Slow invariant manifold of heartbeat model
Jean-Marc Ginoux, Bruno Rossetto

To cite this version:
Abstract

A new approach called Flow Curvature Method has been recently developed in a book entitled Differential Geometry Applied to Dynamical Systems. It consists in considering the trajectory curve, integral of any n-dimensional dynamical system as a curve in Euclidean n-space that enables to analytically compute the curvature of the trajectory - or the flow. Hence, it has been stated on the one hand that the location of the points where the curvature of the flow vanishes defines a manifold called flow curvature manifold and on the other hand that such a manifold associated with any n-dimensional dynamical system directly provides its slow manifold analytical equation the invariance of which has been proved according to Darboux theory. The Flow Curvature Method has been already applied to many types of autonomous dynamical systems either singularly perturbed such as Van der Pol Model, FitzHugh-Nagumo Model, Chua’s Model, ...) or non-singularly perturbed such as Pikovskii-Rabinovich-Trakhtengerts Model, Rikitake Model, Lorenz Model,... Moreover, it has been also applied to non-autonomous dynamical systems such as the Forced Van der Pol Model. In this article it will be used for the first time to analytically compute the slow invariant manifold analytical equation of the four-dimensional Unforced and Forced Heartbeat Model. Its slow invariant manifold equation which can be considered as a "state equation" linking all variables could then be used in heart prediction and control according to the strong correspondence between the model and the physiological cardiovascular system behavior.
1 Introduction

Dynamical systems consisting of nonlinear differential equations are generally not integrable. In his famous memoirs: *Sur les courbes définies par une équation différentielle*, Poincaré [22, 25] faced to this problem proposed to study trajectory curves properties in the phase space.

“... any differential equation can be written as:

\[
\frac{dx_1}{dt} = X_1, \quad \frac{dx_2}{dt} = X_2, \quad \ldots, \quad \frac{dx_n}{dt} = X_n
\]

where \(X\) are integer polynomials.

If \(t\) is considered as the time, these equations will define the motion of a variable point in a space of dimension \(n\).”

– Poincaré (1885, p. 168) –

Let’s consider the following system of differential equations defined in a compact \(E\) included in \(\mathbb{R}\) as:

\[
\frac{d\vec{X}}{dt} = \vec{\mathcal{F}}(\vec{X})
\]

with

\[
\vec{X} = [x_1, x_2, \ldots, x_n]^t \in E \subset \mathbb{R}^n
\]

and

\[
\vec{\mathcal{F}}(\vec{X}) = [f_1(\vec{X}), f_2(\vec{X}), \ldots, f_n(\vec{X})]^t \in E \subset \mathbb{R}^n
\]

The vector \(\vec{\mathcal{F}}(\vec{X})\) defines a velocity vector field in \(E\) whose components \(f_i\) which are supposed to be continuous and infinitely differentiable with respect to all \(x_i\) and \(t\), i.e. are \(C^\infty\) functions in \(E\) and with values included in \(\mathbb{R}\), satisfy the assumptions of the Cauchy-Lipschitz theorem. For more details, see for example [2]. A solution of this system is a trajectory curve \(\vec{X}(t)\) tangent to \(\vec{\mathcal{F}}\) whose values define the states of the dynamical system described by the Eq. (1).

\[\text{1 Except at the fixed points.}\]
Thus, trajectory curves integral of dynamical systems regarded as n-dimensional curves, possess local metrics properties, namely curvatures which can be analytically deduced from the so-called Frénet formulas. For low dimensions two and three the concept of curvatures may be simply exemplified. A three-dimensional curve for example has two curvatures: curvature and torsion which are also known as first and second curvature. Curvature measures, so to speak, the deviation of the curve from a straight line in the neighborhood of any of its points. While the torsion measures, roughly speaking, the magnitude and sense of deviation of the curve from the osculating plane in the neighborhood of the corresponding point of the curve, or, in other words, the rate of change of the osculating plane. Physically, a three-dimensional curve may be obtained from a straight line by bending (curvature) and twisting (torsion). For high dimensions greater than three, say n, a n-dimensional curve has \((n - 1)\) curvatures which may be computed while using the Gram-Schmidt orthogonalization process and provides the Frénet formulas for a n-dimensional curve.

In it has been established that the location of the point where the curvature of the flow, i.e. the curvature of the trajectory curves integral of any slow-fast dynamical systems of low dimensions two and three vanishes directly provides the slow invariant manifold analytical equation associated to such dynamical systems.

In a book recently published the Flow Curvature Method has been generalized to high-dimensional dynamical systems and then extensively exemplified to analytically compute: fixed points stability, invariant sets, center manifold approximation, normal forms, local bifurcations, linear invariant manifolds of any n-dimensional dynamical systems which may be used to build first integrals of these systems.

One of the main applications of the Flow Curvature Method presented in the next section establishes that curvature of the flow, i.e. curvature of trajectory curves of any n-dimensional dynamical system directly provides its slow manifold analytical equation the invariance of which is proved according to Darboux Theorem.

Then, it will be used for the first time to analytically compute the slow invariant manifold analytical equation of the four-dimensional Unforced and Forced Heartbeat Model.

\(^2\) Since only time derivatives of the trajectory curves are involved in the curvature formulas.

\(^3\) A two-dimensional curve, i.e. a plane curve has a torsion vanishing identically.

\(^4\) The notion of curvature of a plane curve first appears in the work of Apollonius of Perga.

\(^5\) The name torsion is due to L.I. Vallée, Traité de Géométrie Descriptive.

\(^6\) The osculating plane is defined as the plane spanned by the instantaneous velocity and acceleration vectors.
2 Slow Invariant Manifold Analytical Equation

The concept of invariant manifolds plays a very important role in the stability and structure of dynamical systems and especially for slow-fast dynamical systems or singularly perturbed systems. Since the beginning of the twentieth century it has been subject to a wide range of seminal research. The classical geometric theory developed originally by Andronov [1], Tikhonov [29] and Levinson [18] stated that singularly perturbed systems possess invariant manifolds on which trajectories evolve slowly and toward which nearby or bits contract exponentially in time (either forward and backward) in the normal directions. These manifolds have been called asymptotically stable (or unstable) slow manifolds. Then, Fenichel [6], [9] theory for the persistence of normally hyperbolic invariant manifolds enabled to establish the local invariance of slow manifolds that possess both expanding and contracting directions and which were labeled slow invariant manifolds.

Thus, various methods have been developed in order to determine the slow invariant manifold analytical equation associated to singularly perturbed systems. The essential works of Wasow [31], Cole [3], O’Malley [20], [21] and Fenichel [6], [9] to name but a few, gave rise to the so-called Geometric Singular Perturbation Theory and the problem for finding the slow invariant manifold analytical equation turned into a regular perturbation problem in which one generally expected, according to O’Malley (1974 p. 78, 1991 p. 21) the asymptotic validity of such expansion to breakdown.

So, the main result of this work established in the next section is that curvature of the flow, i.e. curvature of trajectory curves of any n-dimensional dynamical system directly provides its slow manifold analytical equation which reads:

\[ \text{curvature of the flow, i.e. curvature of trajectory curves of any n-dimensional dynamical system directly provides its slow manifold analytical equation which reads:} \]

2.1 Slow manifold of high-dimensional dynamical systems

In the framework of Differential Geometry trajectory curves \( \vec{X}(t) \) integral of n-dimensional dynamical systems [11] satisfying the assumptions of the Cauchy-Lipschitz theorem may be regarded as n-dimensional smooth curves, i.e. smooth curves in Euclidean n-space parametrized in terms of time.

**Proposition 2.1.** The location of the points where the curvature of the flow, i.e. the curvature of the trajectory curves of any n-dimensional dynamical system vanishes directly provides its \((n-1)\)-dimensional slow invariant manifold analytical equation which reads:
\[
\phi(\vec{X}) = \dot{\vec{X}} \cdot \left( \ddot{\vec{X}} \wedge \ldots \wedge \vec{X} \right) (n)
\]

\[
= \det \left( \dot{\vec{X}}, \ddot{\vec{X}}, \ldots, \vec{X} \right) (n) = 0
\]

where \( \vec{X} \) represents the time derivatives of \( \vec{X} \).

**Proof.** Cf. Ginoux et al. \cite{13} ; Ginoux \cite{14} \qed

### 2.2 Darboux invariance theorem

According to Schlomiuk \cite{26,27} and Llibre et al. \cite{19} it seems that in his memoir entitled: *Sur les équations différentielles algébriques du premier ordre et du premier degré*, Gaston Darboux (1878, p. 71) has been the first to define the concept of invariant manifold. Let’s consider a \( n \)-dimensional dynamical system \( (1) \) describing “the motion of a variable point in a space of dimension \( n \).” Let \( \vec{X} = [x_1, x_2, \ldots, x_n]^t \) be the coordinates of this point and \( \vec{V} = [\dot{x}_1, \dot{x}_2, \ldots, \dot{x}_n]^t \) its velocity vector.

**Proposition 2.2.** Consider the manifold defined by \( \phi(\vec{X}) = 0 \) where \( \phi \) is a \( C^1 \) in an open set \( U \) is invariant with respect to the flow of \( (1) \) if there exists a \( C^1 \) function denoted \( K(\vec{X}) \) and called cofactor which satisfies:

\[
L_{\vec{V}} \phi = K(\vec{X}) \phi(\vec{X})
\]

for all \( \vec{X} \in U \) and with the Lie derivative operator defined as:

\[
L_{\vec{V}} \phi = \vec{V} \cdot \nabla \phi = \sum_{i=1}^{n} \frac{\partial \phi}{\partial x_i} \dot{x}_i = \frac{d\phi}{dt}.
\]

In the following invariance of the slow manifold will be established according to what will be referred as Darboux Invariance Theorem.

**Proof.** Cf. Ginoux et al. \cite{13} ; Ginoux \cite{14} \qed
3 Heartbeat model

3.1 Description of the model

According to di Bernardo et al. [5] "The cardiac conduction system may be assumed to be a network of self-excitatory pacemakers, with the SinoAtrial (SA) node having the highest intrinsic rate. Subsidiary pacemakers with slower firing frequencies are located in the AtrioVentricular (AV) node and the His-Purkinje system. Under physiological conditions, the SA node is the dominant pace-maker and impulses travel from this node to the ventricule through the AV junction, which is traditionally regarded as a passive conduit." Then, starting from the assumptions (17) that between the SA and AV node a bi-directional coupling exists they describe the cardiac conduction system (Cf. Fig. 1 & Fig. 2) by means of two-coupled nonlinear oscillators. For a genesis of the model see di Bernardo et al. [5] and Signorini et al. [28].

![Cardiac Conduction System](image)

**Figure 1: Cardiac Conduction System.**

The model proposed may be also described by an equivalent electrical circuit depicted in Fig. 2. Its structure with two nonlinear oscillators in parallel with a resistance put together the features of the Van der Pol [30] and West [32] models. These two coupled nonlinear oscillators are built from a modification of the Van der Pol model, so that the generated waveforms resemble the action potentials of cells in the SA (resp. AV) node. The AV nonlinear oscillator represents the waveform of the intensity \(x_3\) which satisfactorily replicate the action potential \(x_4\) in the AV node and corresponds exactly to the original Van der Pol model when the resistance is null, i.e. in the uncoupled case. Thus, the nonlinear function \(f(x)\) which represents the tension \(x_3\)-current \(x_4\) characteristic of the nonlinear resistor (e.g. a triode) may be written as:
Figure 2: Equivalent Electrical Circuit.

\[ f(x) = \frac{x^3}{3} - x \]

For the generated waveform of the intensity \((x_2)\) resembles the action potential \((x_1)\) of the SA node cells the tension \((x_1)\)-current \((x_2)\) characteristic of the nonlinear resistor of the oscillator representing the SA node which is also of Van der Pol type must be modified (di Bernardo et al. [5]). Thus, by adding the piecewise linear function \(h(x)\) to the cubic nonlinearity of the Van der Pol oscillator \(f(x)\) its characteristics reads.

\[ g(x) = h(x) + f(x) \quad \text{where} \quad h(x) = \begin{cases} +x & \text{for } x < -0.5 \\ -x^2 - 0.25 & \text{for } |x| \leq 0.5 \\ -x & \text{for } x > 0.5 \end{cases} \]

Moreover, let suppose that the waveform of the voltage generator in (SA) can be sinusoidal of amplitude \(A\) and frequency \(f\). Forcing the system means that a region of the cardiac tissue can become an active pacemaker and so interferes with the normal sinus rhythm generated by the SA node. The model is thus two-coupled nonlinear oscillator implemented in a set of four non-autonomous ordinary differential equations.

\[
\begin{align*}
\dot{X} = & \begin{pmatrix}
\frac{1}{C_{SA}} x_2 \\
-\frac{1}{L_{SA}} [x_1 + g(x_2) + R(x_2 + x_4)] + A \cos(2\pi ft) \\
\frac{1}{C_{AV}} x_2 \\
-\frac{1}{L_{AV}} [x_3 + f(x_4) + R(x_2 + x_4)]
\end{pmatrix}
\end{align*}
\]

(4)
The $R$ parameter models the coupling "strength" between the SinoAtrial (SA) and the AtrioVentricular (AV) node. The parameters value satisfying a normal heartbeat dynamics are:

$$C_{SA} = 0.25F; \quad L_{SA} = 0.05H; \quad C_{AV} = 0.675F; \quad L_{AV} = 0.027H; \quad R = 0.11\Omega \quad (5)$$

By varying this coupling resistance while keeping other parameters as above, a type of arrhythmia known as 2º AV block of the Wenckebach type may be obtained. In order to describe arrhythmia, di Bernardo et al. [5] introduced two integers $n : m$ which means the atria contract $n$ times while the ventricles $m$ times. Thus, the Flow Curvature Method will enable, according to Prop. 2.1, to directly compute the slow manifold analytical equation associated with heartbeat model (1) in both unforced and forced cases for various values of the coupling parameter $R$.

### 3.2 Unforced Heartbeat model

While posing $A = 0$ in Eq. 4 the heartbeat model is then described by an autonomous dynamical system. As soon as $R > 0.11\Omega$, 1 : 1 periodic solutions are observed (Cf. Fig. 3).

![Figure 3: Unforced Heartbeat Model trajectory in the $(x_1, x_2, x_3)$ phase space.](image)

When $R$ decreases this value a series of subharmonic bifurcations undergoes and the attractor resembles one type of arrhythmia known as 2º AV block of the Wenckebach type. By posing $R = 0.018\Omega$ the slow invariant manifold analytical equation corresponding to that case (Cf. Fig. 4) has been computed according to Prop. 2.1 and may be written as:
\[ \phi(\vec{X}) = \det \left( \ddot{X}, \dddot{X}, \ldots, \vec{X} \right) = 0 \]  

(6)

Because of the presence of the piecewise linear function \( h(x) \) in Eq. 4 the slow invariant manifold analytical equation may be computed for each side, i.e. for \( x < -0.5 \) and for \( x > 0.5 \). In both cases it leads to a polynomial depending on the variables: \( x_1, x_2, x_3, x_4 \) the equation of which is given in Appendix.

In Fig. 4 it can be observed that both trajectory curves and slow invariant manifold are in a very close vicinity. This due to the smallness of the parameters such that \( L_{SA} \) and \( L_{AV} \).

3.3 Forced Heartbeat model

When the amplitude \( A \) is different from zero the dynamical system will become non-autonomous and it will be the same for the slow invariant manifold analytical equation. So, in order to avoid such difficulty a suitable variable changes may transform this non-autonomous system into an autonomous one while increasing the dimension of two. Indeed the forcing is modeled by the cosine which is nothing else but the solution of an harmonic oscillator. Thus, the autonomous forced heartbeat model may be written as a set of six ordinary differential equations.
where $x_5$ is the solution of the harmonic oscillator of pulsation $\Omega = 2\pi f$.

Moreover, it may be stated that in the vicinity of the flow curvature manifold both flow curvature manifold and its Lie derivative are merged. Thus, according to Darboux Invariance Theorem and Prop. 2.2 the slow manifold of the Unforced and Forced Heartbeat models are locally invariant.

4 Discussion

In this work a new approach which consists in applying Differential Geometry to Dynamical Systems and called Flow Curvature Method has been partially presented. By considering the trajectory curve, integral of any $n$-dimensional dynamical system, as a curve in Euclidean $n$-space, the curvature of the trajectory curve, i.e. curvature of the flow has been analytically computed enabling thus to define a manifold called: flow curvature manifold. Since such manifold
only involves the time derivatives of the velocity vector field and so, contains information about the dynamics of the system, it enables to find again the main features of the dynamical system studied. Thus, Flow Curvature Method enables to analytically compute: fixed points stability, invariant sets, center manifold approximation, normal forms, local bifurcations, slow invariant manifold and integrability of any n-dimensional dynamical systems but also to “detect” linear invariant manifolds of any n-dimensional dynamical systems which may be used to build first integrals of these systems.

Then, according to \cite{14} Flow Curvature Method has been applied to a 4-dimensional autonomous dynamical system, i.e. the Unforced Heartbeat model and to a 6-dimensional non-autonomous dynamical systems, i.e. the Forced Heartbeat model in order to compute their slow invariant manifold analytical equation which may be considered as a "state equation" linking all variables of such systems and then allowing to express one with respect to all others. Thus, according to the works of di Bernardo et al. \cite{5}; Signorini et al. \cite{28} the slow invariant manifold analytical equation could be used to study different aspects of the heartbeat dynamics such that heart prediction and control of one variable or one parameter from all others. Moreover, the Flow Curvature Method could be also applied to biodynamical model of HIV-1. This will be the subject of another publication.

References


Appendix

This appendix provides the slow invariant manifold analytical equation of the Unforced Heartbeat model for the left and right side, i.e. for $x < -0.5$ and $x > 0.5$. For sake of simplicity variables have been taken such that $x_1 = x$, $x_2 = y$, $x_3 = z$, $x_4 = 0$:

$$
\phi_{lfs}(x, y, z, 0) = 0.0012345x^4 - 0.0022228x^3y + 0.00037511xz^2
- 0.00044596xy^3 + 0.00037448x^3y^3 + 0.00003387y^4 - 0.002672x^2y^4
+ 0.00974419xy^5 + 0.00033587y^6 - 0.0066214x^2y^6 - 0.0033732xyz^7
+ 0.0049183y^8 - 0.0056278xy^9 - 0.0009777y^{10} - 0.0011415y^{12}
- 0.30904x^4z + 1.5x^5z + 0.31868x^2yz + 0.108x^4yz - 0.055861xyz^2
- 3.6691x^3y^2z + 0.064882y^3z + 0.47798x^2y^3z + 4.6666x^4y^3z
- 0.077528xy^4z - 5.1675x^3y^4z + 0.066041y^5z - 3.7898x^2y^5z
- 0.031419xy^6z + 3.1111x^3y^6z - 0.040448y^7z - 5.3475x^2y^7z
- 1.4508xy^8z - 0.077657y^9z + 0.37037x^2y^9z - 1.8265xy^{10}z
- 0.19842y^{11}z - 0.16049xy^{12}z - 0.20739y^{13}z - 0.032921y^{15}z
+ 18.784x^2z^2 - 102.02x^4z^2 + 0.35642xyz^2 - 200.36x^3y^2z^2
+ 3.7585y^2z^2 + 34.327x^2y^2z^2 + 55.555x^4y^2z^2 - 7.2815xy^3z^2
- 439.12x^3y^3z^2 + 3.4234y^4z^2 - 188.62x^2y^4z^2 + 5.0932xyz^5z^2
- 37.037x^3y^5z^2 - 3.9484y^6z^2 - 377.1x^2y^6z^2 - 63.569xy^7z^2
- 2.1979y^8z^2 - 74.074x^2y^8z^2 - 120.14xy^9z^2 - 7.6519y^{10}z^2
- 28.806xy^{11}z^2 - 13.151y^{12}z^2 - 3.4293y^{14}z^2 + 0.67914xz^3
- 8.2025x^3z^3 - 0.016924y^3z^3 + 32.686x^2y^3z^3 + 0.87526xyz^5z^3
+ 9.21999y^3z^3 - 36.513x^2y^3z^3 - 26.337xy^4z^3 + 4.3502y^5z^3
- 47.011xy^6z^3 - 12.868y^7z^3 - 11.917y^8z^3 + 0.0067128z^4
+ 647.95x^2z^4 + 12.536xyz^4 + 129.58y^2z^4 - 352.81x^2y^2z^4
- 235.03xy^3z^4 + 61.791y^4z^4 - 588.02xy^5z^4 - 156.69y^6z^4
- 156.8y^8z^4 + 11.76xz^5 - 7.8403y^3z^5
\[ \phi_{\text{right}}(x, y, z, 0) = 0.0012345x^4 - 0.004692x^3y + 0.0048652x^2y^2 \\
- 0.00078467xy^3 + 0.0037448x^3y^3 + 0.00003387y^4 + 0.0076833xy^4 \\
- 0.03568xy^5 + 0.037643y^6 - 0.0066214x^2y^6 + 0.03633xy^7 \\
- 0.04668y^8 - 0.0056278xy^9 + 0.013603y^{10} - 0.0011415y^{12} \\
- 0.034699x^3z + 1.4356x^2yz - 11.892x^3yz - 0.15531xy^2z \\
+ 54.378x^3y^2z + 0.014991y^3z - 120.87x^2y^3z + 4.6666x^3y^3z + 131.23xy^4z \\
- 37.167x^4y^3z - 55.767y^5z + 110.55x^2y^5z - 145.14xy^6z + 3.1111x^3y^6z \\
+ 70.682y^7z - 17.347x^2y^7z + 31.864xy^8z - 19.091y^9z + 0.37037x^2y^9z \\
- 0.93763xy^{10}z + 0.35116y^{11}z - 0.16049xy^{12}z + 0.3852y^{13}z \\
- 0.032921y^{14}z - 0.31296x^2z^2 + 9.0823x^4z^2 + 0.62489xyz^2 - 95.29x^3yz^2 \\
- 0.072986y^2z^2 + 330.69x^2y^2z^2 + 55.555x^3y^2z^2 - 469.16xy^3z^2 \\
- 290.97x^3y^3z^2 + 232.73y^4z^2 + 425.62x^2y^4z^2 + 4.3027xy^5z^2 \\
- 37.037x^3y^5z^2 - 270.86y^6z^2 + 363.63xy^2y^6z^2 - 998.42xy^7z^2 \\
+ 838.7y^8z^2 - 74.074x^2y^8z^2 + 340.76xy^9z^2 - 383.62y^{10}z^2 \\
- 28.806xy^{11}z^2 + 62.294y^{12}z^2 - 3.4293y^{14}z^2 + 0.054748xz^3 \\
- 8.2025x^3z^3 + 0.036957y^3z^3 + 36.913x^2y^3z^3 - 57.359xy^2z^3 \\
+ 31.972y^3z^3 - 36.513x^2y^3z^3 + 191.33xy^4z^3 - 233.44y^5z^3 \\
- 47.011xy^6z^3 + 110.02y^7z^3 - 11.917y^9z^3 + 0.0061728z^4 \\
- 57.678x^2z^4 + 115.19xyz^4 - 11.168y^2z^4 - 352.81x^2y^2z^4 \\
+ 2117xy^3z^4 - 2778.3y^4z^4 - 588.02xy^5z^4 + 1411.3y^6z^4 \\
- 156.8y^8z^4 + 11.76xz^5 - 7.8403y^3z^5 \\

The complete slow invariant manifold analytical equation of the Unforced and Forced Heartbeat model may be downloaded at: http://ginoux.univ-tln.fr