Using the Wild Bootstrap to Quantify Uncertainty in Fibre Orientations from Q-Ball Analysis

H. A. Haroon[1], and G. J. Parker[1]

[1]Imaging Science and Biomedical Engineering, The University of Manchester, Manchester, England, United Kingdom

Introduction   Bootstrapping of repeated diffusion-weighted image datasets enables non-parametric quantification of the uncertainty in the inferred fibre orientation for probabilistic fibre tracking[1]. Unlike the conventional bootstrap technique, the wild bootstrap method requires a single image dataset to be acquired. Previously, the wild bootstrap method has been presented as an alternative to conventional bootstrapping for diffusion tensor imaging[2,3], as data can be collected in a fraction of the time, bringing bootstrapping into the clinical domain. Here we present a study of two possible implementations of wild bootstrapping using Q-Ball analysis[4] and compare the outputs with conventional bootstrapping.

Methods   MR diffusion-weighted data were acquired on a 3T Philips Achieva scanner (Philips Medical Systems, Best, Netherlands) using an 8-element SENSE head coil. A PGSE EPI sequence was implemented with TE = 54ms, TR = 6000ms, G_{max} = 62mT/m, partial Fourier factor 0.679, 112 × 112 matrix reconstructed to 128 x 128, reconstructed resolution 1.836 mm, slice thickness 2.1 mm, 34 contiguous slices, 61 diffusion sensitisation directions at b = 1200s/mm^2 (Δ = 28.37ms, δ = 13.52ms), 1 at b = 0, SENSE acceleration factor = 2.5. The total imaging time was 7 minutes. This sequence was repeated on 8 occasions in the same volunteer to provide a conventional boostrapping dataset. All diffusion-sensitised images were registered to the corresponding b = 0 image within each slice location and for all scanning repetitions to the first scan, using a 2D affine registration implementing using FLIRT[5] (http://www.fmrib.ox.ac.uk/fsl/flirt).

Software was developed in-house in MATLAB (http://www.mathworks.com/products/matlab/) to implement Q-Ball analysis on our data, and to implement conventional and wild bootstrapping.

Conventional Bootstrapping: Conventional bootstrapping was applied to the 8 diffusion-weighted scan repetitions. Over 1000 iterations, a new image set was created by randomly taking a voxel from any of the 8 repetitions, in the same slice and in matching diffusion-sensitising directions, on a voxel-by-voxel basis.

The image set created by each bootstrap sampling was then processed using the Q-Ball method, which generates diffusion orientation distribution functions (ODF)[4] whose peaks relate to the principle underlying fibre orientations (one or more). The ODF values are reconstructed at 642 discrete points on a unit sphere given by a three-fold tessellated icosahedron, within each voxel. We fit a local 2D quadratic to the ODF values on the sphere to give an interpolated estimate of the actual underlying fibre orientation. Q-Ball also allows us to generate general fractional anisotropy (GFA)[4] maps.

Wild Bootstrapping Variant 1: Wild bootstrapping was applied only to the first of the 8 diffusion-weighted scan repetitions. Firstly this image set was processed with Q-Ball to generate ODFs. The original diffusion signal was then recovered from the ODFs using the following monoexponential approximation derived from equations given in [4]:

$$E(\mathbf{q}(\mathbf{u})) = E_0 \cdot \exp\left[-4\pi \cdot Z^2 \cdot (\mathbf{q}(\mathbf{u}))^2 \cdot (\psi(\mathbf{u}))^2\right] \quad \ldots[1],$$ where $E(\mathbf{q}(\mathbf{u}))$ is the diffusion-weighted signal measured along a direction

vector $\mathbf{u}$, with a given diffusion wavevector $\mathbf{q}$. E_0 is the non-diffusion-weighted signal, i.e. measured with $\mathbf{q}$=0. Z is a normalization constant[4] and $\psi(\mathbf{u})$ is the ODF value along $\mathbf{u}$. The diffusion wavevector is defined as $\mathbf{q}(\mathbf{u}) = (2\pi)^{-1} \cdot \gamma \delta G(\mathbf{u})$, where $G(\mathbf{u})$ is the diffusion gradient vector parallel to $\mathbf{u}$. We first use a 2D quadratic fit to interpolate the ODF values in the direction of the diffusion-sensitizing gradients and then use equation [1] to recover the predicted diffusion-weighted signals in these directions.

Wild Bootstrapping Variant 2: As with variant 1, this image set was first processed with Q-Ball to generate ODFs. The underlying fibre orientations were then interpolated using a local 2D quadratic fit, as for the conventional bootstrap. Using the number of fibres extracted in each voxel from the ODFs we fitted one, two or three diffusion tensors to the original diffusion-weighted signal acquired[6,7], or assumed isotropic diffusion if the number of fibres extracted using Q-Ball was greater than three. The predicted signal was then recovered using the fitted diffusion tensors[6].

Wild Bootstrapping Variants 1 & 2: A residual was calculated by taking the difference between the recovered (predicted) diffusion-weighted signal, from the Q-Ball ODFs (variant 1) or the multi-tensor fitting (variant 2), and the original diffusion-weighted signal acquired on the scanner. For each variant, over 1000 iterations, a new image set was created by randomly shuffling the residuals, for any given voxel, amongst all the diffusion-encoding directions and then adding them on to the recovered (predicted) diffusion-weighted signals. The image set created by each bootstrap sampling was then processed with Q-Ball to extract the estimates of underlying fibre orientations, as described above.

We compared the distribution of fibre orientations, and plotted the mean of the GFA values amongst the 1000 iterations, from the conventional bootstrap against the two variants of wild bootstrapping.

Results and Discussion   Figure 1(a) is a GFA map with the zoomed-in region used for Figs 1(b-d) highlighted by the blue box. Fig 1(b) shows a sample of the fibre orientation estimates derived using conventional Q-Ball bootstrapping. Our derivation of equation [1], used in variant 1, comes from an assumption that a single radial diffusion coefficient is adequate to generate the predicted signal needed to provide residuals for wild bootstrapping. Fig 1(c) shows that in many areas this simplification is justified. However, some voxels demonstrate significantly different structure to that predicted using the conventional bootstrap. The results of variant 2 are shown in Fig 1(d). Most of the recovered structure is very similar to that obtained using the conventional bootstrap, indicating a better derivation of residuals than for variant 1. Fig 1(e) shows a plot of mean GFA from the entire slice obtained using conventional bootstrap versus mean GFA obtained using wild bootstrapping variants 1 (red) and 2 (green). Variant 2 shows greater consistency with conventional bootstrap.

Wild bootstrap Q-Ball allows the generation of fibre orientation PDFs for multi-fibre probabilistic tractography using any diffusion data acquisition that supports the Q-Ball analysis. The benefits of PDF generation in this way are (1) that there is no requirement for calibration of the PDFs against estimated noise levels using test functions[8] and (2) that there is no need for model selection when deciding how many fibres are present in a voxel[9]; both of which introduce approximations into the probabilistic tracking process. We therefore expect that wild bootstrap based on Q-Ball, or other methods for extracting multiple fibre orientations, will be a useful component of probabilistic tracking methodologies.
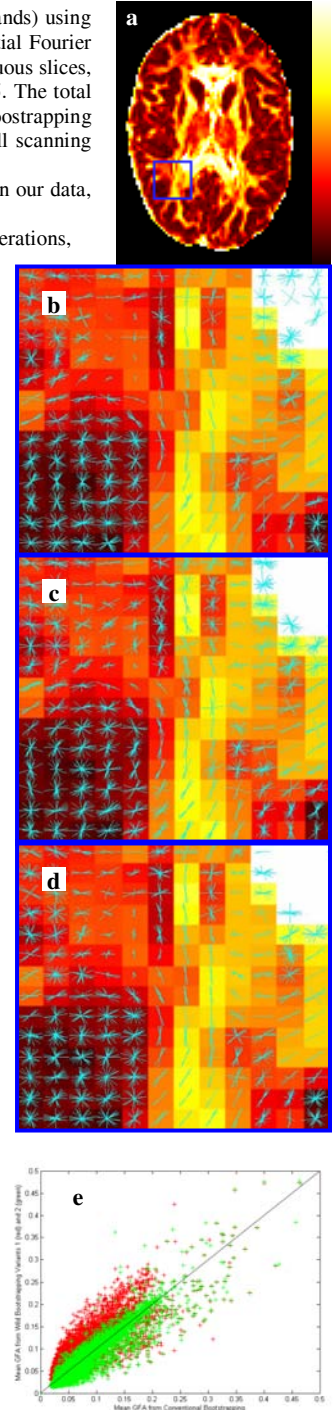
Figure 1. (a-e) Please see text.

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