1. What is Computational Anatomy?

Computational anatomy is a relatively new research field at the intersection of biology/medicine and mathematics that studies and develops methods for comparison and statistical modeling of anatomical shapes (organs, bones, ...) and their variability. In this setting, anatomical shapes are either represented explicitly as surfaces or implicitly by objects embedded in (volumetric) images.

A major challenge in computational anatomy arises from the mathematical structure of the data: Most anatomical shapes do not form a linear vector space but 'live' on or close to nonlinear manifolds. This nonlinear structure prevents the use of traditional techniques from Euclidean statistics and motivates the development of specific techniques suitable for those nonlinear spaces.

2. Basic Concepts

Let $I : \Omega \to \mathrm{R}$ ($\Omega \subset \mathrm{R}^3$) be a 3D grayscale image and $\varphi : \Omega \to \Omega$ a dense and nonlinear spatial transformation that can be used to spatially align two images (e.g., $I_2 = I_1 \circ \varphi^{-1}$).

Orbit model

$$O_{I_T} := \{I_T \circ \varphi^{-1} \mid \varphi \in \mathrm{Diff}(\Omega)\}$$

The orbit O_{I_T} describes the set of all images (= different shape configurations) generated by applying elements φ of the set of diffeomorphic transformations $\mathrm{Diff}(\Omega)$ to a given template image $I_T : \Omega \to \mathrm{R}$.

Diffeomorphic Transformations A diffeomorphic transformation φ is a bijective, smooth, and differentiable function that also has a smooth and differentiable inverse φ^{-1}. These properties guarantee a preservation of the topology of the shapes/images deformed by those transformations.

Usually, diffeomorphic transformations are interpreted as endpoints of a flow ϕ_t

$$\frac{\partial}{\partial t}\phi_t(\mathbf{x}) = v(\phi_t(\mathbf{x}), t) \text{ with } \phi_0(\mathbf{x}) = \mathbf{x} \text{ , } \mathbf{x} \in \Omega \text{ and } \ t \in [0, 1] \tag{1}$$

at time $t = 1$:

$$\varphi(\mathbf{x}) = \phi_1(\mathbf{x}) = \phi_0(\mathbf{x}) + \int_0^1 v(\phi_t(\mathbf{x}), t)\ dt\ . \tag{2}$$

Here, $v : \Omega \times [0, 1] \to \Omega$ describes a time-varying vector field (a so-called velocity field), which parameterizes the path of a particle/voxel that starts at position $\mathbf{x} \in \Omega$ and ends at $\varphi(\mathbf{x})$.

3. Diffeomorphic Image Registration

In practice, a diffeomorphic transformation $\varphi = \phi_1 \in \mathrm{Diff}(\Omega)$ that spatially aligns two images I_1 and I_2 (e.g., $I_2 \approx I_1 \circ \varphi^{-1}$) is estimated via image registration:

$$\arg\min_{v}\ \mathcal{D}(I_1 \circ \varphi^{-1}, I_2) + \alpha\mathcal{S}(v) \ \text{ s.t } \frac{\partial}{\partial t}\phi_t = v_t\ \forall t \in [0, 1] \text{ and } \phi_0 = Id\ . \tag{3}$$

Here, $\mathcal{D}(I_1 \circ \varphi^{-1}, I_2)$ is a similarity measure that quantifies the (dis)similarity of the images after warping. Typical choices for $\mathcal{D}$ include the Sum of Squared Differences (SSD) or Mutual Information (MI). $\mathcal{S}(v)$ denotes a regularizer that measures the smoothness of the velocity field. Typical choices for $\mathcal{S}$ include standard differential operators (e.g., Laplacian operator).

LDDMM The most influential registration approach in this context is called *Large Diffeomorphic Deformation Mapping* (LDDMM). In LDDMM, the regularizer is chosen as $\mathcal{S}(v) = \int_0^1 \|Lv_t\|_2^2 \, dt$, where L denotes a linear operator associated with a space of smooth velocity fields V. Intuitively, this regularizer quantifies the length of the path of the flow parameterized by v along the manifold of diffeomorphic transformations.

Furthermore, $\mathcal{S}(v) = \int_0^1 \|Lv_t\|_2^2 \, dt$ can also be interpreted as the kinetic energy associated with this transformation and $m_t = Lv_t$ denotes the kinetic momentum at time t. Under the assumption that no external forces act on the system (= momentum conservation), the whole path ϕ_t can be parameterized by the initial momentum/initial velocity m_0/v_0, which makes it easier to perform statistics on those diffeomorphisms. This solution scheme is usually called *geodesic shooting*.

Log-Euclidean Framework Although LDDMM is a mathematically sound framework, its usage is oftentimes hampered by its large computational footprint, which is a direct result of relying on time-varying velocity fields. The so-called *Log-Euclidean Framework* tries to circumvent this problem by using stationary (time-independent) velocity fields. To do so, the group of diffeomorphic transformations $(\mathrm{Diff}(\Omega), \circ)$ is interpreted as a Lie group (a smooth manifold) with an associated Lie algebra (a vector space; the tangent space $\mathcal{T}_{Id}\mathrm{Diff}(\Omega)$ at the identity Id).

Elements of the tangent space (= stationary velocity fields) can be mapped to the manifold (space of diffeomorphisms) via the group exponential $\exp_{Id} : \mathcal{T}_{Id}\mathrm{Diff}(\Omega) \to \mathrm{Diff}(\Omega)$. The inverse of the group exponential is the group logarithm $\log_{Id} : \mathrm{Diff}(\Omega) \to \mathcal{T}_{Id}\mathrm{Diff}(\Omega)$ that maps a transformation φ to its stationary velocity field v. Now, it can be shown that $\varphi = \phi_1 = \exp_{Id}(v)$ is a solution of Eq. (3), which allows for the definition of computationally very efficient registration algorithms.

4. Distances and Statistics

LDDMM Distance between an optimal φ and Id:

$$d(Id, \varphi)_V^2 = \int_0^1 \|v_t\|_V^2 \, dt = \int_0^1 \|Lv_t\|_2^2 \, dt \tag{4}$$

Distance between two transformations φ_1 and φ_2:

$$d(\varphi_1, \varphi_2)_V^2 = d(Id, \varphi_2 \circ \varphi_1^{-1})_V^2 \tag{5}$$

Distance between two images (shapes) I_1 and I_2:

$$d(I_1, I_2)_V^2 = \inf_{\varphi} \{ d(Id, \varphi)_V^2 : I_1 \circ \varphi^{-1} = I_2 \} \tag{6}$$

These distances can be used to generalize several measures and techniques known from Euclidean statistics (averages, variances, PCA, regression, ...) to nonlinear spaces.

Log-Euclidean Framework In contrast to the LDDMM setting, the Log-Euclidean framework relies on stationary velocity fields that are elements of the linear tangent space at the identity $\mathcal{T}_{Id}\mathrm{Diff}(\Omega)$. Consequently, the inner product of $\mathcal{T}_{Id}\mathrm{Diff}(\Omega)$ can be used to compute the distance between two transformations φ_1 and φ_2 as

$$d(\varphi_1, \varphi_2)^2 = \|\log_{Id}(\varphi_1) - \log_{Id}(\varphi_2)\|_2^2 = \|v_1 - v_2\|_2^2 \, . \tag{7}$$

Therefore, the use of the Log-Euclidean framework allows us to directly apply techniques from Euclidean statistics to diffeomorphisms via their tangent space representations.