

Software Licence

This software and data licence agreement (the "**Licence**") is a legally binding agreement between **You** (as defined below) and the **MEDICAL RESEARCH COUNCIL**, a public body established by Royal Charter, and incorporated under the laws of England, having a head office address at 2nd Floor David Phillips Building, Polaris House, North Star Avenue, Swindon, SN2 1FL, UK (hereinafter, "**MRC**"¹).

PREAMBLE

(A) MRC aims at (i) promoting and supporting high-quality basic, strategic and applied research; and (ii) advancing and disseminating knowledge and technology; thereby, contributing to the maintenance and improvement of human health.

(B) The Faculty of Sciences of the University of Lisbon (hereinafter, "**FCUL**"²) is committed through teaching, research and innovation to support advancement and dissemination of knowledge and technology.

(C) The MRC, and more specifically the MRC Cognition and Brain Science Unit, and FCUL, and more specifically the FCUL Institute of Biophysics and Biomedical Engineering, contributed to the elaboration of the Software and wish to make the Software available subject to the terms and conditions set out in this License.

IT IS HEREBY AGREED AS FOLLOWS

1 DEFINITIONS

"**Licence**" means this agreement, in relation to the Software.

"**GUI**" means

- (a) the Graphic User Interface and related computer programs in machine-readable object code form (including updates) designed by the MRC; and
- (b) any data, source code, or information incorporated in, or related to, the Graphic User Interface.

"**Protected Function**" means an individual utility which can be either called from the GUI or the command line and any source code or information which directly relates to such individual utility. The source code of the Protected Functions will not be provided.

"**Source Codes**" means only the source codes made available to You by MRC. For the avoidance of doubt, Sources Codes do not include the source codes of the Protected Functions.

"**Software**" means

- (a) the UDKI toolbox as described in the Annex 1 and any data, source code, functions or information incorporated in, or related to, the UDKI toolbox, which aims at Diffusion Kurtosis Imaging (DKI) data processing and analysis;
 - (b) the GUI;
 - (c) the Protected Functions; and
 - (d) the Source Codes;
- whether or not protected or protectable by intellectual property rights and any intellectual property rights in the foregoing.

"**You**" mean the user of the Software; whether an individual, a sole proprietorship, a partnership, a limited partnership, a limited liability partnership, a corporation, a limited

¹ Notices to MRC: FAO General Counsel, MRC Technology, Lynton House, 7-12 Tavistock Square, London WC1H 9LT, UK.

² Notices to FCUL: Faculdade de Ciências da Universidade de Lisboa, Campo Grande, Edifício C5, 1749-016 Lisboa

liability company, a business trust, a joint stock company, a trust, an incorporated association, a joint venture or similar entity or an organization (including a government or political subdivision or department or agency of a government). "**Your**" shall refer to the same and be construed accordingly.

In this Agreement, words denoting the singular include the plural and vice-versa

2 GRANT

- 2.1 Subject to Clause 3, MRC hereby grants to You a non-exclusive, non-transferable, worldwide, revocable right to install and use the Software free of charge at Your premises for the sole purpose of internal non-commercial research.
- 2.2 By using the Software, You confirm that You accept the rights granted under Clause 2.1 and that You agree to comply with the terms and conditions of this Licence. However, if You do not agree to comply with these terms and conditions, You must not use the Software for any purpose.
- 2.3 MRC retains all right, title and interest in and to the Software, the related source code, and any and all associated patents, copyrights, and other intellectual property rights in any jurisdiction worldwide. Except as expressly provided in this Licence no rights are provided to You under any intellectual property rights or other proprietary rights vested in the MRC.
- 2.4 The MRC does not claim ownership of any data, results or intellectual property produced by You as a result of Your use of the Software under this Licence.

3 USE OF THE SOFTWARE

3.1 You may:

(i) Modify, translate, reproduce, improve or otherwise alter any of the Source Codes, provided that the results of such activities are made available to the public under the same terms as the Software has been made available to You under this Licence;

(ii) Publish or disclose any result obtained through the use of the Software in scientific journals and/or scientific meetings, provided that:

- a. You acknowledge the MRC and FCUL in any publication/disclosure of results, in accordance with academic norms and customs; and
- b. You include the following references:

"Neto Henriques, R., Correia, M.M., Nunes, R.G., Ferreira, H.A., 2015. Exploring the 3D Geometry of the Diffusion Kurtosis Tensor - Impacts on the Development of Robust Tractography Procedures and Novel Biomarkers. *NeuroImage* 111, 85-99. doi.: 10.1016/j.neuroimage.2015.02.004."

And

"Neto Henriques, R., Ferreira, H.A., Correia, M.M., 2015. United Diffusion Kurtosis Imaging (UDKI) toolbox. *MAGMA* 28 (S1): 511-512. doi: 10.1007/s10334-015-0490-7."

3.2 You agree NOT:

- (i) To sell, distribute, or sublicense the Software, incorporate it into other software or products for commercial exploitation, or to use the Software other than as provided for under this Licence.
- (ii) To access, translate, modify, alter, decompile, disassemble, reverse engineer, reverse compile, attempt to derive, or reproduce any source code or any information of the Protected Functions included in the Software.
- (iii) To remove any copyright or other proprietary or product identification notices from the Software.
- (iv) To make any use of the Software in any way which breaches any applicable law, including without limitation, any infringement of intellectual property rights of MRC and/or third parties.
- (v) To use the Software as a clinical diagnostic or to support or inform clinical decisions or for providing care to humans.

3.3 You agree that no rights are provided under this Licence to use the Software for commercial purposes, including the provision of a commercial service or to use the Software on behalf of any commercial entity or for use in consulting for a commercial entity.

3.4 You will not provide, or otherwise make available (including by loading the Software onto the Internet or any network or system), the Software in any form, in whole or in part (including but not limited to, program listings, object and source program listings, object code and source code) to any third party without MRC's prior written consent.

3.5 Should you wish to make any other use of the Software other than as set out in this Licence, advance permission will be required from MRC and/or its licensors.

4 OTHER TERMS OF USE

4.1 MRC does not guarantee that the Software will always be available. MRC may, at its sole discretion, suspend, withdraw, discontinue, change, amend and/or update all or any part of the Software without notice. MRC will not be liable to You if for any reason any Software is unavailable at any time or for any period.

4.2 In the event of any breach of these terms and conditions by You, Your right to use the Software will cease immediately and You shall destroy any copies of the Software that you have made.

4.3 In the event of You being an organisation, You will ensure that access to the Software is restricted to Your employees, agents, visiting workers, or students who reasonably have need for such access only for use as permitted under this Licence, and that such persons comply with the provisions of this Licence.

4.4 You acknowledge that if any additional intellectual property, software or hardware is required to use or operate the Software, then You shall be solely responsible for obtaining such licences or equipment, at Your own expense.

4.5 Both Parties recognise that the Software is provided "as is" without warranty of merchantability or fitness for a particular purpose or any other warranty, express or implied, and without any representation or warranty that the use or supply of the

Software will not infringe any patent, copyright, trademark or other right.

- 4.6 In no event shall MRC be liable for Your use of the Software or any results arising from Your use of the Software and for any direct or indirect damages or losses, including any loss of profits, loss of revenue, loss of business, loss of data, loss of contracts or opportunity, resulting from Your use of the Software or any results arising from Your use of the Software. You hereby agree to indemnify and hold harmless the MRC for any loss, claim, damage, or liability, which may arise from Your use of the Software or any results arising from Your use of the Software.

5 TERM AND TERMINATION

- 5.1 This Licence shall come into force and effect as soon as the Software is downloaded by You and shall remain in force for as long as You have possession of the Software.
- 5.2 MRC shall have the right to terminate this Licence without cause; such termination to be effective ten (10) days following the date notice is given.
- 5.3 Upon the termination of this Licence for any reason, You will cease using the Software and delete all copies made.

6 GENERAL PROVISIONS

- 6.1 *Changes to these terms:* MRC may revise these terms and conditions at any time by amending this page. Please check this page from time to time to take notice of any changes we make, as they are binding on You.
- 6.2 *Severability of Provisions:* If any provision of this Licence is declared void or unenforceable by any judicial or administrative authority this will not *ipso facto* nullify the remaining provisions of this Licence and the provision of this Licence so affected will be curtailed and limited only to the extent necessary to bring it within the legal requirements.
- 6.4 *Publicity:* You shall not utilise the name or marks of the MRC in any publication, promotional or advertising context, or press release regarding the subject matter of this Licence without the prior written consent of the MRC.
- 6.5 *Governing Law & Jurisdiction:* This Licence shall be governed by English Law, and subject to the exclusive jurisdiction of the English Courts.

Annex 1

Abstract

United Diffusion Kurtosis Imaging (UDKI) is a toolbox for Diffusion Kurtosis Imaging (DKI) data processing. It includes DKI pre-processing steps and modules to estimate the kurtosis tensor and standard diffusion and kurtosis rotational invariant measures. This toolbox also includes DKI biological modelling for estimation of axonal water fraction and DKI based tractography. UDKI is fully implemented in MATLAB and it is compatible with any operating system (Window, Linux or Mac OS X) with a base installation of MATLAB (version 7.8 onwards). The base MATLAB license is not provided with this toolbox. UDKI functionalities are grouped in six modules: pre-processing; DTI/DKI model fitting; estimation of diffusion tensor rotational invariant measures; estimation of kurtosis tensor rotational invariant measures; fitting of DKI biophysical models; and DKI based tractography reconstruction.

Toolbox Details

Pre-processing: includes optional procedures to smooth diffusion-weighted data, functions for voxel resolution resampling, and functions to remove background voxels. All these procedures are implemented using basic MATLAB functions.

DTI/DKI model fitting: includes the constrained tensor estimation approach as suggested by Tabesh et al. (2011), and the robust fast estimation of the mean diffusivity and kurtosis (Neto-Henriques, 2012a; 2012b).

Estimation of diffusion tensor rotational invariant measures: includes the estimation of the mean diffusivity, axial diffusivity, radial diffusivity, fractional anisotropy according to Pierpaoli and Basser (1996), and the estimation of the linear, planar and spherical anisotropy according to Westin et al. (1997).

Estimation of Kurtosis tensor rotational invariant measures: includes the estimation of mean, axial and radial kurtosis following to Tabesh et al. (2011)

Fitting of DKI biophysical models: includes the DKI based biological model fit as proposed by Fieremans et al. (2011).

DKI based tractography reconstruction: includes the fiber direction estimation algorithms as proposed by Jensen et al. (2014) and Neto Henriques et al. (2015). From the fiber direction estimates, tractography is reconstructed using an adapted version of a brute force streamline algorithm described by Huang et al. (2004), however generalized to handle cases of crossing fibers.

References

- Fieremans, E., Jensen, J.H., Helpert, J.A., 2011. White matter characterization with diffusion kurtosis imaging. *NeuroImage* 58, 177-188. doi: 10.1016/j.neuroimage.2011.06.006
- Huang, H., Zhang, J., van Zijl, P.C., Mori S., 2004. Analysis of noise effects on DTI-based tractography using the brute-force and multi-ROI approach. *Magn Reson Med*. 52(3), 559-65.
- Jensen, J.H., Helpert, J.A., Tabesh, A., 2014. Leading non-Gaussian corrections for diffusion orientation distribution function. *NMR Biomed*. 27, 202-211. doi: 10.1002/nbm.3053
- Neto Henriques, R., Correia, M., Cam-CAN, 2012a. Towards optimization of diffusion Kurtosis imaging to study brain changes with age. Poster presentation at the 29th annual meeting of the European Society for Magnetic Resonance in Medicine and Biology, Lisbon.
- Neto Henriques, R., Ferreira, H.A., Correia, M.M., 2012b. Diffusion Kurtosis Imaging of the Healthy Human Brain. Master Dissertation Bachelor and Master program in Biomedical Engineering and Biophysics, Faculty of Sciences, University of Lisbon. <http://repositorio.ul.pt/handle/10451/8511>
- Neto Henriques, R., Correia, M.M., Nunes, R.G., Ferreira, H.A., 2015. Exploring the 3D Geometry of the Diffusion Kurtosis Tensor - Impacts on the Development of Robust Tractography Procedures and Novel Biomarkers. *NeuroImage* 111, 85-99. doi: 10.1016/j.neuroimage.2015.02.004
- Pierpaoli, C., Basser, P. J., 1996. Toward a quantitative assessment of diffusion anisotropy. *Magnetic Resonance in Medicine*, 36(6), 893-906. doi:10.1002/mrm.1910360612
- Tabesh, A., Jensen, J. H., Ardekani, B. A., Helpert, J. A., 2011. Estimation of tensors and tensor-derived measures in diffusional kurtosis imaging. *Magn. Reson. Med*. 65(3), 823-836. doi:10.1002/mrm.22655
- Westin, C.-F., Peled, S., Gubjartsson, H., Kikinis, R., Jolesz, F., 1997. Geometrical diffusion measures for MRI from tensor basis analysis. *Proc. 5th Annual ISMRM*.