User's manual for `BISM.m`

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The script `BISM.m` (Bayesian Inversion Stress Microscopy) is free to use. It requires `MATLAB`. It should be placed in the directory that contains the movies to be processed (in `.mat` format). Alternatively set the directory path for the file `BISM.m` in `MATLAB`.

See the article *"Inference of internal stress in a cell monolayer"*, V. Nier *et al.*, Biophysical Journal **110** 1625-1635 (2016) (also **arXiv:1603.03694**) for a complete description of Bayesian Inversion Stress Microscopy, and for further introduction to the notations used in the following.

Fig. 1 summarizes the algorithm. An input traction force movie is handled frame by frame in a vector form $\vec{T}$. BISM uses the balance of linear momentum and prior information to determine the internal stress tensor $\boldsymbol{\sigma}$ of the cell monolayer within a Bayesian formalism. If the tissue is confined, boundary conditions for the stress are known and can be embedded in the prior. A regularization parameter Λ, characterizing the respective weight of the prior versus that of the likelihood, has to be determined. In order to do so, it is possible to use either the Maximum A Posteriori (MAP) method or the L-curve approach. A divergence matrix $\mathbf{A}$ and a prior matrix $\mathbf{B}$ are defined. The stress field is estimated as the most likely value of the posterior dstribution (Eq. (14)):

$$\hat{\vec{\sigma}} = \left(\Lambda\mathbf{B} + l^2\mathbf{A}^T\mathbf{A}\right)^{-1} l^2\mathbf{A}^T\vec{T}$$

in vector form. It is linearly interpolated on the same grid as the input traction force

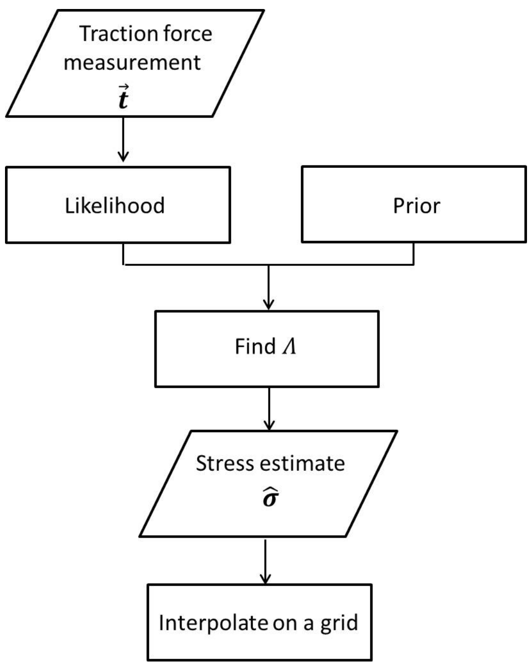

Figure 1: Flow-chart of the algorithm.

field, where l is the mesh size. Given a traction force field in kPa, the internal stress field will be in kPa μm. A stress field in kPa is obtained by dividing the output of `BISM.m` by the monolayer height. When the error bar on the traction force measurement is known, `BISM.m` also estimates error bars on the stress. A coefficient of determination R^2 quantifies the difference between $\vec{T}$ and $\mathbf{A}\vec{\sigma}$.

Parameters Values for the following parameters must be prescribed.

Parameters	Definition
`ForceName`	Name of the traction force file to be processed in `.mat` format.
	The structure has one field for each frame.
	Each field has two cells, one for each traction force component.
`R`	Number of rows
`C`	Number of columns
`kM`	Number of time steps
`coeff`	Conversion factor, in μm/pixel
`xmin, xmax`	x coordinates of the domain boundaries, in μm
`ymin, ymax`	y coordinates of the domain boundaries, in μm
`BC`	Boundary Conditions
	`BC` $= 1$ for a confined tissue
	`BC` $= 0$ otherwise
`meth_Lambda`	Determination of the regularization parameter Λ
	If `meth_Lambda` $= 1$, use Maximum A Posteriori (MAP) optimixation
	If `meth_Lambda` $= 2$, use the L-curve
	If `meth_Lambda` $= 3$, use a given value (default value 10^{-6})
`noise_value`	Noise amplitude on the traction force measurement, in the same unit as the traction force
	Use `noise_value` $= 0$ when unknown
`fplot`	Graphics enabled when `fplot` $= 1$
`mult`	If `fplot` $= 1$, multiplicative coefficient for a better plot of the stress field (default value 1)

Notes

- The main *input* is a time-lapse sequence of cell-substrate traction force measurements with `kM` time steps. Measurements must be given on a regularly spaced grid defined in cartesian coordinates. The parameters defining the grid are the number of columns C, the number of rows R, corresponding respectively to the number of points in the x and y direction. The grid lies between `xmin` and `xmax`, and `ymin` and `ymax` with the same spatial resolution l in both directions. The parameter `coeff` convert pixels into μm if necessary.

- The input file 'Traction_field.mat' contains a MATLAB structure `traction`, with `kM` traction force fields, each corresponding to a time step. For each frame `k0`, framek0 contains itself two $R \times C$-matrices tx and ty, respectively the x and y components of the traction forces.

- When using MAP optimization or a L-curve, run BISM.m first on a few images in order to determine Λ (meth_Lambda= 1 or 2), then set Λ to its optimal value (meth_Lambda= 3). The same value of Λ should be used for all frames in order to be able to compare the internal stress fields obtained.

- The *output* of the script is the structure stress saved in the stress_BISM.mat file. For each frame k0, this structure first contains the regularization parameter Lambda. The stress field components σ_{xx}, σ_{yy} and σ_{xy} are given as $R \times C$ matrices, sxx, syy and sxy where the columns (*resp.* the rows) correspond to the x (*resp.* the y) coordinate. The vectors x and y contain the x and y coordinates of the internal stress field, defined on the same grid as the traction force field. Accuracy is quantified by the coefficient of determination R2_T. The mean values of the inferred stress components are stored as mean_from_sigma. In the case of a confined system, it is possible to calculate exactly the mean value of the different stress components directly from the traction force measurement, using (Eq.S2): $\langle \sigma_{\mathrm{ik}} \rangle = -\langle t_{\mathrm{i}} x_{\mathrm{k}} \rangle$. These values are stored for comparison as mean_from_t.

- When BISM is used with noise_value $\neq 0$, the script generates three additional output fields error_sxx, error_syy and error_sxy corresponding to the error bars on each stress component. When noise_value is not known from the experiment, it may be estimated from the traction force data by MAP optimisation and the L-curve method (meth_Lambda $= 1$ or 2) as noise_value_MAP and noise_value_Lcurve respectively.

- When fplot $= 1$, the traction force and stress fields are represented graphically. At each point, the stress tensor is represented by two line segments oriented along the stress eigenvectors, of lengths proportional to the eigenvalues with the following color code: blue, tensile stress; red, compressive stress. The coefficient of proportionality mult allows to adapt the length of the line segments if necessary. A direct comparison between exact and inferred stresses is also plotted for each component.

- In order to test this code and to familiarize oneself with the format and notations, we provide an example of a force field. The file 'Traction_field.mat' contains one frame, from a confined domain with boundaries xmin=ymin=0 and xmax=ymax=100 μm (R = C = 50, coeff = 1). This traction force field, given in kPa, has been computed from a finite element simulation of a viscous material driven by active force dipoles (see Nier *et al.* 2016) to which we added a random noise of 5% relative amplitude. For comparison, we also provide in the file 'Stress_field.mat' the exact stress field, given in kPa μm, from the same numerical simulation.