computations,

$$\Upsilon(q, T) = \exp\left(\frac{-q\beta\lambda}{\mu^2} \frac{1 - e^{-\mu T}}{1 - (1 - q)e^{-\mu T}} + T\left[\beta\left(\frac{\lambda}{\mu}\right) - (\gamma + \mu)\right]\right).$$

We have introduced the dependence on $q$ and $T$ in order to derive biological insights from this map. If $R_0 < 1$ (see Expression (3)) then $0 < \Upsilon(q, T) < 1$ for all $q > 0$ and $T > 0$. Biologically, if the epidemic is eradicated in Model (2), the introduction of vaccination does not alter it (see Fig. 1 Left). However, if the epidemic is endemic in system (2), the performance of the vaccination is quite subtle. A noticeable result is that less interventions can produce smaller values of $\Upsilon(q, T)$.

To understand this phenomenon, we first notice that $\Upsilon(q, 0) = 0$, $\frac{\partial \Upsilon}{\partial T}(q, 0) < 0$, and

$$\lim_{T \to \infty} \Upsilon(q, T) = \infty,$$

(see Fig. 1 Right). Therefore, for each $q_0 \in (0, 1)$, there exists a minimum of
Υ(₀,𝑇) that is attained at a positive time 𝑇_{opt}. Moreover, there is an interval (0, 𝑇_{thre}) so that Υ(₀,𝑇) < 1 for all 𝑇 ∈ (0, 𝑇_{thre}). These properties imply that for each ₀, the optimum time of intervention is 𝑇_{opt}. In other words, introducing a 𝑇-periodic vaccination scheme in (2) with 𝑇 < 𝑇_{opt} will produce more interventions on the population which could lead to a slower eradication of the epidemic. A similar discussion was carried out in [1, 29] but the authors focused on situations in which 𝐼′(𝑡) < 0 for all 𝑡 > 0, see also [8].

4. Statement of the main results. In this section, we show that an unsuitable vaccination program can produce chaotic dynamics and increase the number of infectious individuals at the same time. To state this result in mathematical terms, we rewrite (6)-(7). Given  > 0, we employ the notation

\[ \lambda = k₁ ₀, \quad \beta = k₂ ₀, \quad q = k₅ ₀ \]

with

\[ k_i > 0 \text{ for all } i = 1, 2, 3, 4, 5. \]

One can recall that if \( R₀ = \frac{λβ}{μ(γ+μ)} > 1 \) (or \( R₀ = \frac{k₁k₄}{k₂(k₃+k₂ ₀)} > 1 \)), the endemic equilibrium

\[ (S*, I*) = \left( \frac{λ}{μR₀}, \frac{μ}{β}(R₀ - 1) \right) \]

is a global attractor of System (2). In the sequel, we argue as follows: we fix the parameters \( k₁, ..., k₅ \) in advance and move the parameters \( ₀ > 0 \) and \( T > 0 \).

**Theorem 4.1.** Fix \( k_i > 0 \) for all \( i = 1, ..., 5 \) with

\[ \frac{k₁k₄}{k₂(k₃+k₂ ₀)} > 1. \quad (13) \]

Then, there exists \( T^* > 0 \) with the following property: for each \( T > T^* \), we can find \( 0 < < 1 \) so that the map \( A \) associated with (6)-(7) has chaotic dynamics on two symbols relative to two disjoint compact sets \( K₀ \) and \( K₁ \) provided \( 0 < < \). Moreover,

\[ K₀ ∪ K₁ ⊂ \{ (S, I) ∈ (0, ∞)^2 : I > I* \}. \quad (14) \]

**Remark 1.** The conclusion of the previous theorem also holds true for the map \( B \). That is, if we fix \( k_i > 0, ₀, \) and \( T \) satisfying the conditions of Theorem 4.1 then, \( B \) has chaotic dynamics on two symbols relative to two disjoint compact sets \( \tilde{K}_0 \) and \( \tilde{K}_1 \) with

\[ \tilde{K}_0 ∪ \tilde{K}_1 ⊂ \{ (S, I) ∈ (0, ∞)^2 : I > I* \}. \quad (15) \]

The precise definition of chaotic dynamics is given in the next section. Notice that condition (13) means that \( R₀ > 1 \) for all \( 0 < < 1 \). A remarkable fact is that the map \( A \) admits an invariant set \( Λ \) with chaotic dynamics contained in the set in which the number of infected individuals is greater than the infected individuals without vaccination, (see (14) and Theorem 2.2 in [20]). As indicated in Remark 1, this fact is not affected by the time in which we count the population. The reader can consult [6] for numerical simulations about chaotic dynamics and paradoxical phenomena in the classical SEIR model with pulse vaccination.

5. Proof of Theorem 4.1. The proof of this theorem is divided into five steps. First, we give some mathematical background on chaotic dynamics. Then, we employ several changes of variables in the system. Finally, we propose a new geometrical construction to generate chaotic dynamics in model (6)-(7).
5.1. Mathematical tools. In this section we give the precise definition of chaotic dynamics and the tools that we use in the paper. The results and definitions are taken from [20], (see also [24, 19]).

Definition 5.1 (Definition 2.2 in Medio et al. [20]). Consider \((\mathcal{J},d)\) a metric space and \(D \subset \mathcal{J}\) an open set. We say that a continuous map \(\psi: D \rightarrow \mathcal{J}\) induces chaotic dynamics on two symbols if there exist two disjoint compact sets \(K_0, K_1 \subset D\) such that, for each two-sided sequence \((s_i)_{i \in \mathbb{Z}} \in \{0,1\}^\mathbb{Z}\), there exists a corresponding sequence \((\omega_i)_{i \in \mathbb{Z}} \in (K_0 \cup K_1)\) such that
\[
\omega_i \in K_{s_i} \quad \text{and} \quad \omega_{i+1} = \psi(\omega_i) \tag{16}
\]
for all \(i \in \mathbb{Z}\), and, whenever \((s_i)_{i \in \mathbb{Z}}\) is a \(k\)-periodic sequence (that is, \(s_{i+k} = s_i\) for all \(i \in \mathbb{Z}\)) for some \(k \geq 1\), there exists a \(k\)-periodic sequence \((\omega_i)_{i \in \mathbb{Z}} \in (K_0 \cup K_1)^\mathbb{Z}\) satisfying (16).

This definition guarantees the common properties of chaotic dynamics such as sensitive dependence on the initial conditions and the presence of an invariant set \(\Lambda\) being transitive and semiconjugate with the Bernoulli shift. In addition, our definition of chaos guarantees the existence of periodic points of any period. The reader can consult [20], specially Theorem 2.2, for a list of properties of maps satisfying Definition 5.1 and a deep comparison with other definitions of chaotic dynamics.

Next we give some notions related to the method of stretching along the paths.

Definition 5.2. Consider a set \(\mathcal{R}\) homeomorphic to \([0,1] \times [0,1]\). We say that the pair \(\tilde{\mathcal{R}} = (\mathcal{R}, \mathcal{R}^-)\) is an oriented topological rectangle if \(\mathcal{R}^- = \mathcal{R}^-_l \cup \mathcal{R}^-_r\) where \(\mathcal{R}^-_l\) and \(\mathcal{R}^-_r\) are two disjoint compact arcs contained in the boundary of \(\mathcal{R}\).

Definition 5.3. Take \((\mathbb{R}^2, \| \cdot \|)\) with the Euclidean distance. Given two oriented rectangles \(\tilde{\mathcal{R}} := (\mathcal{R}, \mathcal{R}^-)\) and \(\tilde{\mathcal{B}} := (\mathcal{B}, \mathcal{B}^-)\) with \(\mathcal{B}, \mathcal{R} \subset \mathbb{R}^2\) and a compact set \(\mathcal{K} \subset \mathcal{R}\), we say that a continuous map
\[
\psi: D \subset \mathbb{R}^2 \rightarrow \mathbb{R}^2
\]
\((\mathcal{K}, \psi)\) stretches \(\tilde{\mathcal{R}}\) and \(\tilde{\mathcal{B}}\) along the paths and write
\[
(\mathcal{K}, \psi): \tilde{\mathcal{R}} \rightarrow\leftarrow \tilde{\mathcal{B}}
\]
if the following condition holds: for every path \(\gamma: [0,1] \rightarrow \mathcal{R}\) such that \(\gamma(0) \in \mathcal{R}^-_l\) and \(\gamma(1) \in \mathcal{R}^-_r\), there exists a sub-interval \([t', t'']\) \(\subset [0,1]\) so that
\[
\gamma(t) \in \mathcal{K}, \quad \psi(\gamma(t)) \in \mathcal{B}
\]
for all \(t \in [t', t'']\) and moreover, \(\psi(\gamma(t'))\) and \(\psi(\gamma(t''))\) belongs to different components of \(\mathcal{B}^-\).

Theorem 5.4 (Theorem 2.3 in [20]). Consider \(\psi: D \rightarrow \mathbb{R}^2\) a continuous map and \(\tilde{\mathcal{R}} = (\mathcal{R}, \mathcal{R}^-)\) an oriented rectangle as above. Assume that there are two disjoint compact sets \(K_0, K_1\) such that
\[
(\mathcal{K}_i, \psi): \tilde{\mathcal{R}} \rightarrow\leftarrow \tilde{\mathcal{R}} \quad \text{for all } i = 0, 1,
\]
then \(\psi\) induces chaotic dynamics on two symbols relative to \(K_0 \cup K_1\).
5.2. Changes of variable. For each $0 < \epsilon < 1$, we know that $R_0 > 1$ by condition (13). Therefore, the endemic equilibrium of system (2) exists. Inspired by Smith’s paper [27], we first employ the change of variable

$$x = \frac{S - S_\ast}{\beta S_\ast I_\ast} \quad \text{and} \quad y = \frac{I - I_\ast}{I_\ast}$$

that transforms system (6)-(7) into

$$\begin{cases}
x'(t) = -y(t) - \mu x(t) - \beta I_\ast (1 + y(t))x(t) \\
y'(t) = \beta^2 I_\ast S_\ast x(t)(1 + y(t))
\end{cases} \quad (17)$$

with

$$x(nT^+) = (1 - q)x(nT^-) - \frac{q}{\beta I_\ast}. \quad (18)$$

Notice that

$$\begin{aligned}
\beta I_\ast &= k_2 \epsilon \left( \frac{k_1 k_4}{k_2 (k_3 + k_2 \epsilon^2)} - 1 \right) \rightarrow 0 \\
\beta^2 I_\ast S_\ast &= k_1 k_4 \left( 1 - \frac{k_2 (k_3 + k_2 \epsilon^2)}{k_1 k_4} \right) \rightarrow k_1 k_4 - k_2 k_3 \\
\frac{q}{\beta I_\ast} &= \frac{k_5}{k_2 \left( \frac{k_1 k_4}{k_2 (k_3 + k_2 \epsilon^2)} - 1 \right)} \rightarrow k_1 k_4 - k_2 k_3
\end{aligned} \quad (19)-(21)$$

as $\epsilon \rightarrow 0^+$. In system (6), the region $[0, \infty)^2$ is transformed into $[\frac{1}{\beta I_\ast}, \infty) \times [-1, \infty)$. Moreover, the equilibrium $(S_\ast, I_\ast)$ is carried out to $(0, 0)$. Using the notation of the beginning of the previous section, we can re-write model (17)-(18) as

$$\begin{cases}
x'(t) = -y(t) - k_2 \epsilon x(t) - k_2 \epsilon \left( \frac{k_1 k_4}{k_2 (k_3 + k_2 \epsilon^2)} - 1 \right) (1 + y(t))x(t) \\
y'(t) = k_1 k_4 \left( 1 - \frac{k_2 (k_3 + k_2 \epsilon^2)}{k_1 k_4} \right) x(t)(1 + y(t))
\end{cases} \quad (22)$$

with

$$x(nT^+) = (1 - k_5 \epsilon)x(nT^-) - \frac{k_5}{k_2 \left( \frac{k_1 k_4}{k_2 (k_3 + k_2 \epsilon^2)} - 1 \right)}. \quad (23)$$

For each $\epsilon \in [0, 1)$, we define $AC_\epsilon$ as

$$AC_\epsilon(x_0, y_0) = ((1 - q)x(T; (x_0, y_0)) - \frac{q}{\beta I_\ast}, y(T; (x_0, y_0)))$$

where $(x(t; (x_0, y_0)), y(t; (x_0, y_0)))$ is the solution of (22) with initial condition $(x_0, y_0)$. This map is continuous with respect to $\epsilon \in [0, 1)$. For $\epsilon = 0$, system (22)-(23) is

$$\begin{cases}
x'(t) = -y(t) \\
y'(t) = (k_1 k_4 - k_2 k_3) x(t)(1 + y(t))
\end{cases} \quad (24)$$

with

$$x(nT^+) = x(nT^-) - \frac{k_5 k_3}{k_1 k_4 - k_2 k_3}. \quad (25)$$

By condition (13), we have that $k_1 k_4 - k_2 k_3 - k_2^2 > 0$. Hence $k_1 k_4 > k_2 k_3$.

Next we apply a second change of variable to (22)-(23), namely $z = \ln(1 + y)$ (the first variable remains unaltered). We arrive at

$$\begin{cases}
x'(t) = -(e^{z(t)} - 1) - k_2 \epsilon x(t) - k_2 \epsilon \left( \frac{k_1 k_4}{k_2 (k_3 + k_2 \epsilon^2)} - 1 \right) e^{z(t)}x(t) \\
z'(t) = k_1 k_4 \left( 1 - \frac{k_2 (k_3 + k_2 \epsilon^2)}{k_1 k_4} \right) x(t)
\end{cases} \quad (26)$$
with
\[ x(nT^+) = (1 - k_5 \varepsilon)x(nT^-) - \frac{k_5}{k_2 \left(\frac{k_1 k_4}{k_2 (k_3 + k_2 \varepsilon)} - 1\right)}. \]  
(27)

For \( \varepsilon = 0 \), we obtain
\[
\begin{align*}
\begin{cases}
x'(t) = -e^{z(t)} + 1 \\
z'(t) = (k_1 k_4 - k_2 k_3)x(t)
\end{cases}
\end{align*}
\]  
(28)

with
\[ x(nT^+) = x(nT^-) - \frac{k_5 k_3}{(k_1 k_4 - k_2 k_3)}. \]  
(29)

The orbits of system (28) (without condition (29)) are closed curves determined by
the energy levels of the map
\[ V(x, z) = -e^{z} + z - (k_1 k_4 - k_2 k_3)\left(\frac{x^2}{2}\right). \]

In fact, we can write system (28) (after a simple change of variable) as the second
order equation
\[ x'' + (k_1 k_4 - k_2 k_3)(e^x - 1) = 0. \]
Furthermore, by Proposition 3.1 (i) and Corollary 2.5 in [7], the period function of
this equation is strictly increasing with respect to the energy levels. That is, the
required time to travel the whole orbit increases with respect to the energy levels.
Note that the parameter \( \Delta \) in [7] is identically zero.

**Remark 2.** After the two changes of variable, the equilibrium \((S_*, I_*)\) of the au-
tonomous system (6) and the regions
\[ \{(S, I) : I > I_*\} \]
and \([0, \infty)^2\) are transformed into \((0, 0)\) and \((x, y) : y > 0\) and \([\frac{-1}{\Delta^2}, \infty) \times \mathbb{R}^2\)
respectively. Observe that, by (13), \(\beta I_* = \mu(R_0 - 1) > 0\) for all \(0 < \varepsilon < 1\).
Therefore, \(\frac{-1}{\Delta^2} \rightarrow -\infty\) as \(\varepsilon \rightarrow 0^+\). Roughly speaking, for the limit case \(\varepsilon = 0\),
the admissible initial conditions are transformed into \(\mathbb{R}^2\).

**5.3. Construction of the topological rectangles.** For each \(T > 0\) and \(\varepsilon \geq 0\),
we define \(P_\varepsilon\) the Poincare map of system (26) at time \(T\) and
\[ \psi_\varepsilon(x, z) = \left((1 - k_5 \varepsilon)x - \frac{k_5}{k_3 \left(\frac{k_1 k_4}{k_2 (k_3 + k_2 \varepsilon)} - 1\right)}, z\right). \]
The map \(\Psi_\varepsilon(x_0, z_0) = \psi_\varepsilon \circ P_\varepsilon(x_0, z_0)\) is that associated with system (26)-(27)
following the same scheme as for the map \(A\).

In the sequel, we argue as follows: We first prove that \(\Psi_0\) has chaotic dynamics
when \(T > T^*\) for a suitable constant \(T^* > 0\). Notice that \(\Psi_0 = t_v \circ P_0\) with
\[ t_v(x, z) = \left(x - \frac{k_5 k_3}{k_1 k_4 - k_2 k_3}, z\right), \]
that is, the translation according to the vector
\[ v = \left(\frac{k_5 k_3}{k_1 k_4 - k_2 k_3}, 0\right). \]  
(30)

Then, for each time \(T > T^*\), we apply a perturbative argument to conclude that
\(\Psi_\varepsilon\) has chaotic dynamics if \(0 < \varepsilon < \varepsilon^*\) for an adequate \(\varepsilon^* > 0\). We stress that \(\Psi_\varepsilon\)
is continuous with respect to \(\varepsilon\).
The orbits of system (28) are determined by $L_e = \{(x,z) : V(x,z) = e\}$ with $e \in \mathbb{R}$. For each value of $e$, $L_e$ is a closed curve that is symmetric with respect to the $z$-axis. The minimum and maximum values of the $z$-coordinate satisfy $z_{\text{min}} < 0 < z_{\text{max}}$. Moreover, $L_e$ can be written as

$$
\{(f_+(z), z) : z \in [z_{\text{min}}, z_{\text{max}}]\} \cup \{(f_-(z), z) : z \in [z_{\text{min}}, z_{\text{max}}]\}
$$

where $f_+ : [z_{\text{min}}, z_{\text{max}}] \rightarrow [0, \infty)$ and $f_- : [z_{\text{min}}, z_{\text{max}}] \rightarrow (-\infty, 0]$ are continuous functions with the following conditions:

C1): $f_+(z_{\text{max}}) = f_+(z_{\text{min}}) = f_-(z_{\text{max}}) = f_-(z_{\text{min}}) = 0$.

C2): $f_+$ is strictly increasing in $(z_{\text{min}}, 0)$ and strictly decreasing in $(0, z_{\text{max}})$.

C3): $f_-$ is strictly decreasing in $(z_{\text{min}}, 0)$ and strictly increasing in $(0, z_{\text{max}})$.

See Fig. 2 for an illustration of the geometry of the curves. Next we fix a point of the form $(x_0, z_0)$ with $x_0 = \frac{v_1}{2} = \frac{k_5k_4}{2(k_1k_4 - k_2k_3)}$ and $z_0 > 0$ an arbitrary positive constant. Recall that the vector in expression (30) can be written as $v = (-v_1, 0)$. Take the curve

$$
\Gamma_{x_0} = \{(x,z) : V(x,z) = V(x_0, z_0)\}
$$

and its image by the translation according to the vector $v = (-v_1, 0)$, i.e. $t_v(\Gamma_{x_0})$. By the choice of $x_0$ together with C1) and C2), we have that

$$
\Gamma_{x_0} \cap t_v(\Gamma_{x_0}) = \{(p_1,p_2),(q_1,q_2)\}
$$

with $q_2 < 0 < p_2$. Observe that $p_1 = q_1 = -x_0$ by the symmetry with respect to the $z$-axis, (see Fig. 3). Denote by $\tilde{z}_{\text{max}}$ the maximum of the $z$-coordinate of $\Gamma_{x_0}$. Now we “inflate” the curve $\Gamma_{x_0}$. Specifically, we take $\delta > 0$ small enough so that the curve

$$
\Gamma_{x_0+\delta} = \{(x,z) : V(x,z) = V(x_0+\delta, z_0)\}
$$

has the following property:

$$
\Gamma_{x_0+\delta} \cap t_v(\Gamma_{x_0+\delta}) = \{(p_1,\delta,p_2,\delta),(q_1,\delta,q_2,\delta)\}
$$

with

$$
\tilde{z}_{\text{max}} > p_2, \delta > 0 > q_2, \delta,
$$

see Fig. 4. Let $A_1$ and $A_2$ be the annulus defined by
Figure 3. Pictorial description of \( \Gamma_{x_0} \) (continuous curve) and \( t_v(\Gamma_{x_0}) \) (dashed curve).

Figure 4. Pictorial description of \( \Gamma_{x_0}, \Gamma_{x_0+\delta} \) (continuous curves), and \( t_v(\Gamma_{x_0}) t_v(\Gamma_{x_0+\delta}) \) (dashed lines). Geometrically, condition (31) means that the intersection of both annulus is below the line \( z = z_{max} \), (red line).

\[
A_1 = \{(x, z) : V(x_0, z_0) \leq V(x, z) \leq V(x_0 + \delta, z_0)\}
\] and \( A_2 = t_v(A_1) \), see Fig. 5. Consider

\[
Q = A_1 \cap A_2 \cap \{(x, z) : z > 0\}.
\]

Obviously, \( Q \) is a topological rectangle. Moreover,

\[
Q \subset A_2 \cap \{(x, z) : p_2 \leq z \leq p_2, \delta\}.
\] (32)

To see this property, we use that the maximum and minimum values of the \( z \)-coordinate of the set \( Q \) are attained at the points \( \Gamma_{x_0+\delta} \cap t_v(\Gamma_{x_0+\delta}) \) and \( \Gamma_{x_0} \cap t_v(\Gamma_{x_0}) \) respectively, see Fig. 5. Recall that \( \Gamma_{x_0} \) and \( \Gamma_{x_0+\delta} \) can be parameterized as indicated at the beginning of the step, (see properties \( C2 \) and \( C3 \)).
Finally we construct two topological rectangles $R_1$ and $R_2$ as follows. $R_1$ is the topological rectangle with the following boundary: $r_1$ the segment with ends at $(x_0, z_0)$ and $(x_0 + \delta, z_0)$; the arc $\Gamma_{x_0+\delta} \cap \{(x, z) : p_2 \leq z \leq p_{2, \delta}\}$; $r_2$ the segment with ends at $(\alpha_1, p_{2, \delta})$ and $(\alpha_2, p_{2, \delta})$ where $(\alpha_1, p_{2, \delta}) = \Gamma_{x_0} \cap \{(x, z) : z = p_{2, \delta}, x > 0\}$ and $(\alpha_2, p_{2, \delta}) = \Gamma_{x_0+\delta} \cap \{(x, z) : z = p_{2, \delta}, x > 0\}$; the arc $\Gamma_{x_0} \cap \{(x, z) : p_2 \leq z \leq p_{2, \delta}\}$. The topological rectangle $R_2$ is $t_v(R_1)$, see Fig. 5.

5.4. Stretching properties and conclusion. Define

$$Q_u = \{(x, z) \in Q : V(x, z) = V(x_0 + \delta, z_0)\}$$

and

$$Q_l = \{(x, z) \in Q : V(x, z) = V(x_0, z_0)\}.$$

Let $\tau(x, z)$ be the time employed by the orbit of system (28) with initial condition $(x, z)$ to return to $(x, z)$. As discussed at the end of Section 5.2, $\tau$ is strictly increasing as a function of the energy. Notice that the point $(x_0 + \delta, z_0)$ is of a higher level of energy than $(x_0, z_0)$. Therefore,

$$\tau(x_0 + \delta, z_0) > \tau(x_0, z_0).$$

Take

$$T^* = \frac{6\tau(x_0 + \delta, z_0)\tau(x_0, z_0)}{\tau(x_0 + \delta, z_0) - \tau(x_0, z_0)}.$$

Fix $T > T^*$ and define $n^*$ as the largest integer that satisfies

$$\frac{T}{\tau(x_0, z_0)} > n^*$$

and $n_*$ as the smallest integer that satisfies

$$\frac{T}{\tau(x_0 + \delta, z_0)} < n_*.$$
By the choice of $T$, $n^* - n_s > 4$. Condition (33) implies that after a time $T$, any solution of (28) with initial condition
\[(x, z) \in \{(x, z) : V(x, z) = V(x_0, z_0)\}\]
meets $(x, z)$ at least $n^*$ times during interval $[0, T]$. Analogously, condition (34) says that any solution of (28) with initial condition
\[(x, z) \in \{(x, z) : V(x, z) = V(x_0 + \delta, z_0)\}\]
meets $(x, z)$ at most $n_s$ times during the interval $[0, T]$. Now, we define the compact sets
\[
\mathcal{K}_1 = \{(x, z) \in Q : \frac{T}{\tau(x, z)} \in [n_s, n_s + 2]\}
\]
\[
\mathcal{K}_0 = \{(x, z) \in Q : \frac{T}{\tau(x, z)} \in [n^* - 2, n^*]\}.
\]
Our goal is to prove that
\[
(\mathcal{K}_i, \Psi_0) : \tilde{Q} \xrightarrow{\tau} \tilde{Q} \text{ for all } i = 0, 1
\]
for the oriented rectangle
\[
\tilde{Q} = (Q, Q_u \cup Q_l).
\]
Recall that $\Psi_0 = t_v \circ P_0$ with $P_0$ the Poincaré map of system (28) at time $T$ and $t_v$ the translation according $v = (-v_1, 0)$. Indeed, take a path $\gamma : [0, 1] \rightarrow Q$ with $\gamma(0) \in Q_u$ and $\gamma(1) \in Q_l$. Since $\tau(\gamma(s))$ is a continuous map, there are two disjoint intervals $[a_1, a_2]$ and $[b_1, b_2]$ so that
\[
\frac{T}{\tau(\gamma(s))} \in [n_s, n_s + 2]
\]
for all $t \in [a_1, a_2]$ and
\[
\frac{T}{\tau(\gamma(s))} \in [n^* - 2, n^*]
\]
for all $t \in [b_1, b_2]$. Now, we can find a sub-interval $[\tilde{a}_1, \tilde{a}_2] \subset [a_1, a_2]$ so that $P_0(\gamma(\tilde{a}_1)) \in r_1$, $P_0(\gamma(\tilde{a}_2)) \in r_2$, and $P_0(\gamma(s)) \in \mathcal{R}_1$ for all $s \subset [\tilde{a}_1, \tilde{a}_2]$. The analogous argument holds for $\mathcal{K}_0$.

Roughly speaking, we are proving a rather intuitive fact. Since the annulus is invariant under (28) and the angular velocity is decreasing, the image of any arc with ends at $Q_u$ and $Q_l$ by $P_0$ (for a large time) is a type of “spiral”.

Finally, given a path $\beta : [0, 1] \rightarrow \mathcal{R}_1$ so that $\beta(0) \in r_1$ and $\beta(1) \in r_2$, it is clear that there is a sub-interval $[c_1, c_2] \subset [0, 1]$ so that
\[
\beta([c_1, c_2]) \subset t_{-v}(Q)
\]
with $\beta(\beta(c_1)) \in t_{-v}(Q_u)$ and $\beta(c_2) \in t_{-v}(Q_l)$ where $t_{-v}$ is the translation according to the vector $(v_1, 0)$. Recall that $Q \subset \mathcal{R}_2 = t_{v}(\mathcal{R}_1)$ and so $t_{-v}(Q) \subset t_{-v}(\mathcal{R}_2) = \mathcal{R}_1$. Thus,
\[
t_v(\beta([c_1, c_2])) \subset Q
\]
with
\[
t_v(\beta(c_1)) \subset Q_u
\]
\[
t_v(\beta(c_2)) \subset Q_l.
\]

Collecting all the information we have proved that for any path $\gamma : [0, 1] \rightarrow Q$ with $\gamma(0) \in Q_u$ and $\gamma(1) \in Q_l$, there are two sub-intervals $[a_1, \beta(1)]$ and $[\beta(2), b_2]$ so that
• $\gamma(\alpha_1, \beta_1) \in K_0$ and $\gamma(\alpha_2, \beta_2) \in K_1$,
• $\Psi_0(\gamma(\alpha_1, \beta_1))$ and $\Psi_0(\gamma(\alpha_2, \beta_2))$ are two arcs contained in $Q$ with ends at $Q_u$ and $Q_l$.

To conclude the proof of the theorem we employ a perturbative argument. By the construction, there is $\rho > 0$ small enough so that if

$$\|\Psi_0(x, z) - F(x, z)\| < \rho$$

for all $(x, z) \in Q$ then

$$(K_i, F) : \bar{Q} \to \bar{Q} \quad \text{for all } i = 0, 1.$$  

By this remark together with the continuous dependence on $\varepsilon > 0$, we deduce that there is $\bar{\varepsilon} > 0$ so that

$$(K_i, \Psi_\varepsilon) : \bar{Q} \to \bar{Q} \quad \text{for all } i = 0, 1,$$

and $0 < \varepsilon < \bar{\varepsilon}$. Now we simply undo the changes of variable (see Remark 32) to complete the proof of the theorem.

The proof of Remark 1 is a direct consequence of conjugacy (10).

**Remark 3.** In light of the proof of Theorem 5.4, we observe that the same statement of Theorem 5.4 (with the same proof) remains true if we re-write (6)-(7) with the notation

$\lambda = k_1\varepsilon$, $\mu = k_2\varepsilon$, $\gamma = k_3\varepsilon$, $\beta = k_4\varepsilon$, $q = k_5\varepsilon$ with $k_i > 0$ for all $i = 1, 2, 3, 4, 5$ and $\varepsilon > 0$.

6. **Discussion.** Theoretical biologists have long studied the multiple implications of vaccination in epidemic models [26, 9, 17, 8, 6, 23, 30, 4]. Despite many advances, some fundamental questions remain unsolved. An optimum design of a vaccination program requires, apart from financial and logistical considerations, subtle results in epidemiology that are currently not available in the literature. This demand has been magnified because of many populations being subject to vaccination behave in a completely unpredictable manner [2, 6]. To overcome this challenge, we have analyzed the role of the pulse vaccination in the classical SIR model. Our analysis revealed that the parameters inherent in infectious disease dynamics can interact in complex ways with the birth and death rates of the population to produce chaotic behaviors.

As indicated in Section 3, the global eradication of an epidemic by means of pulse vaccination is always possible, provided the vaccination coverage is sufficiently strong. In the model (6)-(7), the quantity $\Upsilon$ serves to establish a threshold and to measure the velocity of eradication. The analysis of $\Upsilon$ indicated that if the disease-free equilibrium is a global attractor in the absence of vaccination, the introduction of pulse vaccination does not alter it. However, unexpected behaviors appear when the disease is endemic in the absence of vaccination. For a specific vaccination coverage $q \in (0, 1)$, there exists a pulse interval $(0, T_{thr})$ that ensures the effective implementation of this campaign; that is, the $T$-periodic administration of doses with $T \in (0, T_{thr})$ leads to the global eradication of the disease. Furthermore, there exists an optimum time $T_{op} > 0$ that determines the fastest eradication. A remarkable fact is that reducing the time between pulses could produce a slower eradication. In other words, less interventions could lead to better results. This fact has been already mentioned in [1, 26, 8] when $I'(t) < 0$. Based on experimental data, the WHO recommends that the time between successive pulses should be as short
as possible [14]. Our analysis indicated that this is an adequate recommendation but it could be improved depending on the particular target population.

An active area of research is the understanding of the presence of chaotic dynamics in biological systems particularly in epidemic models. In Section 4, we have detected two different mechanisms to generate chaotic dynamics when the vaccination coverage is low, (see Theorem 4.1 and Remark 3). The fist mechanism is a consequence of the interaction among low birth and death rates and high contact rate, and the second mechanism is the result of the interplay between high birth rate and low contact rate. From an applied perspective, our results could be useful for the optimum designing of vaccination programs. One of the main challenges of the WHO is the global eradication of certain diseases in countries with low incomes and high birth rates [13, 3]. Our results stress that an insufficient vaccination coverage in these countries can generate chaotic dynamics and increase the number of infectious individuals.

There are many results on the dynamic behavior of models (4)-(5) or some variants of it in the literature [26, 9, 17, 8, 6, 23, 30, 4]. Necessary and sufficient conditions for the eradication of diseases are very well-known. Regarding the presence of chaotic dynamics, numerical simulations have already suggested that the classical SEIR model could exhibit chaotic dynamics [6]. To the best of our knowledge, this is the first time in which a theoretical proof of chaotic dynamics is given for an epidemic model subject to pulse vaccination. The method for proving this consists of the application of the method of stretching along the paths and some changes of variable. The geometrical construction seems new and could be applied in different biological situations. The reader can consult [2] for different applications of the method of stretching along the paths in epidemiology.

In summary, the main strength of our findings is that based on the analysis of a simple model, it was possible to derive new biological insights on the presence of chaotic dynamics in epidemiology. Our approach provides us with a source of rich and new phenomena with impactful repercussions for real control.

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E-mail address: ruizalfonso@uniovi.es