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Joint prediction of longitudinal development of cortical surfaces and white matter fibers from neonatal MRI

Islem Rekik[a,b], Gang Li[a], Pew-Thian Yap[a], Geng Chen[a], Weili Lin[a], Dinggang Shen[a,c,*]

[a] Department of Radiology and BRIC, University of North Carolina at Chapel Hill, NC, USA
[b] CVIP, Computing, School of Science and Engineering, University of Dundee, UK
[c] Department of Brain and Cognitive Engineering, Korea University, Seoul 02841, Republic of Korea

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ABSTRACT

The human brain can be modeled as multiple interrelated shapes (or a multishape), each for characterizing one aspect of the brain, such as the cortex and white matter pathways. Predicting the developing multishape is a very challenging task due to the contrasting nature of the developmental trajectories of the constituent shapes: smooth for the cortical surface and non-smooth for white matter tracts due to changes such as bifurcation. We recently addressed this problem and proposed an approach for predicting the multishape developmental spatiotemporal trajectories of infant brains based only on neonatal MRI data using a set of geometric, dynamic, and fiber-to-surface connectivity features. In this paper, we propose two key innovations to further improve the prediction of multishape evolution. First, for a more accurate cortical surface prediction, instead of simply relying on one neonatal atlas to guide the prediction of the multishape, we propose to use multiple neonatal atlases to build a *spatially heterogeneous* atlas using the multidirectional varifold representation. This individualizes the atlas by locally maximizing its similarity to the testing baseline cortical shape for each cortical region, thereby better representing the baseline testing cortical surface, which founds the multishape prediction process. Second, for temporally consistent fiber prediction, we propose to reliably estimate *spatiotemporal* connectivity features using low-rank tensor completion, thereby capturing the variability and richness of the temporal development of fibers. Experimental results confirm that the proposed variants significantly improve the prediction performance of our original multishape prediction framework for both cortical surfaces and fiber tracts shape at 3, 6, and 9 months of age. Our pioneering model will pave the way for learning how to predict the evolution of anatomical shapes with abnormal changes. Ultimately, devising accurate shape evolution prediction models that can help quantify and predict the severity of a brain disorder as it progresses will be of great aid in *individualized* treatment planning.

Introduction

Multimodal MR imaging offers unprecedented insights into different facets of brain development. With the increasing availability of longitudinal postnatal brain imaging data, one can now track dramatic spatiotemporal changes in both white matter (Dubois et al., 2014) and gray matter (Gilmore et al., 2007) during the first years of postnatal development. The trajectories of these changes are often characterized using spatiotemporal shape models. However, great challenges arise when the shapes of different structures exhibit contrasting developmental behaviors. For instance, the cortical surface can be modeled as a shape that undergoes a *diffeomorphic* (i.e., smooth and invertible) evolution, whereas white matter pathways undergo a *non-diffeomorphic* evolution as they elongate and bifurcate with growth due to active myelination (Deoni et al., 2011).

Devising a robust and accurate framework for predicting, based on *neonatal* data, the development of multiple interlinked shapes, such as cortical surfaces and white matter tracts, is of great clinical interest. This allows identification of aberrant developmental patterns in case-control settings. There is a growing body of evidence in the neuroscience literature indicating that the shapes of structures in the developing brain can be used as biomarkers for many neurodevelopmental disorders. For instance, hemispheric shape asymmetries appeared to be influenced by sexually dimorphic factors or by schizophrenia pathophysiology (Narr et al., 2007). In addition, the morphology of cortical gyri and sulci at birth is found to be predictive of the pathological functioning in certain developmental and neuropsychiatric disorders (Dubois et al., 2008). This motivates designing shape-

* Corresponding author at: Department of Radiology and BRIC, University of North Carolina at Chapel Hill, NC, USA.
E-mail address: dgshen@med.unc.edu (D. Shen).

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based developmental prediction models to allow early diagnosis of neurodeveopmental and psychiatric illnesses that are rooted in early infancy (Lyall et al., 2014) as well as neurodevelopmental impairments in preterm infants (Kapellou et al., 2006).

Existing approaches to brain growth prediction are mainly focused on predicting the evolution of low-dimensional scalar data. For instance, Sadeghi et al. used nonlinear mixed-effects modeling to infer individual developmental trajectories for the radial diffusivity of the posterior thalamic radiation (Sadeghi et al., 2013, 2014; Gerig et al., 2016). Extension of methods as such to high-dimensional data involving multiple shapes poses significant challenges, as pointed out in Gerig et al. (2016). Fishbaugh et al. (2013) proposed a geodesic shape regression model rooted in the theory of currents to predict back in time subcortical shapes at 6 months from shapes at between 9 and 24 months of age. This model was further extended to integrate image data to evolve image and shape following the slope of the initial momenta vectors (Fishbaugh et al., 2014). However, for image-shape prediction, this model requires measurements at least at two time points. Even more advanced approaches still required more than one time point for prediction such as the works of Nie et al. (2010, 2012) where a mechanical cortical growth model was devised to simulate the dynamics of cortical folding from longitudinal MRI data in the first postnatal year.

To address these problems, we introduced in Rekik et al. (2015a,b,c) learning-based frameworks for predicting subject-specific spatiotemporal growth of the cortical surface solely from *neonatal* data acquired at a single time point. Although promising, these frameworks are focused only on predicting one shape (i.e., the cortical surface) and ignore other important shapes such as the white matter tracts. To the best of our knowledge, our work introduced in Rekik et al. (2016b) is the first attempt to address this limitation by *multishape* modeling of both cortical surfaces derived from structural MRI and the white matter fibers derived from diffusion MRI. Building on Rekik et al. (2015b,a,c), the proposed framework (Rekik et al., 2016a,b) employs a geodesic multidirectional varifold shape regression model to estimate a time-varying deformation velocity field that flows shapes diffeomorphically. In addition, the proposed framework harnesses fiber-to-surface connectivity for non-diffeomorphic modeling of the growth of white matter tracts. Specifically, our framework includes training and testing stages. In the training stage, for each infant, we learn from the training subjects (1) the geometric features of the cortical surface, (2) the dynamic features (i.e., evolution trajectories) of the baseline cortical surface, and (3) the fiber-to-surface connectivity features. In the testing stage, for the multishape of a testing neonatal subject, we select the best features that simultaneously predict the triangular faces on the cortical surface mesh and all the fibers traversing them at the 3, 6 and 9 months time points. Our framework affords several advantages. First, it does not require the computationally expensive process of registering thousands of fibers to establish tract-to-tract correspondence for prediction, which is prohibitive using a conventional diffeomorphic multishape registration setting as in Durrleman et al. (2014). Second, it guides fiber prediction using the diffeomorphic cortical surface deformation trajectory, which is less complex and can be estimated more accurately than that of fiber growth trajectory. More importantly, this enables us to account for fiber connectivity changes and the occurrence of new fibers, which can cause topological changes in the connections.

However, this first work on multishape prediction had a number of limitations, which we aim to address in this paper. First, our early approaches (Rekik et al., 2015b,a, 2016b) use a single-atlas approach where shape information from a single neonatal subject in the training dataset was used to obtain the shape predictions, failing to take into account possible spatial and topographic variability. To address this, we propose to use multiple atlases to estimate a *spatially heterogenous* atlas that best approximates the cortical shape of a testing subject. For this purpose, we use the multidirectional varifold shape similarity metric introduced in Rekik et al. (2015c, 2016a). Second, in our work (Rekik et al., 2016b), the fiber-surface relationship was determined based only on the neonatal time point, hence does not enforce temporal consistency. To address this, we propose to estimate *spatiotemporal* connectivity features from neonatal connectivity features using low-rank tensor completion (Kressner et al., 2014) to further refine the fiber selection process. Experimental results indicate that the two strategies mentioned above significantly improve the prediction accuracy in comparison with our previous method (Rekik et al., 2016b).

Table 1
Major mathematical notations used in this paper.

Mathematical notation	Definition
x	3D position in $\mathbb{R}^3$
W^*	space of currents and varifolds
W	testing space
ω	testing vector field in W
K_W	shape Gaussian kernel of RKHS
K_V	deformation Gaussian kernel
σ_W	decay rate of the Gaussian kernel K_W
σ_V	decay rate of the Gaussian kernel K_V
k_e	linear kernel for varifold definition
n	oriented unit normal vector in $\mathbb{R}^3$
$\overleftrightarrow{n}$	nonoriented unit normal vector in $\mathbb{R}^3$
ϕ_t	diffeomorphism (invertible and smooth mapping) at time t
v_t	the deformation velocity field at time t
p_k	initial deformation momentum in $\mathbb{R}^3$ located at the control point c_k
S_i	observed surface at timepoint t_i
$\tilde{S}_0$	reconstructed virtual shape
$\tilde{S}_i$	predicted surface, $i > 0$
$\mathcal{V}$	the dynamic cloud
$\mathcal{A}_i$	atlas at timepoint t_i
κ	principal curvature direction
F_i	ensemble of fibers
$\tilde{F}_0$	virtual ensemble of fibers
$\tilde{F}_i$	predicted fibers, $i > 0$
M_i	multishape (S_i, F_i) observed at timepoint t_i
$\pi^S(F)$	projecting fibers F onto a surface S
f^k	the two extremeties of fiber f, $k \in \{1, 2\}$
ξ	a triangular face (mesh)
μ	a vertex in $\mathbb{R}^3$
μ_l	a vertex belonging to a labeled region l
$\mathcal{F}(\xi)$	set of fibers that hit the face ξ
$d(\xi, \xi')$	similarity measure between two faces ξ and xi' in fiber properties
ϵ	radius of the local neighborhood search
$\mathcal{T}_\mu$	low-rank tensor of size $N_k \times N_t \times N_s$ defined at vertex μ
$\mathcal{E}_\mu$	masking tensor of size $N_k \times N_t \times N_s$ defined at vertex μ
$\mathbf{r}$	multilinear rank of dimension 1×3
N_k	number of faces in k-ring neighborhood centered at vertex μ
N_t	number of acquisition timepoints (including the first observation)
N_s	number of all training subjects + the new testing subject
$\mathcal{M}_\mathbf{r}$	smooth manifold of tensors
P_Ω	linear tensor projection onto Ω

Fundamental works on longitudinal multishape prediction from a single measurement

In this section, we provide a comprehensive overview of the first works related to learning-based shape prediction for the developing infant brain. These present the building blocks of the *enhanced* multishape prediction model devised in this paper. For easy reference and to enhance the readability, we summarized the major mathematical notations in Table 1.