
TemplateFlow: FAIR-sharing of multi-scale, multi-species brain models

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Supplementary Text 1

Inter-template registration workflow

To enable the flow of knowledge across template spaces, *TemplateFlow* includes a workflow for computing robust transformations between any pair of adult human template spaces. To compute a transformation between two template spaces, the inter-template registration workflow makes use of 10 of the high-quality T₁-weighted (T1w) adult human brain images used in the creation of the MNI 152 template portfolio. In the first step of the workflow, these 10 images are registered to both template spaces using the symmetric normalization (SyN) algorithm (Avants et al., 2008). SyN is an algorithm for nonlinear registration of images, which has the objective of identifying a diffeomorphic transformation that maximizes the cross-correlation between the (*moving*) image it transforms and a target (*fixed or reference*) image. Here, each of the 10 subject T1w images is input as a moving image, and each of the two template spaces to be connected is input as a reference image to a single transform. Thus, 20 total transforms are estimated in the first stage of the workflow. We use the SyN algorithm in conjunction with an affine initialization, which computes a preliminary alignment between images before they are input to the SyN algorithm.

Next, in the second stage of the workflow, we exploit the multi-channel registration capacity of the SyN algorithm to estimate a single, composite template-to-template transformation in each direction. In further detail, the second stage begins with a brain extraction step, which uses template-based priors to remove skull and extracranial voxels from each of the 10 T1W images aligned to each template. Next, we correct for intensity non-uniformities (INU) in each image using the N4ITK bias field correction algorithm (Tustison et al., 2010). The SyN algorithm then permits each of the skull-stripped, INU-corrected images to be input as registration targets on a separate registration channel. Thus, we optimize a 10-channel registration, wherein the 10 moving images are the 10 skull-stripped subject T1w images that we registered to one template space in the first step, and the 10 reference images are the same skull-stripped T1w images, this time registered to the other template space. To estimate the inverse template-to-template transform, we repeat this process, reversing the assignments of reference and moving images. Thus, the workflow computes a single transformation that simultaneously optimizes the alignment between all 10 images in both coordinate spaces.

If *FreeSurfer*-formatted *.aparc* parcellation files are available for each image, they are warped to each template space. The warped parcellation labels are then used as inputs to a joint label fusion (JLF) procedure (Wang et al., 2013), which returns both a deterministic parcellation and a set of label prior maps for each template. Additionally, reconstructed subject surfaces are warped into each template space using a point-wise version of the transformations computed in the first step, applied to the vertices of each subject's cortical surface. After vertices are transformed, surfaces are reconstituted using Poisson surface reconstruction (Kazhdan and Hoppe, 2013).

"MNI space" text mining analysis

To investigate the coupling between software libraries and standard spaces, we conducted an exploratory text mining analysis of the term "MNI" in the neuroimaging literature. For this, we used the Elsevier API to download the entire corpus of two leading journals of neuroimaging methodology, *NeuroImage* and *NeuroImage: Clinical*. In this way, we retrieved a total 16,812 full-text articles that were subsequently segmented into lists of sentences. A scan of these sentences revealed 14,870 sentences across 6,048 articles that contained the word "MNI". Sentences were cleaned (i.e., removing punctuation, single letters, accents, numbers) and tokenized into words, which were subsequently lemmatized (i.e., converted to base form) using the NLTK wordnet lemmatizer. From the lemmatized words, we filtered out stopwords (i.e., NLTK stopwords and a custom list) and included words with a frequency above 10 as part of our "dictionary"; this yielded a dictionary size of 2,324 words.

Next, we computed a sparse dictionary size by article count matrix (i.e., $2,324 \times 6,048$), on which we performed topic modelling with latent Dirichlet allocation (LDA; Blei et al., 2003, implementation from scikit-learn with the learning decay hyperparameter set to 0.7). The number of topics ($k=15$) was selected by identifying the LDA model yielding the lowest perplexity (Blei et al., 2003) sweeping the interval [8-16] for the parameter. The 20 words from the dictionary that loaded the highest on the 15 topics were visualized using word clouds. Topics were sorted by descending dominance, and the dominance fraction (number of articles where the topic is the most loaded with respect to the total 6,048 documents) was included above the corresponding topic's word cloud (Supplementary Figure 1).

Our topic model identified a clear coupling between the reporting of spatial standardization and software libraries. Out of 15 topics we modeled, two of the most dominant topics (Topics 3 and 5) contained software tool names as well as the names of related scientists. As shown in Supplementary Figure 1, around 500 articles (each term) contained either "SPM" (9% of the documents, Topic #3) or "FSL" (8%, Topic #5) in the same sentence as "MNI". The two words do not ever appear together, suggesting that researchers stick with one or another in their analyses. Additional topics that seemingly relate to the provenance of templates and atlases—beyond the ubiquitous "Montreal", "Neurological" and "Institute" for MNI—are those that ranked #4, #13, #14, which include "SPM" and other terms such as "McGill", "Wellcome", "UCL", or the "statistical", "parametric", and "mapping" in SPM (see Supplementary Figure 1). The remainder of topics appears to relate to miscellaneous aspects of spatial standardization, such as "anatomical", "smoothness", "standard", "normalization", "(re)align/alignment", etc., with no immediately apparent relationship to the origin of the resource. Nonetheless, our results suggest that the MNI templates bundled with SPM and FSL have historically gained broader currency as a result of the widespread use of these software libraries.

Our text mining results are consistent with a previous investigation by Carp (2012) in the domain of functional MRI, which similarly illustrated a strong coupling between software library and authors' choices of templates and atlases. In this prior work, Carp (2012) analysed 241 functional MRI studies, 90.9% of which reported normalizing brain images to a common template. Of those, 79.0% indicated the target space used for spatial normalization. Few studies reported critical parameters such as image modality, and only 50 out of 241 specified the template image, out of which 26.0% used "the MNI152 template", and 26.0% the "SPM library's echo-planar imaging template". Unfortunately, template selection is seen as a default parameter of the software library, which leads to the assumption that the target normalization space is implicitly reported by identifying the software tools of choice. The risks and limitations of this reporting scheme are further underscored by a recent comparison of analytic outcomes across software libraries. In this study, Bowring et al. (2019) implemented analogous image processing pipelines using tools from each of three software suites (AFNI, FSL and SPM) in order to identify challenges to reproducing published studies with openly shared raw data. When discussing the differences among software pipelines, they noted that, "while all packages are purportedly using the same MNI atlas space, an appreciable amount of activation detected by AFNI and FSL fell outside of SPM's analysis mask."



Supplementary Figure 1. The FSL and SPM software tools associate with dominant topics of sentences including the term “MNI” across the literature. We performed topic modeling with latent Dirichlet allocation (LDA; *Blei et al., 2003*) on text sentences extracted from 6,048 articles that contained the word “MNI”. For each topic identified, the 20 words with the highest loadings on that topic are displayed in a word cloud with larger font size indicating higher loading of the word on the corresponding topic. Word clouds are sorted by descending topic dominance. Ranking and relative dominance are shown above each topic’s cloud. Two top-dominant topics —#3 and #5— are associated with SPM and FSL respectively.

Furthermore, the coupling between templates and software likely limits the use of templates other than those defaulted by the software. Custom templates (i.e., those not included as a default option for the software tool) range from population-specific templates to *ad hoc* templates created by averaging images of the study at hand. In some settings, the use of default templates risks introducing “template effects” that confound the interpretation of results (such as those introduced when an adult template is used in pediatric imaging studies, *Yoon et al., 2009*). As the target population moves away from the population used to create a default template—generally, a neurotypical adult population—“template effects” become more concerning and custom templates more necessary. The problem is exacerbated in the case of nonhuman imaging, as the scarcity (or absence) of specific templates available within software packages hinders already challenging translational endeavors. Further, the consistency across templates and atlases is reportedly low (*Bohland et al., 2009*), and although there has not been any programmatic comparison to understand the extent to which this inconsistency alters the spatial interpretation of results, it is reasonable that templates and atlases introduce a decision point and therefore are sources of some analytical variability.

Supplementary Text 2

The role of templates and atlases in the progress of neuroscience

Brains are morphologically variable, exhibiting diversity in such features as overall size (*Lüders et al., 2002*), sulcal curvature (*Tosun et al., 2015*), and functional topology (*Tavor et al., 2016; Mars et al., 2018*). Morphological variability manifests not only in differences between brains but also in the way that a brain changes across its lifespan, as it is remodelled by development, aging, and degenerative processes (*Courchesne et al., 2000; Good et al., 2001; Sowell et al., 2003*). These morphological differences often correspond with the effects of interest in neuroimaging studies and hinder direct spatial comparisons between brain maps (*Brett et al., 2002*). The substantial variability within and between individual brains necessitates a means of formalizing population-level knowledge about brain anatomy and function. Neuroscientists have answered this need by creating brain atlases as references for understanding and contextualizing morphological variability. Atlases map landmarks, features, and other knowledge about the brain as annotations that are consistent across individual brains.

The development of atlases in neuroscience has accelerated knowledge discovery and dissemination. Early endeavors, epitomized by the groundbreaking work of *Brodman* (2006, originally published in German in 1909) and complemented by *Von Economo and Koskinas* (2008, originally published in German in 1925), leveraged careful scrutiny of microanatomy and cytoarchitectonic properties in small numbers of brains. Talairach’s assiduous postmortem examination of a single brain (*Talairach et al., 1957*) remarkably incorporated stereotaxy by defining three spatial reference axes over the brain that allowed anchoring neural landmarks to coordinates.

This first stereotaxic atlas saw wide use with a later, improved version (*Talairach and Tournoux, 1988*). Stereotaxy also prompted the development of the earliest surgical neuronavigation systems. *Schurr and Merrington* (1978) developed a stereotaxic apparatus to surgically induce targeted brain lesions on cats. This work informed early sectional atlases of the rodent (*Paxinos and Watson, 1997*) and macaque (*Martin and Bowden, 2000*) brains.

On account of its implicit stereotaxy, its capacity to image the entire brain, and its non-invasive acquisition protocols, magnetic resonance imaging (MRI) has revolutionized neuroscience in general and the atlasing endeavor (*Evans et al., 2012*) in particular. In combination with software instruments’ progress to map homologous features between subjects supported by regular grids (*Avants et al., 2008*) or reconstructed anatomical surfaces (*Robinson et al., 2014*), MRI has enabled researchers to create population-average maps of a particular image modality and/or particular sample with relative ease. These maps, called “templates”, are typically created by averaging features across individuals that are representative of the population of interest to a study (*Dickie et al., 2017*). As a result, atlasing endeavours have been made contingent on templates, and have shifted away from the search for a single universal neuroanatomical pattern, instead making use of increasingly large samples with the aim of representing a population average of the distribution of morphological patterns (*Evans et al., 1993*).

The problem of “template effects” and the influence of distribution modes

Although neurotypical human adults have historically been the most comprehensively templated brains (*Evans et al., 1993; Mazziotta et al., 1995, 2001; Evans et al., 2012; Satterthwaite et al., 2016*), researchers have also generated templates and atlases for diseased (*Dickie et al., 2015*), infant (*Matsuzawa et al., 2001; Fonov et al., 2011; Shi et al., 2011*), and elderly (*Buckner et al., 2004*) human populations. Similarly, nonhuman MRI templates have seen parallel development, e.g., rodents (*Calabrese et al., 2013; Szulc et al., 2015*), and primates (*Schilling et al., 2017; Jung et al., 2021*).

Advancing beyond the volumetric constraints of stereotaxy, researchers of the primate neocortex have also devised standard spaces based on geometric reconstructions of the cortical surface (*Fischl et al., 1999*). This surface-based approach has the advantage of respecting the intrinsic topology of cortical folds, a development that has led to further improvements in spatial localization (*Van Essen et al., 2012; Coalson et al., 2018*).

Such resources as atlases and templates, which provide standardized prior knowledge, have become an indispensable component of modern neuroimaging data workflows for two cardinal reasons. First, group inference in neuroimaging studies requires that individuals’ features are aligned into a common spatial frame of reference where their location can be called standard (*Brett et al., 2002*). Second, templates engender a stereotaxic coordinate system in which atlases can be delineated or projected. Associating atlases with template coordinates also facilitates the mapping of prior population-level knowledge about the brain into images of individual subjects’ brains (for instance, to sample and average the functional MRI signal indexed by the regions defined in an atlas; *Yeo et al. (2011)*). Because they are integral to analytic workflows, the most widely-used templates and atlases are typically distributed along with neuroimaging software libraries. Alternatively, researchers distribute their templates through, e.g., the *NeuroImaging Tools and Resources Collaboratory* [NITRC; RRID:SCR_003430], institutional websites, or data storage systems such as FigShare [RRID:SCR_004328] or Dryad [RRID:SCR_005910]. However, using the default templates of their analyses’ software toolbox is the most common practice, as shown by *Carp* (2012) in a review of 241 functional MRI studies.

Design and implementation of TemplateFlow

In sum, a number of challenges have derived from management, stewardship, distribution, reuse and reporting of templates that merit attention. In an early perspective, *Van Essen* (2002) called for connecting templates in an aggregation of databases with “powerful and flexible options for searching, selecting, and visualizing data” and stressed the importance of resource accessibility. *TemplateFlow* provides a framework that satisfies all of the

Supplementary Note 1. The FAIR Guiding Principles. Reproduced from (Wilkinson et al., 2016, Box 2).

To be Findable:

- F1. (meta)data are assigned a globally unique and persistent identifier
- F2. data are described with rich metadata (defined by R1 below)
- F3. metadata clearly and explicitly include the identifier of the data it describes
- F4. (meta)data are registered or indexed in a searchable resource

To be Accessible:

- A1. (meta)data are retrievable by their identifier using a standardized communications protocol
 - A1.1. the protocol is open, free, and universally implementable
 - A1.2. the protocol allows for an authentication and authorization procedure, where necessary
- A2. metadata are accessible, even when the data are no longer available

To be Interoperable:

- I1. (meta)data use a formal, accessible, shared, and broadly applicable language for knowledge representation.
- I2. (meta)data use vocabularies that follow FAIR principles
- I3. (meta)data include qualified references to other (meta)data

To be Reusable:

- R1. (meta)data are richly described with a plurality of accurate and relevant attributes
 - R1.1. (meta)data are released with a clear and accessible data usage license
 - R1.2. (meta)data are associated with detailed provenance
 - R1.3. (meta)data meet domain-relevant community standards

forementioned desiderata while following the “Findability, Accessibility, Interoperability, and Reusability (FAIR) Guiding Principles” (Supplementary Note 1; Wilkinson et al., 2016). To implement several of the FAIR Principles, the *TemplateFlow Archive* features a tree-directory structure, metadata files, and data files following an organization inspired by the Brain Imaging Data Structure (BIDS; Gorgolewski et al., 2016). The online documentation hub and the resource browser located at www.templateflow.org provide further details for users.

TemplateFlow enables next-generation neuroimaging workflows: innovation and contributions

BIDS-inspired structure for template and atlas archival following FAIR Principles

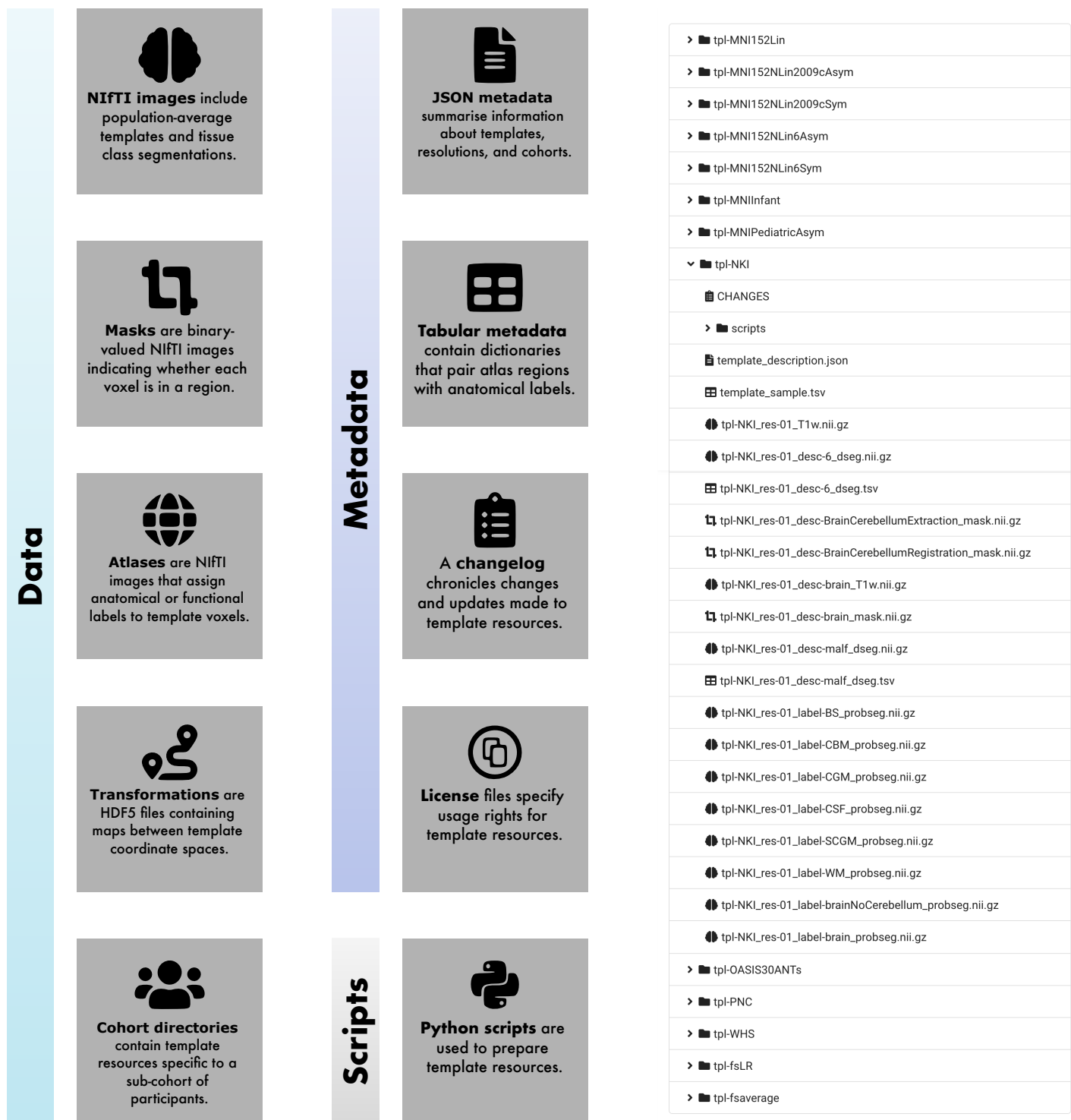
BIDS prescribes a file naming scheme comprising a series of key-value pairs (called “entities”). Mirroring BIDS’ patterns for participants, each template is associated with an identifier, which is an alphanumeric label. Template identifiers are unique across the *Archive*, and signified with the key **tpl-** (e.g., **tpl-MNI152Lin**), which is analogous to **sub-** of BIDS. Hence, every template and all associated metadata, atlases, etc. are assigned a unique and persistent identifier (Supplementary Note 1, F1). The adaptation of BIDS to the domain of templates and atlases affords the tool with a robust implementation of the principles I1-3 in Supplementary Note 1.

For each template, the *TemplateFlow* database includes reference volumetric template images (e.g., one T_1 -weighted MRI), a set of atlas labels and voxelwise annotations defined with reference to the template image, and additional files containing the template and atlas metadata. Correspondingly, *TemplateFlow* allows surface-based resources such as average features, geometry files, annotations, or metadata. The only requirement for feature averages and atlases sharing a unique template identifier is that they must be spatially in register, regardless of the data sampling strategy (i.e., volume, surface, or mixed, and corresponding resolution or mesh density). Although the most widely used templates generally represent MRI-derived features, *TemplateFlow* is not limited to any specific set of modalities. Supplementary Table 1 has been programmatically generated by the accompanying code examples, and enumerates the templates currently distributed with the *Archive* indicating their corresponding unique identifiers and including a short description.

Template resources are described with rich metadata (Supplementary Note 1, F2 and R1), ensuring that the data usage license is clear and accessible (Supplementary Note 1, R1.1), data and metadata are associated with detailed provenance (Supplementary Note 1, R1.2), and data and metadata follow a domain-relevant structure transferred from the neuroimaging community standards of BIDS (R1.3). Supplementary Figure 2 summarizes the data types and metadata that can be stored in the *Archive*. Supplementary Figure 3 provides an overview of the *Archive*’s metadata specification, showing that metadata clearly and explicitly include the identifier of the data they describe (Supplementary Note 1, F3). Data and metadata are retrievable using several open, free, standard communications protocols without need for authentication (Supplementary Note 1, A1) by using *DataLad* (Halchenko et al., 2021). Cloud storage for the *Archive* is supported by the Open Science Framework (<https://osf.io>) and Amazon’s Simple Storage Service (S3). Version control, replication, and synchronisation of template resources across filesystems is managed with *DataLad*. Leveraging *DataLad*, metadata are stored on GitHub, ensuring accessibility to metadata even when corresponding data are no longer available (Supplementary Note 1, A2). *DataLad* is based on *Git* and *Git-Annex*, which index all data and metadata (Supplementary Note 1, F4).

TemplateFlow provides humans and machines with flexible and granular access to templates

TemplateFlow’s Python client provides human users and software tools with reliable and programmatic access to the archive. The client can be integrated seamlessly into image processing workflows to handle requests for template resources on the fly. It features an intuitive application programming interface (API) that can query the *TemplateFlow Archive* for specific files (Supplementary Figure 4). The BIDS-inspired organization



Supplementary Figure 2. The TemplateFlow Archive contains template resources. Left, common file formats included in the *TemplateFlow Archive*. Right, view of the *TemplateFlow Archive*'s browser, accessible at templateflow.org/browse/, with a single template resource directory expanded. Template data are archived using a BIDS-like directory structure, with top-level directories for each template. Each directory contains image files, annotations, and metadata for that template. Following BIDS specifications, volumetric data are stored in NIfTI-1 format. Further surface-based data types are supported with GIFTI (surfaces) and CIFTI-2 (mixed volumetric-and-surface data).

```

{
  "Authors": [
    "Fonov V",
    "Evans AC",
    "Botteron K",
    "Almli CR",
    "McKinstry RC",
    "Collins DL"
  ],
  "Curators": [
    "Esteban O"
  ],
  "Identifier": "MNIPediatricAsym",
  "License": "MIT-derived. See LICENSE file",
  "Name": "MNI's unbiased standard MRI template for pediatric data from the 4.5 to 18.5y age range",
  "RRID": "SCR_008796",
  "ReferencesAndLinks": [
    "https://doi.org/10.1016/j.neuroimage.2010.07.033",
    "https://doi.org/10.1016/S1053-8119(09)70884-5",
    "http://nist.mni.mcgill.ca/?p=974",
    "https://doi.org/10.1007/3-540-48714-X_16"
  ],
  "TemplateFlowVersion": "1.0.0",
  "cohort": {
    "1": {
      "age": [
        4.5,
        18.5
      ],
      "name": "whole age range",
      "units": "yr"
    },
    "2": {
      "age": [
        4.5,
        8.5
      ],
      "name": "prepuberty",
      "units": "yr"
    },
    . . .
  },
  "res": {
    "1": {
      "origin": [
        -98.0,
        -134.0,
        -72.0
      ],
      "shape": [
        197,
        233,
        189
      ],
      "zooms": [
        1.0,
        1.0,
        1.0
      ]
    },
    . . .
  }
}

```

General metadata

Field	Type	Description
Authors	Array (String)	Names of authors who created the template.
Curators	Array	Names of TemplateFlow curators who contributed or manage the dataset.
Identifier	String	Unique human-readable template identifier within TemplateFlow.
License	String	License under which template resources are available.
Name	String	Full descriptive name of the template.
RRID	String	Research Resource Identifier for the TemplateFlow dataset.
ReferencesAndLinks	Array	Publications to reference when using the template, and salient links for template information.
TemplateFlowVersion	String	Version of TemplateFlow under which the dataset was distributed.

Cohort metadata

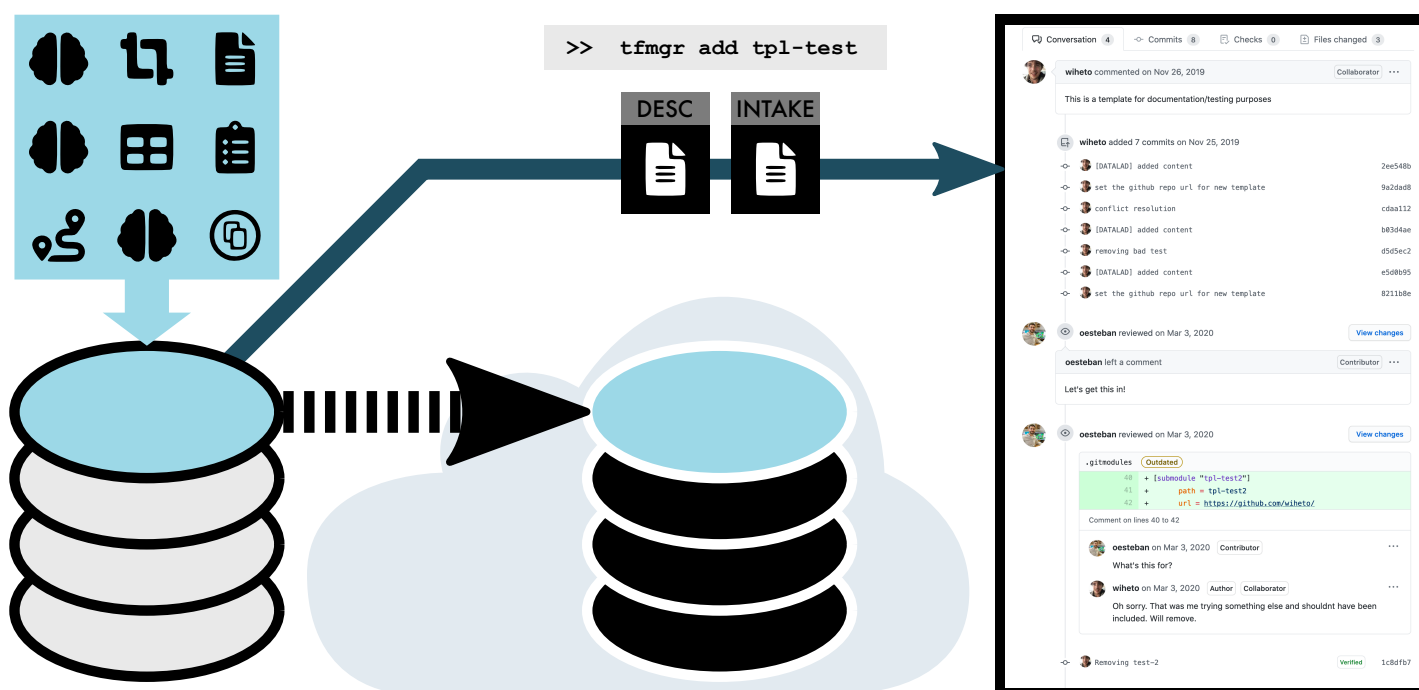
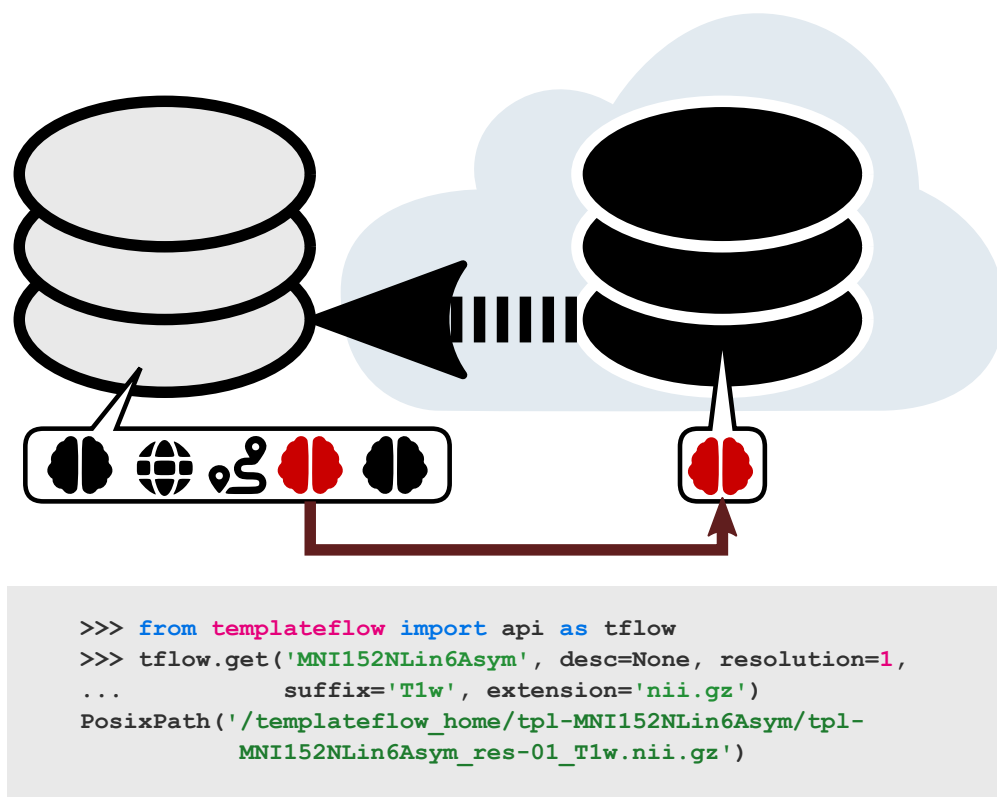
Field	Type	Description
cohort	Object	Top-level field containing all cohort metadata objects.
1, 2, ...	Object	Cohort identifiers. Each has a subdirectory in the template data directory, and each has a metadata object nested in the cohort field.
age	Array (Number)	2-tuple array indicating the lower and upper bounds for participant age in the cohort, if the cohorts are stratified by age.
name	String	Full descriptive name of the cohort..
units	String	Units for cohort age bounds.

Resolution metadata

Field	Type	Description
res	Object	Top-level field containing all resolution metadata objects.
1, 2, ...	Object	Resolution identifiers. Each has a metadata object nested in the res field. The metadata for each resolution apply to all images whose name includes res- <i><identifier></i> . The identifier itself does not necessarily correspond to the voxel size.
origin	Array	(x, y, z) spatial location of the voxel origin relative to the physical origin in mm.
shape	Array	(x, y, z) shape of the image in voxels.
zooms	Array	(x, y, z) size of each voxel in mm.

Supplementary Figure 3. Overview of the metadata specification of the TemplateFlow Archive. TemplateFlow's metadata are formatted as JavaScript Object Notation (JSON) files located within each template set. An example `template_description.json` metadata file is displayed at the left for `MNIPediatricAsym`. In addition to general template metadata, datasets can contain cohort-level and resolution-level metadata, which are nested within the main metadata dictionary and apply only to subsets of images in the dataset.

Supplementary Figure 4. Example usage of the Python-based *TemplateFlow* Client. After importing the API, the user submits a query for the T₁-weighted FSL version of the MNI template at 1 mm resolution. The client first filters through the archive, identifies any files that match the query, and finds their counterparts in cloud storage. It then downloads the requested files and returns their paths in the local *TemplateFlow* installation directory. Future queries for the same resource can be completed without any re-downloading.



Supplementary Figure 5. Contributing a new resource with the *TemplateFlow* Manager. To contribute a new template to *TemplateFlow*, members of the community first organize template resources to conform to the BIDS-like *TemplateFlow* structure. Next, *tfmgr* (the *TemplateFlow* Manager, see Supplementary Table 3) synchronizes the resources to OSF cloud storage and opens a new pull request proposing the addition of the new template. A subsequent peer-review process ensures that all data are conformant with the *TemplateFlow* standard. Finally, *TemplateFlow* curators merge the pull request, thereby adding the template into the archive.

Supplementary Table 1. Digital templates included in *TemplateFlow*. *TemplateFlow* is designed to maximise the discoverability and accessibility of new templates, minimise redundancies in template creation, and promote standardisation of processing workflows. To enhance visibility of existing templates, *TemplateFlow* includes a web-based browser indexing all files in the *TemplateFlow Archive* (templateflow.org/browse/). This table has been automatically generated using the *TemplateFlow Client* tooling.

Template ID	Description
Fischer344	MRI-Derived Neuroanatomical Atlas of the Fischer 344 Rat Brain (Goerzen et al., 2020).
MNI152Lin	Linear ICBM Average Brain (ICBM152) Stereotaxic Registration Model (Mazziotta et al., 1995).
MNI152Nlin2009cAsym	ICBM 152 Nonlinear Asymmetrical template version 2009c (RRID:SCR_008796; Fonov et al., 2009).
MNI152Nlin2009cSym	ICBM 152 Nonlinear Symmetrical template version 2009c (RRID:SCR_008796; Fonov et al., 2009).
MNI152Nlin6Asym	FSL's MNI ICBM 152 non-linear 6th Generation Asymmetric Average Brain Stereotaxic Registration Model (RRID:SCR_002823; Evans et al., 2012).
MNI152Nlin6Sym	ICBM 152 non-linear 6th Generation Symmetric Average Brain Stereotaxic Registration Model (RRID:SCR_008364; Grabner et al., 2006).
MNI305	MNI Average Brain (305 MRI) Stereotaxic Registration Model (Collins et al., 1994).
MNIInfant	MNI Unbiased nonlinear Infant Atlases 0-4.5yr. (RRID:SCR_008796; Fonov et al., 2009).
MNIPediatricAsym	MNI's unbiased standard MRI template for pediatric data from the 4.5 to 18.5y age range (RRID:SCR_008796; Fonov et al., 2011).
MouseIn	In Vivo MP2RAGE Templates of the C57Bl6/J Mouse Brain.
NKI	ANTs' NKI-1 template (Avants et al., 2011).
NMT31Sym	The NIMH Macaque Template v2 (NMT v2) (Jung et al., 2021).
OASIS30ANTS	OASIS30 - Generated with ANTs for MICCAI 2016 (Avants et al., 2011).
PNC	Philadelphia Neurodevelopmental Cohort template (Satterthwaite et al., 2016).
RESILIENT	Age-specific adult rat brain MRI templates and tissue probability maps. (MacNicol et al., 2021)
UNCInfant	UNC Infant 0-1-2 Atlases (Shi et al., 2011).
VALIDATE29	The VALIDATE29 MRI Based Multi-Channel Atlas of the Squirrel Monkey Brain (RRID:SCR_015542; Schilling et al., 2017).
WHS	Waxholm Space atlas of the Sprague Dawley rat brain (Papp et al., 2014).
fsLR	HCP Pipelines' fsLR template (Van Essen et al., 2012).
fsaverage	FreeSurfer's fsaverage template (Fischl et al., 1999).

enables easy integration of tools and infrastructure designed for BIDS (e.g., the Python client uses *PyBIDS*; Yarkoni et al., 2019). To query *TemplateFlow*, a user can submit a list of arguments corresponding to the BIDS-like key-value pairs in each entity's file name.

To integrate template resources into neuroimaging workflows, traditional approaches required deploying an oftentimes voluminous tree of prepackaged data to the filesystem. By contrast, the *TemplateFlow* client implements lazy loading, which permits the base installation to be extremely lightweight. Instead of distributing neuroimaging data with the installation, *TemplateFlow* allows the user to dynamically pull from the cloud-based storage only those resources they need, as they need them. After a resource has been requested once, it remains cached in the filesystem for future utilization.

The uniform interface provided by the BIDS-like directory organisation and metadata enables straightforward integration of new templates into workflows equipped to use *TemplateFlow* templates. Further examples of tools leveraging *TemplateFlow* include *MRQC* (Esteban et al., 2017) for quality control of MRI; *PyNets* (Pisner and Hammonds, 2020), a package for ensemble learning of functional and structural connectomes; *ASLPrep* (Adebimpe et al., 2021), an ASL pre-processing pipeline that makes use of *TemplateFlow* through *sMRIPrep* —the spin-off structural pipeline from *fMRIPrep*;— and *NetPlotBrain* (Thompson and Fanton, 2021), which uses *TemplateFlow* to display spatially standardized brain network data.

TemplateFlow eases the dissemination of templates and opens their vetting and maintenance to the community

Beyond redistributing the templates most commonly used in the literature, the resource has the vision of becoming a centralized and standard way for researchers to disseminate their new templates. *TemplateFlow*'s pipeline for submission of new templates integrates peer-review with minimal technical overhead. This review process is proposed as a complement to the traditional assessment of template resources prior to publication, in which reviewers and editors focus on academic merit over accessibility and reusability potential. This submission pipeline is easily initiated with the Python-based *TemplateFlow Manager*.

TemplateFlow's management infrastructure also eases maintenance. The lack of infrastructure for templates and atlases has given rise to static development modes where templates are packaged once and rarely revised. As a result, templates and atlases have remained outside version control because it is considered too onerous and requires informatics expertise that may exceed the resources of research teams. Although uncommon, errors in template and atlas resources have nonetheless been reported (e.g., Rohlfing, 2013; Halchenko, 2013), and the common denominator across these instances is template reuse for the discovery of issues. In our experience with *OpenfMRI* and *OpenNeuro* (Markiewicz et al., 2021), reuse is a top cause for dataset revision after the first release of data. Because of the flexibility and exposure that *TemplateFlow* affords templates and atlases will substantially lower barriers to reuse and feedback reporting, the resource will stimulate the early identification of problems and promote the request of new features to improve available assets.

Inspired by the Conda-forge community repository and the Journal of Open Source Software, the GitHub-based “templateflow” organization is a site for dialogue between members of the neuroimaging community and *TemplateFlow Archive* curators. GitHub issues offer any community member the ability to share their needs with developers and *Archive* curators, for instance by identifying templates or workflow features for potential inclusion in the project. “Pull requests” provide a means for members of the community to directly contribute code or template resources to the *TemplateFlow Archive*.

Decoupling software and templates is indispensable for more reliable and more reproducible study designs

Although there is not yet any standard distance function that can objectively determine whether a template choice is phenotypically proximal to the study's sample, selecting an inappropriate template may introduce so-called “template effects” that bias morphometric analyses and produce incorrect results (Yoon et al., 2009). For example, since most generally used templates were created with a sample of adults of European ancestry, a study involving

Supplementary Table 2. *TemplateFlow* data entities.

Data entity	API query example	Description
Template	"MNI152Lin"	The template dataset to which an image or other data file belongs.
Resolution	resolution=1	The image resolution. Each resolution is assigned a key, which is defined in the <code>res</code> field of <code>template_description.json</code> .
Mask	desc="brain", suffix="mask"	Indicates that the image is a binary-valued annotation, where voxels labelled 1 are part of the mask.
Discrete segmentation	desc="malf", suffix="dseg"	Indicates that the image is an integer-valued annotation. Each segmentation image file (<code>.nii.gz</code> format) is paired with a dictionary of segment names (<code>.tsv</code> format).
Probabilistic segmentation	label="CSF", suffix="probseg"	Indicates that the image is a probabilistic annotation, wherein the value of each voxel indicates the probability of that voxel belonging to the specified label.
Atlas	atlas="Schaefer", desc="7Network"	The atlas to which a segmentation file belongs.
Transformation	from="MNI152Lin", suffix="xfm"	File containing a mapping between 2 stereotaxic coordinate spaces. The source space is defined in the <code>from</code> field, while the target space is defined in the <code>tpl</code> field.
Image modality	suffix="T1w"	For non-annotation brain images, the suffix indicates whether the image is T1-weighted (<code>T1w</code>), T2-weighted (<code>T2w</code>), proton density-weighted (<code>PD</code>), or T2*-weighted (<code>T2star</code>).
Template cohort	cohort=1	Subsample of a dataset used to generate an average template.

Supplementary Table 3. Command-line interface for *TemplateFlow Manager*.

Argument	Environment variable	Specifications
<code>template_id</code>		Identifier of the template. This is the value of the <code>tpl</code> field in all file names.
<code>--osf-project</code>	<code>OSF_PROJECT</code>	The OSF project where the template data are to be stored. The project must be writable by the user account whose credentials are specified in the <code>--osf-user</code> and <code>--osf-password</code> arguments.
<code>--osf-user</code>	<code>OSF_USERNAME</code>	Account username or identifier for OSF cloud storage.
<code>--osf-password</code>	<code>OSF_PASSWORD</code>	Account password for OSF cloud storage.
<code>--osf-overwrite</code>		Flag that indicates that the OSF client should force the overwrite of any existing files in the OSF project that have names conflicting with those of new files.
<code>--gh-user</code>	<code>GITHUB_USER</code>	Account username for GitHub. The user account whose credentials are provided must have a fork of the <i>TemplateFlow</i> repo.
<code>--gh-password</code>	<code>GITHUB_PASSWORD</code>	Account password for GitHub.
<code>--path</code>	<code>OSF_PROJECT</code>	Path to a local directory where template resources are located. The path must either be a directory whose name is <code>tpl-<template_id></code> or contain such a directory.
<code>--nprocs</code>		Maximum number of parallel processes to run when uploading to or fetching from OSF.

East Asian adults might require a non-default template. More evidently, because of the relative scarcity of nonhuman imaging resources, exposure to template effects is even more pressing in the nonhuman context: e.g., is it appropriate to use a mouse template for the spatial standardization of rat images? Not only are nonhuman templates and atlases fewer, accommodation of such resources in popular software tools is generally limited. For instance, AFNI (Cox and Hyde, 1997) includes a rat template that can be applied in some contexts, while SPM provides functionality only through third-party add-ons (e.g., Sawiak et al., 2009). Second, deviating from software defaults places a knowledge burden on the user. Once the researcher has selected a reference standard space that is suitable for their study population, if their choice is not included by default with the software they plan to use, they must then locate and download the reference template or atlas and integrate it within their analytic pipeline. To our knowledge, only AFNI have made efforts on this direction with their relatively recent `@Install_<template_name>` command, although the tool (i) is not designed to be compatible with other analysis alternatives, and (ii) only provides a minimal set of *TemplateFlow*'s features (i.e., resource download).

Supplementary Note 3 shows how *TemplateFlow* works with *fMRIPrep* to automate preprocessing of outputs in multiple standard spaces. This facilitates assessment of the robustness of a result with respect to the template or atlas of choice in accordance with the multiverse approach. Botvinik-Nezer et al. (2020) also promoted pre-registration of studies as a powerful means to fixate methodological choices before the authors have access to intermediate and final results. Here, *TemplateFlow* emerges as a powerful tool to unambiguously document template and atlas choices at pre-registration time.

Limitations of *TemplateFlow*

TemplateFlow affords researchers substantial analytical flexibility in the choice of standard spaces of reference. Such flexibility helps researchers minimize "template effects" —by easily inserting the most adequate template— but also opens opportunities for incomplete reporting of experiments. Using *DataLad* or the *TemplateFlow Client*, researchers have at their disposal the necessary tooling for precise reporting: unique identifiers, provenance tracking, version tags, and comprehensive metadata. Therefore, the effectiveness of *TemplateFlow* to mitigate selective reporting is bounded by the user's discretion.

As a research resource, the scope of this manuscript is limited to describing the framework and infrastructure of *TemplateFlow*, highlighting how neuroscientists can leverage this new data archive and the tooling around it. Therefore, some fundamental issues related to this work must be left for future investigation: (i) the overarching problems of cross-template and cross-atlas consistency (Bohland et al., 2009); (ii) comparative evaluation of

methodological alternatives for producing new templates, atlases and related data; (iii) providing neuroimagers with more objective means to determine the most appropriate template and atlas choices that apply to their research, as well as better understanding “template effects”; (iv) the adequacy of original (MRI, nuclear imaging, etc.) and derived (regularly gridded images, surfaces, etc.) modalities for a specific research application; or (v) the study of the validity and reliability of inter-template registration, as well as the evaluation of such a component of the *TemplateFlow* framework. However, the proposed framework serves as an ideal keystone to investigate some of the issues above. For instance, the [Supplementary Text 1](#) describe one of the resource’s tools to estimate nonlinear spatial mappings between templates that would be powerful in investigating the issue of consistency (i).

Supplementary Note 2. Quick start with the *TemplateFlow Client API*. The *TemplateFlow Client* offers a versatile application programmer interface (API) leveraging BIDS.

Finding templates At the time of writing there are 25 templates available within the resource, and all the unique identifiers can be accessed with the `templates()` method:

```
>>> from templateflow.api import templates
>>> f"{' '.join(templates())} ({len(templates())} templates)"
"""Fischer344, MNI152Lin, MNI152Nlin2009aAsym, MNI152Nlin2009aSym, MNI152Nlin2009bAsym, MNI152Nlin2009bSym,
MNI152Nlin2009cAsym, MNI152Nlin2009cSym, MNI152Nlin6Asym, MNI152Nlin6Sym, MNI305, MNIColin27, MNIInfant,
MNIPediatricAsym, MouseIn, NKI, NMT31Sym, OASIS30ANTs, PNC, RESILIENT, UNCInfant, VALiDATE29, WHS,
fsLR, fsaverage (25 templates)"""
```

Accessing Metadata We can query metadata associated to individual data files (e.g., a volume or a surface) or general metadata of the template. For example, the `get_metadata(<template_id>)` returns the general metadata as a dictionary. Hence, consulting the full name corresponding to some template identifiers yields:

```
>>> from templateflow.api import get_metadata
>>> [(tpl, get_metadata(tpl)["Name"]) for tpl in templates()[:3]]
[("Fischer344", "MRI-Derived Neuroanatomical Atlas of the Fischer 344 Rat Brain"),
 ("MNI152Lin", "Linear ICBM Average Brain (ICBM152) Stereotaxic Registration Model"),
 ("MNI152Nlin2009cAsym", "ICBM 152 Nonlinear Asymmetrical template version 2009c")]
```

Similarly, we can check the license of a given template:

```
>>> get_metadata("UNCInfant")["License"]
"CC-BY"
```

Or the proper citations (please note that the output in this example has been manipulated for demonstration purposes):

```
>>> from templateflow.api import get_citations
>>> print(get_citations("UNCInfant", bibtex=True)[0])
@article{uncinfant1,
  doi = {10.1371/journal.pone.0018746},
  year = 2011,
  volume = {6},
  number = {4},
  pages = {e18746},
  author = {Feng Shi and Pew-Thian Yap and Guorong Wu and Hongjun Jia and John H. Gilmore and
    Weili Lin and Dinggang Shen},
  title = {Infant Brain Atlases from Neonates to 1- and 2-Year-Olds},
  journal = {{PLOS ONE} {ONE}}
```

```
>>> from templateflow.api import get
>>> print(get("MNI152Nlin6Asym", desc=None, resolution=1, suffix="T1w"))
Downloading https://templateflow.s3.amazonaws.com/tpl-MNI152Nlin6Asym/tpl-MNI152Nlin6Asym_res-01_T1w.nii.gz
100%|#####| 3.29M/3.29M [00:01<00:00, 2.11MB/s]
/home/oesteban/.cache/templateflow/tpl-MNI152Nlin6Asym/tpl-MNI152Nlin6Asym_res-01_T1w.nii.gz
```

Supplementary Note 3. Integration of *TemplateFlow* in processing workflows. The uniform interface provided by the BIDS-like directory organisation and metadata enables straightforward integration of new templates into workflows equipped to use *TemplateFlow* templates.

For example, let's reuse the base configuration file for FSL FEAT we proposed in our paper ([Esteban et al., 2019](#)). The design file `design.fsf` specifies a simple preprocessing workflow with FSL tools. The simplified code listing below shows that, just to make non-default templates available to FSL using the graphical user interface (GUI), at least five steps are necessary:

```
# 1. User determines two nondefault templates they want to spatially normalize into
# 2. User manually downloads templates, extracts the required files from packages
$ curl -sSL <url> | tar xzv --no-same-owner -C /data/templates/
# 3. User opens FSL's GUI, edits the target template box content pointing to the appropriate files
# 4. User generates FSL configuration files to permit batch execution on the command line
# 5. For the default and the two nondefault templates, execute FSL's feat:
$ feat design_<template>.fsf
```

The outputs of each `feat design_<template>.fsf` call will follow the pre-specified patterns of FSL, with whatever customization the user has introduced into the design file. The user, therefore, must then adapt the downstream analysis tools to correctly interpret the derived dataset, in each standard space, or reformat the output dataset according to the expectations of the analysis tools.

The user is also responsible for all aspects of provenance tracking and adequately reporting them in their communications. Information such as version of the template (or download date), citations to relevant papers, and other metadata (e.g., RRIDs) must be accounted for manually throughout the research process.

In contrast, tools using *TemplateFlow* dramatically simplify the whole process (note that `MNI152Nlin2009cAsym` and `OASIS30Ants` are the two templates not found within the FSL distribution, and `MNI152Nlin6Asym` denotes *FSL's MNI space* (i.e., the default FSL template):

```
$ fmriprep /data /derivatives participant --output-spaces MNI152Nlin2009cAsym MNI152Nlin6Asym OASIS30Ants
```

fMRIPrep generates the results with BIDS-Derivatives organization for the three templates. The tool also leverages *TemplateFlow* to generate a *boilerplate citation text* that includes the full names, versions and references to credit the template's authors for each of the templates involved.

fMRIPrep internally stages one spatial normalization workflow for each of the output spaces. Each of these normalization sub-workflows uses a simple line of Python code to retrieve the necessary resources from *TemplateFlow* using the *TemplateFlow Client* interface (Supplementary Figure 4):

```
>>> from templateflow.api import get
>>> tpl_ref_file = get("MNI152Nlin6Asym", desc=None, resolution=1, suffix="T1w", extension="nii.gz")
```

One detail overseen in the FSL example is that, for a robust spatial normalization process, a precise binary mask of the brain is generally used. While FSL would require the user to manually set this mask up in the GUI, in the case of *TemplateFlow*, it requires a second minimal call:

```
>>> msk_ref_file = get("MNI152Nlin6Asym", desc="brain", resolution=1, suffix="mask", extension="nii.gz")
```

These examples are extreme simplifications of what a pipeline developer can automate and make more robust by integrating *TemplateFlow* in their workflows.

For further examples on how *TemplateFlow* can be leveraged, *PyNets* is a package for ensemble learning of functional and structural connectomes ([Pisner and Hammonds, 2020](#)), and *NetPlotBrain* for visualization ([Thompson and Fanton, 2021](#)).

Supplementary Table 4. *TemplateFlow* and NITRC are complementary resources with very different scope, goals and implementations. While *TemplateFlow* is specifically designed for sharing template and atlas resources, the NeuroImaging Tools & Resources Collaboratory (NITRC) “is an award-winning free web-based resource that offers comprehensive information on an ever expanding scope of neuroinformatics software and data” (https://www.nitrc.org/include/about_us.php). Indeed, NITRC provides a fundamental service to the neuroimaging community under open-ended, generalistic purposes, and it has not found a comparable alternative. Indeed, *TemplateFlow* is a narrowly-scoped tool that resolves a very specific set of issues around template, atlases, their sharing and reuse, and their reporting. Reflecting such a hierarchy of resources and acknowledging the relevance of NITRC, *TemplateFlow* was registered therein (<https://www.nitrc.org/projects/templateflow>).

	<i>TemplateFlow</i>	NITRC
Scope	N-D template/atlas resources	General purpose neuroimaging resource cataloging and distribution
Storage	Outsourced: leverages (and replicates across) GIN/g-Node, OSF, and Amazon AWS	Fundamental component of NITRC services
Data Structure	Data must comply with a BIDS-inspired structure	Fully open to resource owner's choice
Programmatic access	Available with <i>DataLad</i> and/or the <i>Python Client</i>	Not available. Some availability through NITRC-IR, an XNAT instance
Ability to store and retrieve individual data files and metadata of templates and atlases	Built-in	Not available
Ability to query specific pieces of data or metadata with filters	Yes, based on <i>PyBIDS</i>	Limited to Web search or XNAT search when available
Versioning	Full version-control with <i>DataLad</i>	Limited to creating “snapshot” packages
Application Programming Interface (machine operable)	Available, with <i>DataLad</i> and/or <i>PyBIDS</i>	Not available
Quality control	Peer-review at submission time: After submission, feedback is tracked and processed through GitHub Issues	Limited to feedback through Web Discussion Forum, which can be disabled by the owner
Unique identifiers	Templates & Sub-template components (e.g., atlases)	Resource
Licensing	Resources must be distributed with a license file, which should be permissive and allow derivative works	A license is chosen and can be presented at download time; however, the author is afforded sufficient flexibility to override this

Supplementary Discussion

Distribution with general-purpose, manually-curated repositories such as NITRC may be more problematic. Beyond the absence of a shared data format because repositories do not mandate any standard, additional problems arise that hinder or block access and reuse. We have found templates at NITRC flagged as available for *freeware noncommercial* use as a general category, but the actual terms for reuse are not accessible. More worryingly, authors may post private resources with the appearance of being open. NITRC's interface allows resources to be nominally released under a permissive open license, but before the data can be accessed, resources' authors may require signing a Data Usage Agreement that forbids redistribution. Further details of the advantages of *TemplateFlow* over NITRC for the particular case of template and atlas resource distribution are provided in the Supplementary Table 4. Long term sustainability of the resource is ensured by using minimal cost services (all free at the time of writing) and open source tools.

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