Corrections

APPLIED MATHEMATICS, SYSTEMS BIOLOGY

The authors note that on page 9252, Equations 2 and 5 appeared incorrectly. The corrected equations appear below. These errors do not affect the conclusions of the article.

\[
x(u,v,w) = \frac{-K_N + K_N u \cos(v - K_B w) + K_T u \sin(v - K_B w)}{K_T^2 + K_N^2}, \tag{2}
\]

\[
N = \begin{bmatrix}
-K_T \cos(v - K_B w) - K_N \sin(v - K_B w) \\
-K_N \cos(v - K_B w) + K_T \sin(v - K_B w) \\
u \\
-K_B \\
1
\end{bmatrix}. \tag{5}
\]

CELL BIOLOGY

The authors note that the author names Tanesha Naïken and Karine Ilk should instead appear as Tanesha Naiken and Karine Ilc. The corrected author line appears below. The online version has been corrected.

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www.pnas.org/cgi/doi/10.1073/pnas.1218232109
Heart wall myofibers are arranged in minimal surfaces to optimize organ function

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Edited by Vladimir Rokhlin, Yale University, New Haven, CT, and approved April 3, 2012 (received for review December 26, 2011)

Heart wall myofibers wind as helices around the ventricles, strengthening them in a manner analogous to the reinforcement of concrete cylindrical columns by spiral steel cables [Richart FE, et al. (1929) Univ Illinois, Eng Exp Stn Bull 190]. A multitude of such fibers, arranged smoothly and regularly, contract and relax as an integrated functional unit as the heart beats. To orchestrate this motion, fiber tangling must be avoided and pumping should be efficient. Current models of myofiber orientation across the heart wall suggest groupings into sheets or bands, but the precise geometry of bundles of myofibers is unknown. Here we show that this arrangement takes the form of a special minimal surface, the generalized helicoid [Blair DE, Vanstone JR (1978) *Minimal Submanifolds and Geodesics* 13–16], closing the gap between individual myofibers and their collective wall structure. The model holds across species, with a smooth variation in its three curvature parameters within the myocardial wall providing tight fits to diffusion magnetic resonance images from the rat, the dog, and the human. Mathematically it explains how myofibers are bundled in the heart wall while economizing fiber length and optimizing ventricular ejection volume as they contract. The generalized helicoid provides a unique foundation for analyzing the fibrous composite of the heart wall and should therefore find applications in heart tissue engineering and in the study of heart muscle diseases.

Histological studies of the mammalian heart (1–4) corroborate the finding that individual myofibers in the left ventricle (LV) are aligned to form helical curves (Fig. 1B). Several formal analyses (1, 2, 5–7) support the view that this alignment is mechanically optimal. Moving beyond considerations of individual fibers has proved difficult. An advantage of certain fibrous composites, such as those in plant cell walls, bone, insect cuticle, and fiberglass, is that their fiber geometries offer efficient reinforcement (8) by equalizing stiffness in all directions parallel to the plane in which fibers lie. Our approach has been to retain the mathematical precision available for the analysis of individual fibers while switching scales to that of the composite arrangement. Anatomical studies reveal that at such scales, fibers remain almost parallel locally (9), as illustrated in Fig. 1C with the colors depicting changes in orientation. We show that they are packed together to achieve this organization, while maintaining their helical form (4), via a unique structural arrangement in which they bundle into a special surface: a generalized helicoid (10–14). Because this object is a minimal surface (15, 16), it generalizes the geodesic properties of the individual helices (1, 2, 5–7) to the more global scale of the ventricular wall. We also show that this minimal surface structure can be maintained as the heart beats, with simulations revealing the power of using the proper mathematical coordinates. Previous models (1, 2, 5–7) apply to selected regions of the LV myocardium but exclude the apex. They describe the orientation of individual fibers but not volumetric bundles of them.

The arrangement of myofibers in generalized helicoids characterizes their orientation throughout the heart wall.

Model

Setting up the right local coordinate frame is critical to developing the generalized helicoid model (GHM). Fig. 1D depicts a myofiber passing through a particular location (voxel) in a rectangular grid in three-dimensional Euclidean space, with its tangent vector lying in the plane of the page, along with fibers passing through neighboring voxels. An orthogonal coordinate frame is placed using the fiber orientation for tangent vector T, the in-page direction for the binormal vector B, and their cross-product for the normal vector N. The differential geometry of the collection of myofibers can now be characterized by specifying the rates of change of fiber orientation for displacements in the directions of T, N, and B.

The GHM expresses fiber orientation in terms of these curvatures by prescribing an orientation function $\theta(x, y, z) : R^3 \rightarrow S^1$ given by

$$\theta(x, y, z) = \arctan \left( \frac{K_T x + K_N y}{1 + K_T x - K_N y} \right) + K_B z,$$

at each point $(x, y, z)$ within the LV wall with respect to a local coordinate frame (17, 18). Here $\theta(x, y, z)$ represents the orientation in the $x$–$y$ plane with respect to the $x$ axis, which is aligned with the local fiber direction, and with the $z$ axis taken to be the component of the heart wall orthogonal to it (following heart myofiber geometry literature, refs. 19 and 20). This choice ensures that the reference frame rotates smoothly and consistently throughout the LV myocardium. Because it is small (21, 22) we do not directly model the component of fiber orientation out of the $x$–$y$ plane in the local neighborhood of $(x, y, z)$.

Fig. 2 illustrates the effects of the parameters of the GHM, with the orientation $\theta$ shown by a unit length vector field in the $x$–$y$ plane and with fibers abstracted by streamline traces in $\theta(23)$. The $K_T$ parameter causes bending in the direction tangent...

Author contributions: P.S., G.J.S., S.W.Z., and K.S. designed research; P.S. and K.S. wrote the paper.

The authors declare no conflict of interest.

*This Direct Submission article had a prearranged editor.

Freely available online through the PNAS open access option.

Data deposition: The data analyzed in this paper is archived at the following location: http://www.cbm.jhu.edu/research/DTMRIDS.php with rat diffusion MRI datasets that were collected at the Eindhoven University of Technology. The database combines human and dog diffusion MRI datasets that are publicly available at http://www.cbm.jhu.edu/research/DTMRIDS.php with rat diffusion MRI datasets that were collected at the Eindhoven University of Technology.

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This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1120785109/-/DCSupplemental.
Fig. 1. Fiber geometry in the left ventricle of a rat. (A) An axial slice (gray) with both a single helical fiber passing through a voxel (B) and a bundle of fibers passing through neighboring locations (C–E). (B) The geometry of a single fiber is characterized locally by its rate of bending in the osculating tangent-normal (TN) plane (curvature) and out of it (torsion). The TN plane is shown in blue. (C) The geometry of a bundle of fibers is more complex. Here we show a narrow slice of fibers arranged across the thickness of the wall, emerging from the slice in A. The colors are used to visualize changes in orientation. (D) More abstractly, we now show fibers passing through a plane of voxels in green, and those in a neighboring plane in a cubic lattice in blue. The placement of a local coordinate frame allows fiber bundle geometry to be characterized by curvature measures in directions T, N, and B. (E) Comparing the model to data: The orientations corresponding to GHM fitting are overlaid in color on the principal eigenvector direction e1 (shown with gray to black shading in the direction from below to above the slice plane), for an axial slice of the rat heart DT-MRI data (compare with C).

tial to a fiber (Fig. 2A). With positive KN added, the fibers fan out. Finally, KB defines angular change in the z direction. In this example, KB has the effect of creating rotated copies of the same streamlines in planes parallel to the x–y plane (Fig. 2C).

Mathematically the GHM’s scalar parameters KT, KN, and KB correspond locally to the three curvatures of the myofiber bundle, describing the amount that the fiber orientation changes for displacements in the directions T, N, and B, respectively (17, 18). As such it provides coordinates for describing the geometry of a bundle of myofibers in three dimensions. In contrast, a helix (1, 2, 5–7) only describes the geometry of a single fiber viewed as a one-dimensional curve.

A fundamental property of the GHM, as shown in ref. 17 and in the Appendix, is that (x, y, z, θ(x, y, z)) is a minimal surface when embedded in R4; i.e., its mean curvature, given by the trace of the shape operator, vanishes everywhere. A more familiar example of a minimal surface is the bubble that results from dipping a wire frame into a soapy film; that is, the minimal surface required to enclose a given volume of air. Blair and Vanstone show in ref. 10 that complete ruled minimal n-dimensional hypersurfaces δn in E n+1 are products of E n−2 and a helicoid in E 3. As such, in E 3, a generalized helicoid is the product of a helicoid in E 3 and the real line. Barbosa et al. (11) and Thas (13, 14) independently derive the parametric equations of such minimal generalized helicoids. There is a relationship between these results and those on generalized helical curves. In ref. 24, Hayden proves that, in Riemannian spaces of n dimensions, with n even, at least one of the curvatures of a generalized helix must vanish. One can deduce from this result that, in E 4, a generalized helix can have non-null curvature and torsion, but its higher-order curvatures must be null. Thus, in E 4, a generalized helix must be the ordinary 3D helix with a linear coordinate function describing its fourth dimension.

Results

We have tested our model against data from diffusion tensor (DT) MRI from three different mammals: rat, dog, and human. DT-MRI provides estimates of myofiber orientation over the full myocardial volume at high spatial resolution by measuring the orientation dependence of the Brownian motion of water molecules (25). Diffusion in the myocardium is anisotropic due to its fibrous structure. Several studies (26–28) show that the principal eigenvector e1 of a DT is locally aligned with myofiber orientation at the spatial scale of a typical image voxel. The use of DT-MRI has advantages over earlier dissection studies which were typically restricted to a small set of locations (3) and are therefore difficult to reproduce.

Returning to Fig. 1D, let T and B represent the x and z axis directions at each voxel. Applying GHM fitting to the fiber bundle shown in Fig. 1C, one expects a large binormal curvature KB, capturing the variation of fiber angle in the direction perpendicular to the heart wall. In contrast, the curvatures KT and KN along and across fibers, respectively, appear to be small. Our results confirm this trend throughout the LV myocardium, consistent with the anatomical observation that fibers are almost parallel locally but turn as one penetrates the heart wall (1–3, 26, 29). Fig. 1E compares our model to the data by overlaying the orientations corresponding to the best fit GHMs in color on the DT-MRI based fiber directions (gray to black) in an axial slice of rat LV myocardium.

In Fig. 3, we plot histograms of the distributions of KB, KN, and KT for one human, three dog, and four rat DT-MRI datasets. The human, dog, and rat datasets have spatial resolutions of 0.4297 × 0.4297 × 1.0, 0.3125 × 0.3125 × 0.8, and 0.25 × 0.25 × 0.25 mm3, respectively. To perform a cross-species comparison, all curvature parameters were normalized based on the maximum epicardial cross-sectional diameter (MD). The histograms were then normalized with respect to the number of voxels contained in the dataset. The histogram of normalized KB values for each dataset peaks around −0.15 to −0.22 rad/mm, revealing a remarkable consistency of design across these three species. The mean KB value for each dataset is also an order of magnitude larger than the mean KN and KT values, which are both centered at zero. The rightmost column of Fig. 3 depicts the spatial varia-
tion of the $K_B$ parameter in a long-axis slice from a single dataset of each species, showing it to be homogeneous throughout the LV myocardial wall, including the apex, an area excluded by other models (1, 2, 5–7). GHM fits for transmural penetrations at locations near the base, the equator, and the apex of a rat heart dataset are shown in Fig. 4. Table 1 and Fig. 5 provide a quantitative and qualitative assessment of the GHM fitting angular errors over all the heart datasets. A von Mises distribution (30) fit shows these errors to be consistently low, with the $\mu$ parameter ranging from $2.63°$ ($0.046$ rad) to $7.63°$ ($0.128$ rad), and to have concentration $\kappa$ higher than 100 (or equivalently, low variance). Locations of high error coincide with dataset boundaries, or are close to the base or insertions of the right ventricle.

In a second experiment, we assess the effect of increasing neighborhood size ($N = 3, 5, 7, 9$) on GHM fits for the human heart dataset. Here we measure error for all voxels within the associated spherical neighborhood, not just the closest voxel neighbors. The von Mises analysis, presented in Table 2, shows that, although the error increases slightly, the larger number of error samples now leads to much tighter von Mises fits, with the concentration parameter $\kappa$ increasing by a factor of 4 or more. In interpreting these results, it is important to recall that because the mathematical framework we follow is motivated by Cartan’s moving frame construction, we adapt the local coordinate frame to the object under consideration. When this frame is made too large, the tangent plane approximation to the heart wall becomes less accurate.

The changes implied by a beating heart, including fiber shortening and wall thickening (31), reveal another surprising aspect of the curvature parameter $K_B$. Chen et al. (26) have reported DT-MRI measurements of fiber orientation along transmural penetrations from epicardium to endocardium on rat hearts fixed at end systole and end diastole. Their results show the heart wall to thicken significantly as myofibers contract, but the total change in fiber orientation from outer wall to inner wall to be quantitatively preserved. Using parameters consistent with their findings and our GHM fits for a transmural sampling at a location near the equator of the dataset in Fig. 4, Fig. 6 and Movie S1 show how this rearrangement of fiber geometry is predicted simply by a decrease in $K_B$. Remarkably, throughout the contraction process, the minimal surface structure provided by the GHM is preserved.

**Discussion**

Our bundling of heart wall myofibers into generalized helicoids adds significant dimensions to current knowledge of LV myofiber structure and function. First, this organization shows that myofi-
his orientation as a function of position is a minimal surface (15, 16) throughout the myocardium. Whereas previous models have considered only the geometry of individual (one-dimensional) fibers (1, 2, 6, 7) or their groupings in (two-dimensional) sheets (9, 19, 26, 28), our analysis of fiber orientation applies in three dimensions across the entire ventricular volume. The property that a minimal surface is locally area minimizing (15, 16) generalizes current understanding that individual helical fibers, being geodesic (1, 2, 6, 7), are length minimizing. Other properties of minimal surfaces are also inherited by the generalized helicoid organization. For example, for a harmonic minimal surface defined on a plane, it can be shown that the second variation of its area depends only on the component of a variation normal to it (15, 16). This property suggests that shortening fibers along their length in the direction given by $\theta$ could contribute to an efficient shrinkage of volume by yielding a displacement in the direction normal to the heart wall. It has in fact been established that a helical orientation of myofibers is essential to achieve a transmurally homogeneous workload for all myocytes within the healthy myocardium (32–34). More globally, the helicoidal myocardial architecture induces torsion of the left ventricle during contraction. Second, our GHM fits with small $K_T$ and $K_N$ but high $K_F$ formalize Neville’s stacked helicoids model (8) and Bouligand’s generalized twisted model (35). These two models have been used as qualitative descriptions of helicoidal arrangements in a variety of biological and man-made fibrous composites (8, 35), but without a formal mathematical underpinning. Furthermore, they have never before been applied to the heart wall. Our formalization along with our experimental fits to DT-MRI data reveal an additional purpose of the generalized helicoid or- more, they have never before been applied to the heart wall. They have been used as qualitative descriptions of helicoidal arrangements of higher error in the rat dataset coincide with anatomically interesting regions, where $K_F$ has a different sign (red arrows in Fig. 3). (Lower) A statistical analysis obtained by fitting a von Mises distribution (30) (solid lines), with the $\mu$ and $\kappa$ parameters shown in Table 1, to the angular errors from discretized GHM fits (open circles).

Table 1. Quantitative assessment of the GHM fits for all heart DT-MRI datasets

<table>
<thead>
<tr>
<th></th>
<th>$K_{\mu}$, rad/mm</th>
<th>$K_{\nu}$, rad/mm</th>
<th>$K_{\tau}$, rad/mm</th>
<th>$\mu$, rad</th>
<th>$\kappa(-)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human</td>
<td>$-0.17 \pm 0.18$</td>
<td>$0.003 \pm 0.085$</td>
<td>$-0.005 \pm 0.081$</td>
<td>$0.046 \pm 0.002$</td>
<td>$108 \pm 8$</td>
</tr>
<tr>
<td>Dog 1</td>
<td>$-0.15 \pm 0.16$</td>
<td>$0.001 \pm 0.101$</td>
<td>$-0.001 \pm 0.101$</td>
<td>$0.098 \pm 0.002$</td>
<td>$141 \pm 9$</td>
</tr>
<tr>
<td>Dog 2</td>
<td>$-0.17 \pm 0.15$</td>
<td>$0.004 \pm 0.096$</td>
<td>$-0.011 \pm 0.090$</td>
<td>$0.078 \pm 0.001$</td>
<td>$136 \pm 9$</td>
</tr>
<tr>
<td>Dog 3</td>
<td>$-0.17 \pm 0.16$</td>
<td>$0.006 \pm 0.099$</td>
<td>$-0.011 \pm 0.096$</td>
<td>$0.128 \pm 0.003$</td>
<td>$157 \pm 7$</td>
</tr>
<tr>
<td>Rat 1</td>
<td>$-0.19 \pm 0.14$</td>
<td>$0.008 \pm 0.053$</td>
<td>$0.003 \pm 0.053$</td>
<td>$0.109 \pm 0.003$</td>
<td>$128 \pm 9$</td>
</tr>
<tr>
<td>Rat 2</td>
<td>$-0.21 \pm 0.12$</td>
<td>$0.008 \pm 0.045$</td>
<td>$0.005 \pm 0.043$</td>
<td>$0.090 \pm 0.002$</td>
<td>$132 \pm 7$</td>
</tr>
<tr>
<td>Rat 3</td>
<td>$-0.22 \pm 0.11$</td>
<td>$0.008 \pm 0.043$</td>
<td>$0.006 \pm 0.049$</td>
<td>$0.107 \pm 0.003$</td>
<td>$121 \pm 9$</td>
</tr>
<tr>
<td>Rat 4</td>
<td>$-0.20 \pm 0.14$</td>
<td>$0.008 \pm 0.053$</td>
<td>$0.000 \pm 0.053$</td>
<td>$0.101 \pm 0.001$</td>
<td>$144 \pm 6$</td>
</tr>
</tbody>
</table>

*All values reported as mean ± standard deviation. A neighborhood of $5 \times 5 \times 5$ around the central voxel $v$ is used for each fit. Errors are measured only for the voxels closest to $v$. $K_{\mu}$, $K_{\nu}$, and $K_{\tau}$ are species-normalized values.

Table 2. Quantitative assessment of the effect of increasing neighborhood size on the GHM fit for the human heart dataset

<table>
<thead>
<tr>
<th>Neighborhood</th>
<th>$\mu$, rad</th>
<th>$\kappa(-)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 x 3 x 3</td>
<td>$0.125 \pm 0.00077$</td>
<td>$610 \pm 23$</td>
</tr>
<tr>
<td>5 x 5 x 5</td>
<td>$0.145 \pm 0.00156$</td>
<td>$478 \pm 33$</td>
</tr>
<tr>
<td>7 x 7 x 7</td>
<td>$0.162 \pm 0.00198$</td>
<td>$444 \pm 37$</td>
</tr>
<tr>
<td>9 x 9 x 9</td>
<td>$0.173 \pm 0.00213$</td>
<td>$430 \pm 38$</td>
</tr>
</tbody>
</table>

*All values reported as mean ± standard deviation. The errors are now measured for all voxels within the sphere of maximal radius inscribed in the neighborhood.
Generalized Helicoidal Model Fitting. In each dataset, the left ventricle was manually segmented by an expert. A GHM fit was obtained at each voxel \(v\) by searching over \(K_F, K_R, K_N, K_B\) values in the range \([-0.7, ..., 0.7]\) rad/mm, in increments of 0.1 rad/mm for the human and dog datasets (a total of \(15 \times 15 \times 15 = 3,375\) \([K_F, K_R, K_N]\) triplets) and a range of \([-2.75, ..., 2.75]\) rad/mm, in increments of 0.25 rad/mm, for the rat datasets (a total of \(23 \times 23 \times 23 = 12,167\) \([K_F, K_R, K_N]\) triplets). For each triplet, the GHM equation was applied within a local neighborhood \(N\) of size \(5 \times 5 \times 5\) voxels with origin at \(v\) to provide a 3D orientation \(\alpha\) at each voxel \(v\) in \(N\). This neighborhood size is about the largest that can be used for the rat heart datasets, where we have approximately 10 voxels from outer wall to inner wall. In our implementation, for storage reasons, we discretized a GHM’s orientation \(\alpha\) to the closest direction among 100 uniformly distributed samples on the hemisphere. The angle between \(u\) and the fiber direction, indicated by the DT principal eigenvector \(e_i\) at \(v\) was then computed, and this angular difference was averaged over all \(v\) in \(N\) to provide a goodness-of-fit measure for the model. We note that, due to the discretization of the GHM’s orientation, even a perfect fit would result in an average error of about 5.4°. The goodness-of-fits measure was used to determine the best-fitting set of \([K_F, K_R, K_N]\) parameters. In order to control for overall heart size differences, the \([K_F, K_R, K_N]\) parameters were normalized with respect to the MD of the human heart, such that, for example, \(K_{num} = K_F \times \text{MD} / \text{MDhuman}\). For each fit, the x axis of the GHM frame at \(v\) was aligned with \(e_i\), with its z axis aligned with the projection of the local normal vector to the heart wall onto the plane orthogonal to \(e_i\). The heart wall normal direction was estimated using the local gradient to a Euclidean distance function (40) within the heart wall. In this manner, the frame rotated smoothly throughout the heart wall and allowed the z axis to be associated with the penetration direction used to define a fiber angle in the literature (19, 20).

Quantitative Assessment of GHM Fitting Errors. The angular error of fit \(\beta\) at \(v\) was computed as the average angular difference between data and model direction, within the six nearest neighbors of \(v\). The calculated \(\beta\) values were placed in bins corresponding to the inherent discretization of the data directions and were statistically analyzed by obtaining a least squares fit of a von Mises probability density function (30):

\[ f(\beta | \mu, \kappa) = \frac{e^{\kappa \cos(\beta - \mu)}}{2\pi I_0(\kappa)} . \]

Here \(\mu\) is a measure of the amount of angular error \(\beta\) with \(\kappa\) a measure of its concentration at that amount——i.e., \(1/\kappa\) is analogous to the variance of a normal distribution. We report the mean and standard deviation of \(K_F, K_R, K_N, K_B\) and the \(\mu\) and \(\kappa\) parameters for each dataset in Table 1, with an associated quantitative and qualitative assessment in Fig. 5. We carry out an additional experiment to assess the effect of increasing neighborhood size \((N = 3, 5, 7, 9)\) on the human heart dataset, measuring the error for all voxels within the associated spherical neighborhood. The \(\mu\) and \(\kappa\) parameters resulting from a von Mises fit are presented in Table 2.

Appendix: The GHM Model for \(\theta\) Is a Minimal Surface

A minimal surface is one whose mean curvature vanishes everywhere (15, 16). The mean curvature is given by the trace of the shape operator, which is the differential dN expressed in terms of the local coordinates of the tangent space \(T_p(S)\) at a point \(p\) of the surface normal vector \(N\). We begin by expressing \((x, y, z, \theta)\) in the parametric form \(h(u, v, w) = (x(u, v, w), y(u, v, w), z(u, v, w), \theta(u, v, w))\), where \(\theta\) is a three-dimensional surface in four-dimensional Euclidean space \(\mathbb{E}^4\). We rearrange the GHM expression for \(\theta\) as

\[ \tan(\theta - K_B z^2) = \frac{K_T x^2 + K_N z^2}{1 + K_N x^2 - K_T y^2} \]

and let \(z(u, v, w) = w\) and \(\theta(u, v, w) = v\) to get tan\((v - K_B w) = \sin(v-K_B w)\). Multiplying the numerator and the denominator of the right-hand side of this equation by the parameter \(u\) and requiring equality with the right-hand side of [1] leads to the parametric equations

\[ x(u, v, w) = \left( K_T^2 + K_N^2 - K_T^2 u \sin(v - K_B w) \right) K_T \left( K_T^2 + K_N^2 \right) \]

\[ y(u, v, w) = K_T + K_N u \sin(v - K_B w) - K_T u \cos(v - K_B w) \]

\[ z(u, v, w) = w, \quad \theta(u, v, w) = v. \]

An expression for the normal vector \(N\) at a given point of the surface is found by solving for the null space of \(J\), where \(J\) is the Jacobian matrix of parametrization \(h\). The solution space is a line in \(\mathbb{R}^4\), and so \(N\) is taken as the direction vector of that line:

\[ N = \begin{bmatrix} -K_T \cos(v-K_B w) - K_N \sin(v-K_B w) \\ K_T (K_T^2 - K_N^2 \sin(v-K_B w)) \\ K_N (K_T^2 - K_N^2 \sin(v-K_B w)) \\ -K_B \end{bmatrix} \]

Projected in the local coordinates of the tangent space \(T_p(S)\) at \(p\), which are given by \(dh/d\theta = (dx/d\theta, dy/d\theta, dz/d\theta, d\theta/d\theta)\), and \(dh/dv, dh/dw, dN\) becomes

\[ dN = \begin{bmatrix} dN_x \frac{\partial h}{\partial x} & dN_y \frac{\partial h}{\partial y} & dN_z \frac{\partial h}{\partial z} & dN_\theta \frac{\partial h}{\partial \theta} \\ dN_x \frac{\partial h}{\partial x} & dN_y \frac{\partial h}{\partial y} & dN_z \frac{\partial h}{\partial z} & dN_\theta \frac{\partial h}{\partial \theta} \\ dN_x \frac{\partial h}{\partial x} & dN_y \frac{\partial h}{\partial y} & dN_z \frac{\partial h}{\partial z} & dN_\theta \frac{\partial h}{\partial \theta} \\ dN_x \frac{\partial h}{\partial x} & dN_y \frac{\partial h}{\partial y} & dN_z \frac{\partial h}{\partial z} & dN_\theta \frac{\partial h}{\partial \theta} \\ \end{bmatrix} \]

The number of points (44,462) at each stage of the motion was the same as in the previous study (46) with a statistical technique used to analyze the data and compare the fitted results with the measured results. The calculations are performed on a powerful computer using high-speed parallel processing. The results are then compared with the measurements and the fit is refined until the best agreement is achieved. The parameters resulting from the fitting procedure are reported in Table 2.
where $\langle \cdot , \cdot \rangle$ denotes the Euclidean dot product in $\mathbb{R}^4$. With the expressions for $h = (x, y, z, \theta)$ provided in [2–4] and with the expression for the normal vector $N$ provided in [5], one can verify that \[
\text{trace}(\nabla N) = \langle \nabla N/\partial w, \nabla h/\partial w \rangle + \langle \nabla N/\partial w, \nabla h/\partial w \rangle + \langle \nabla N/\partial w, \nabla h/\partial w \rangle = 0, \forall (x, y, z, \theta), \] which completes the proof.

ACKNOWLEDGMENTS. We thank Patrick A. Helm and Raimond L. Winslow at the Center for Cardiovascular Bioinformatics and Modeling, and Elliot McVeigh at the National Institutes of Health (NIH), for provision of the human and dog DT-MRI data; G. B. Pike for helpful discussions; and I. Siddiqi and O. Siddiqi for comments on the manuscript. P.S. is supported by the NIH. G.J.S. is supported by the Dutch Technology Foundation, the applied science division of the Netherlands Organization for Scientific Research and the Technology Program of the Ministry of Economic Affairs (Grants 07952 and 10191). S.W.Z. is supported by the NIH (National Institute on Alcohol Abuse and Alcoholism) and the National Science Foundation. K.S. is supported by the Natural Sciences and Engineering Research Council of Canada, Fonds de recherche du Québec—Nature et technologies, and McGill University.