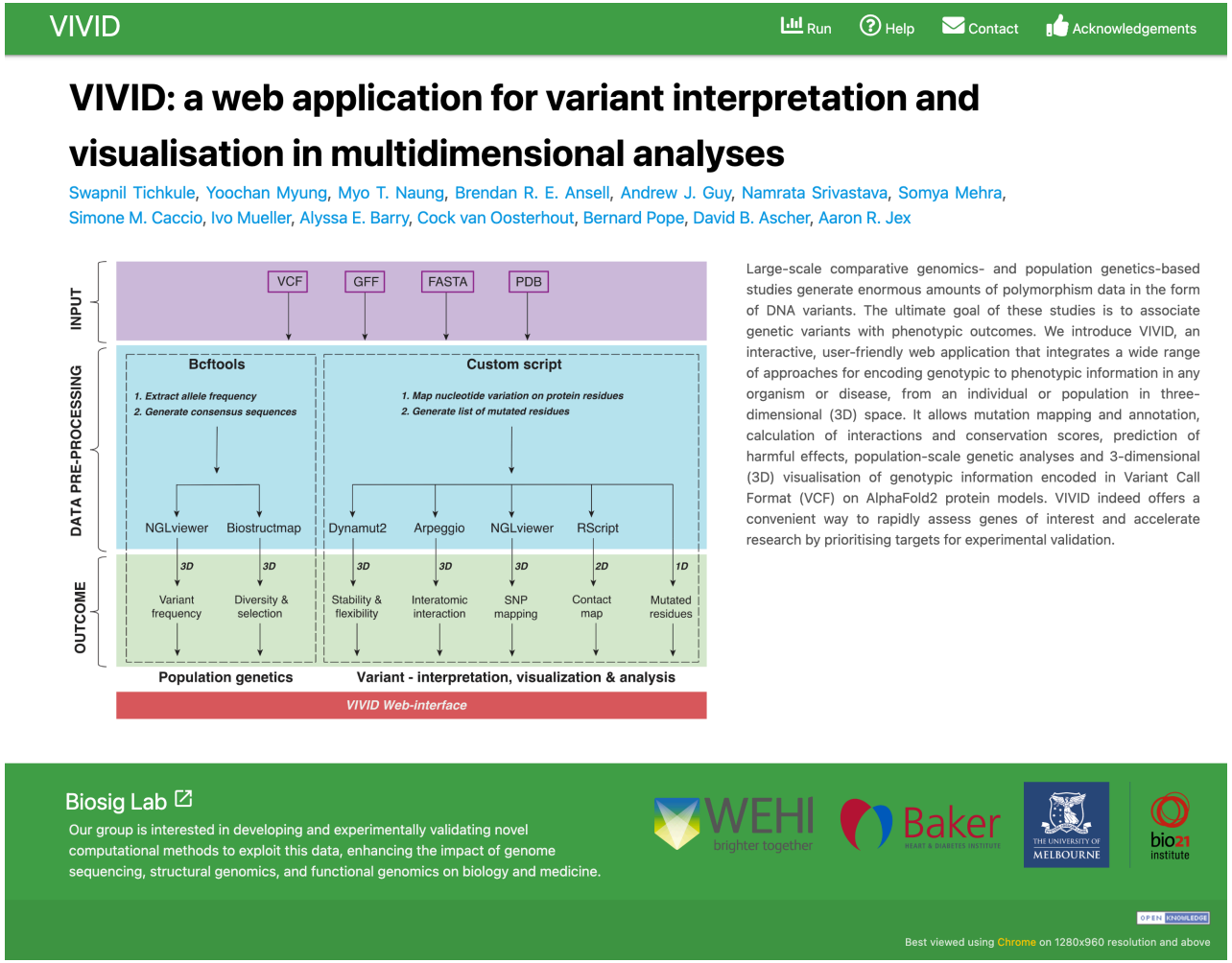



# About VIVID

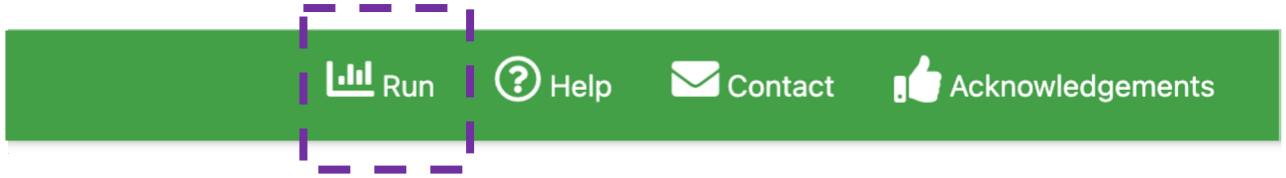
VIVID is a user-friendly web server that allows users to visualise genomic mutations from single-individual to population-scale for their impact on protein structure, function, and evolution.

Read more here:
https://doi.org/10.1101/2021.11.16.468904

Download example dataset 1
Plasmodium falciparum: Erythrocyte binding antigen protein

Download example dataset 2
SARS-CoV-2: Spike protein

[Source of example dataset 1] https://www.malariagen.net/data/pf3k-5
[Source of example dataset 2] https://usegalaxy.org/u/carlosfarkas/h/snpeffsars-cov-2



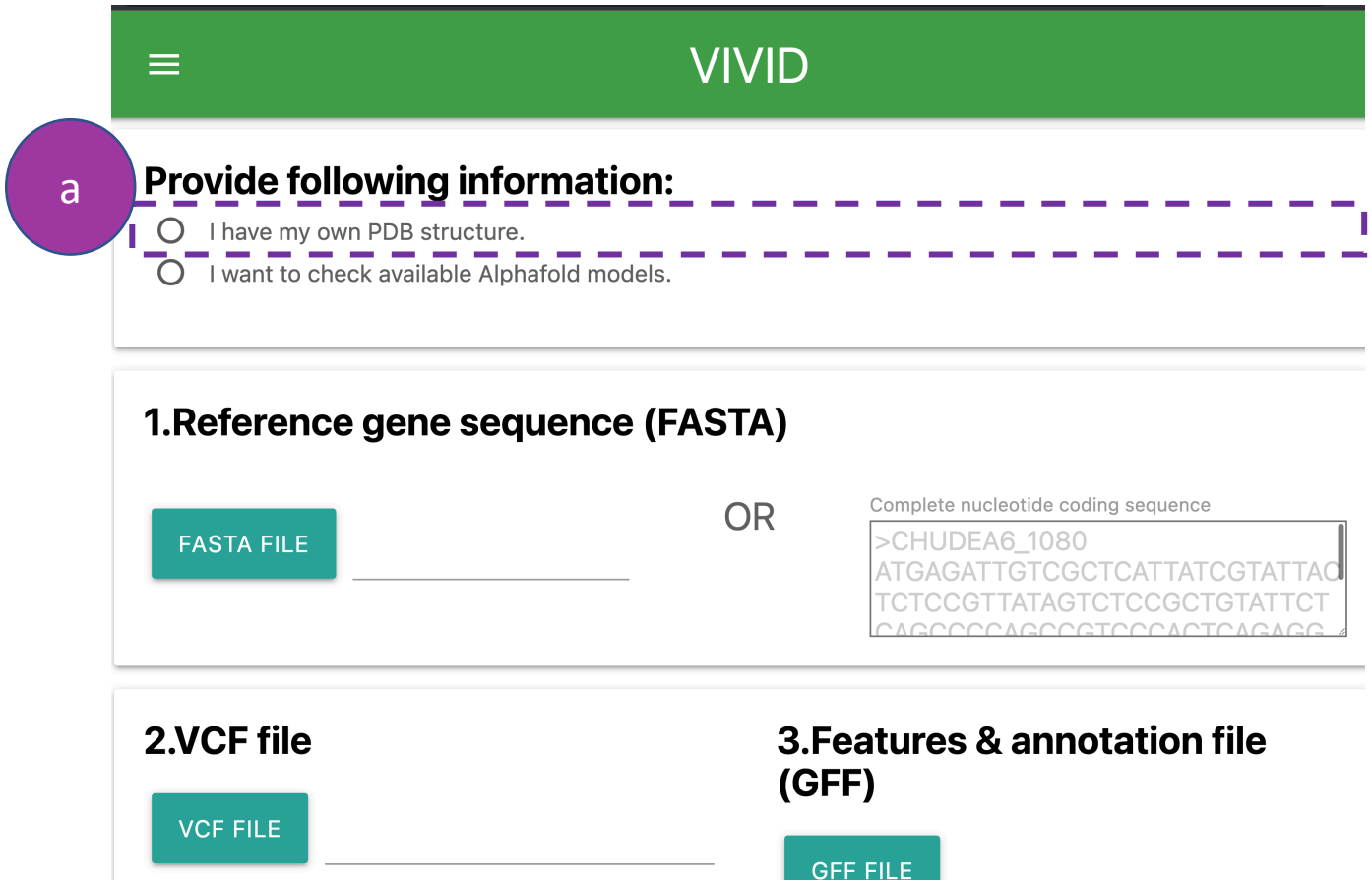

nt interpretation and analyses

ndrew J. Guy, Namrata Srivastava, Somya Mehra,
d Pope, David B. Ascher, Aaron R. Jex

Large-scale comparative genomics- and population genetics-based studies generate enormous amounts of polymorphism data in the form of DNA variants. The ultimate goal of these studies is to associate genetic variants with phenotypic outcomes. We introduce VIVID, an interactive, user-friendly web application that integrates a wide range of approaches for encoding genotypic to phenotypic information in any organism or disease, from an individual or population in three-dimensional (3D) space. It allows mutation mapping and annotation, calculation of interactions and conservation scores, prediction of harmful effects, population-scale genetic analyses and 3-dimensional

# Run Analysis

The job submission page for input files can be accessed via the menu item **Run** on the top bar menu.



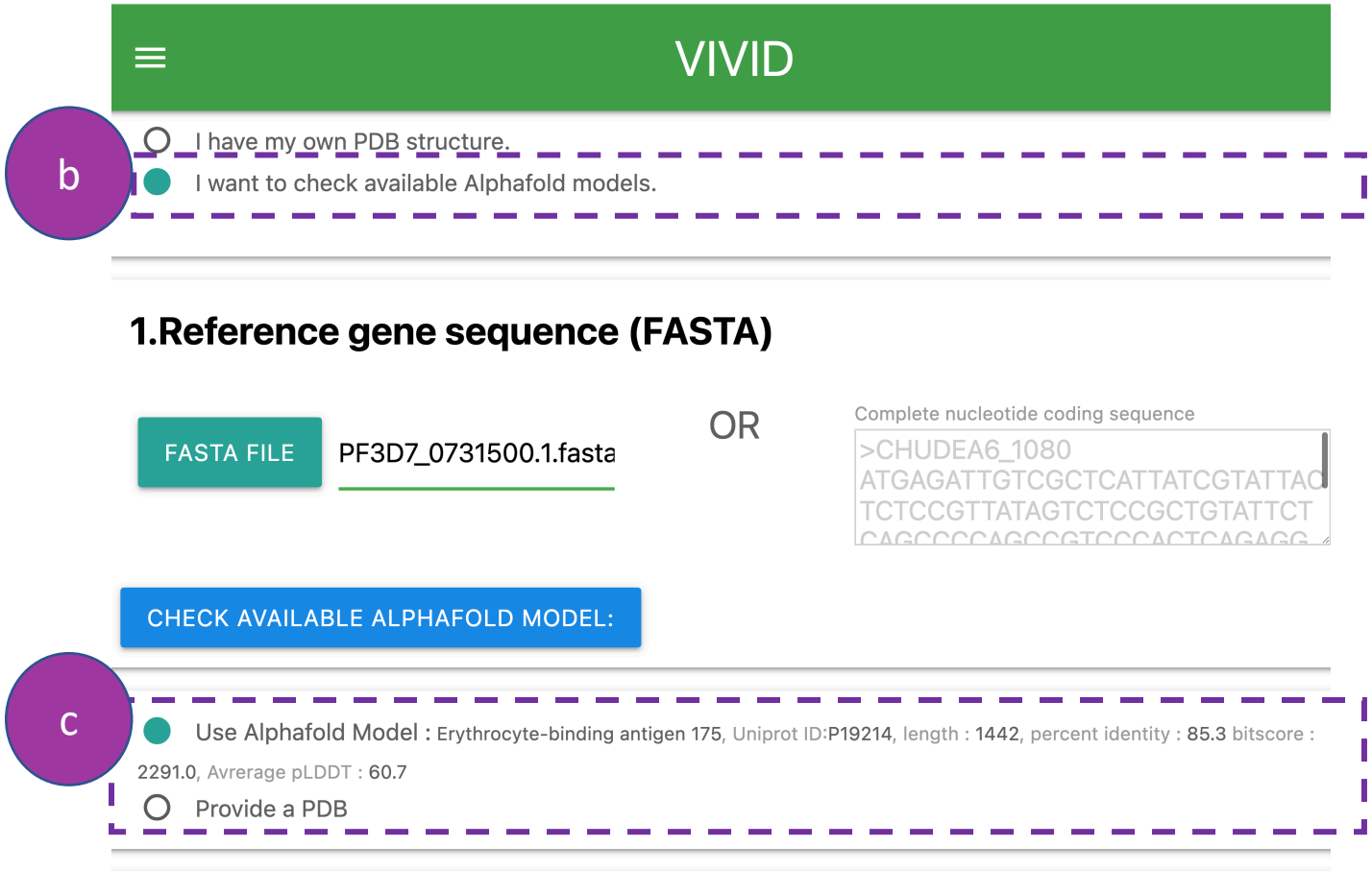

# Run Analysis

## Provide following information

At this input step users have two options to provide a protein structure (PDB file):

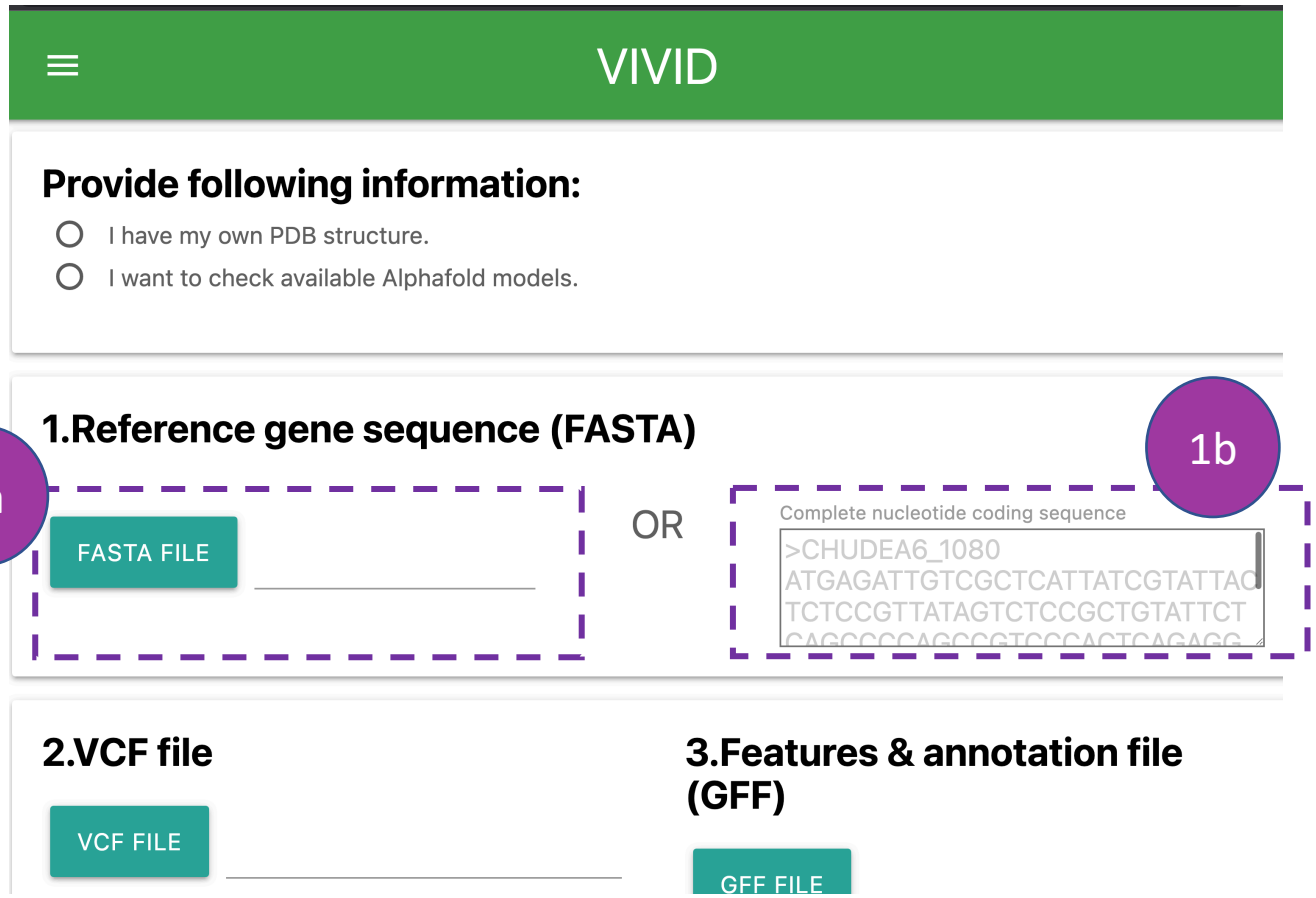
**(a)** Upload a protein structure from the local system or access it via the RCSB PDB database.

# Run Analysis




## Provide following information

**(b)** Request through VIVID to check the availability of a protein structure in the AlphaFold Protein Structure Database. First, this is done by blasting the query sequence against the SWISS-PROT database to obtain the UniProt ID of the top blast search hit. Second, the UniProt ID is then searched in AlphaFold Protein Structure Database to obtain the protein structure. After this search, VIVID provides information such as UniProt ID, sequence identity, and average PLDDT score of the model structure to allow the user to decide whether to proceed with the analyses **(c)**.




# Run Analysis

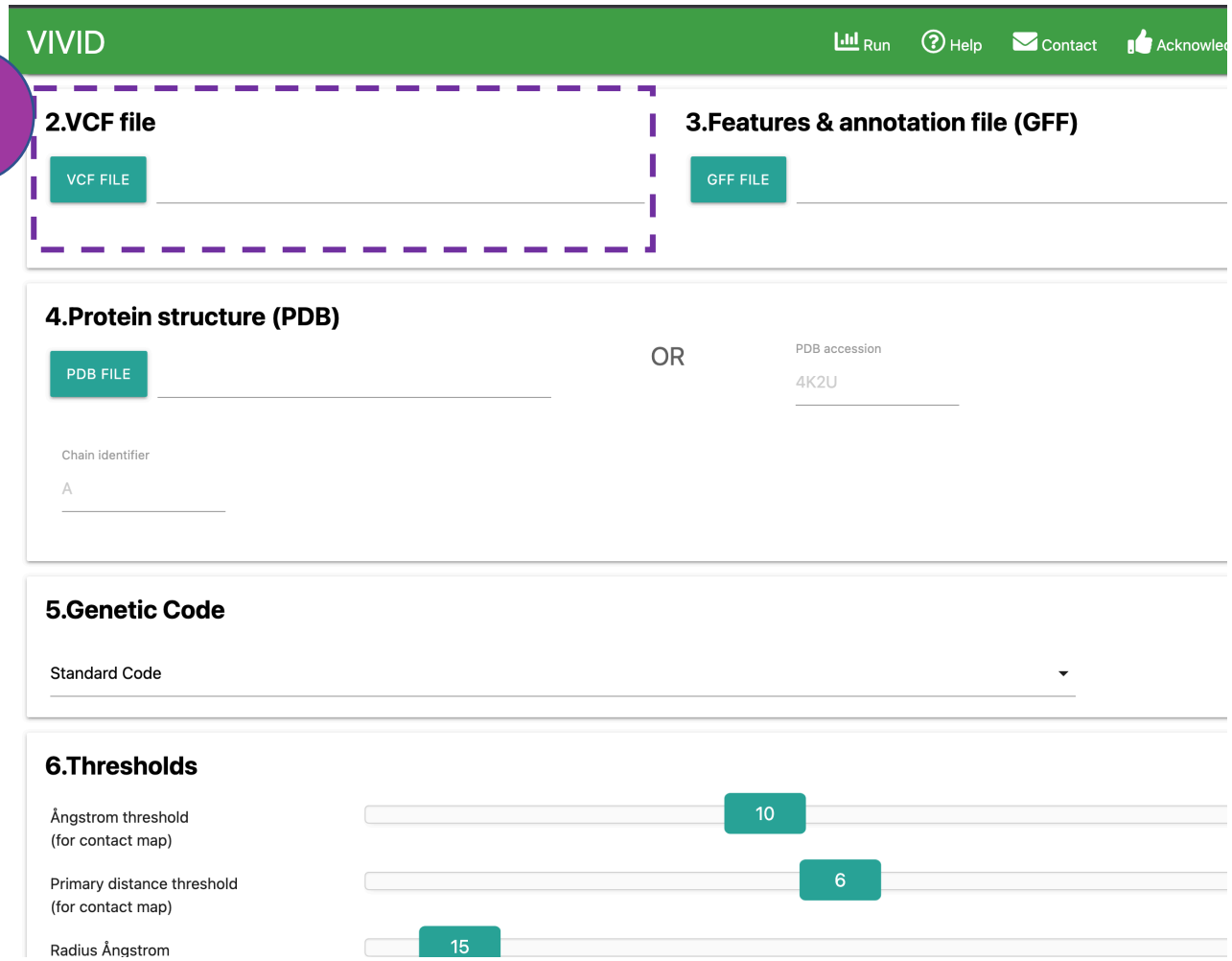
## Reference gene sequence (FASTA)

The complete nucleotide coding sequence of a gene can be provided by either uploading the FASTA file from the local system **(1a)** or by pasting the sequence along with the gene id into the box **(1b)**.

**Please note:**

The header in a FASTA file should contain only '>gene_id' without any additional information such as delimiters ('|', 'space', 'tab', etc.) or annotation **(1b)**.

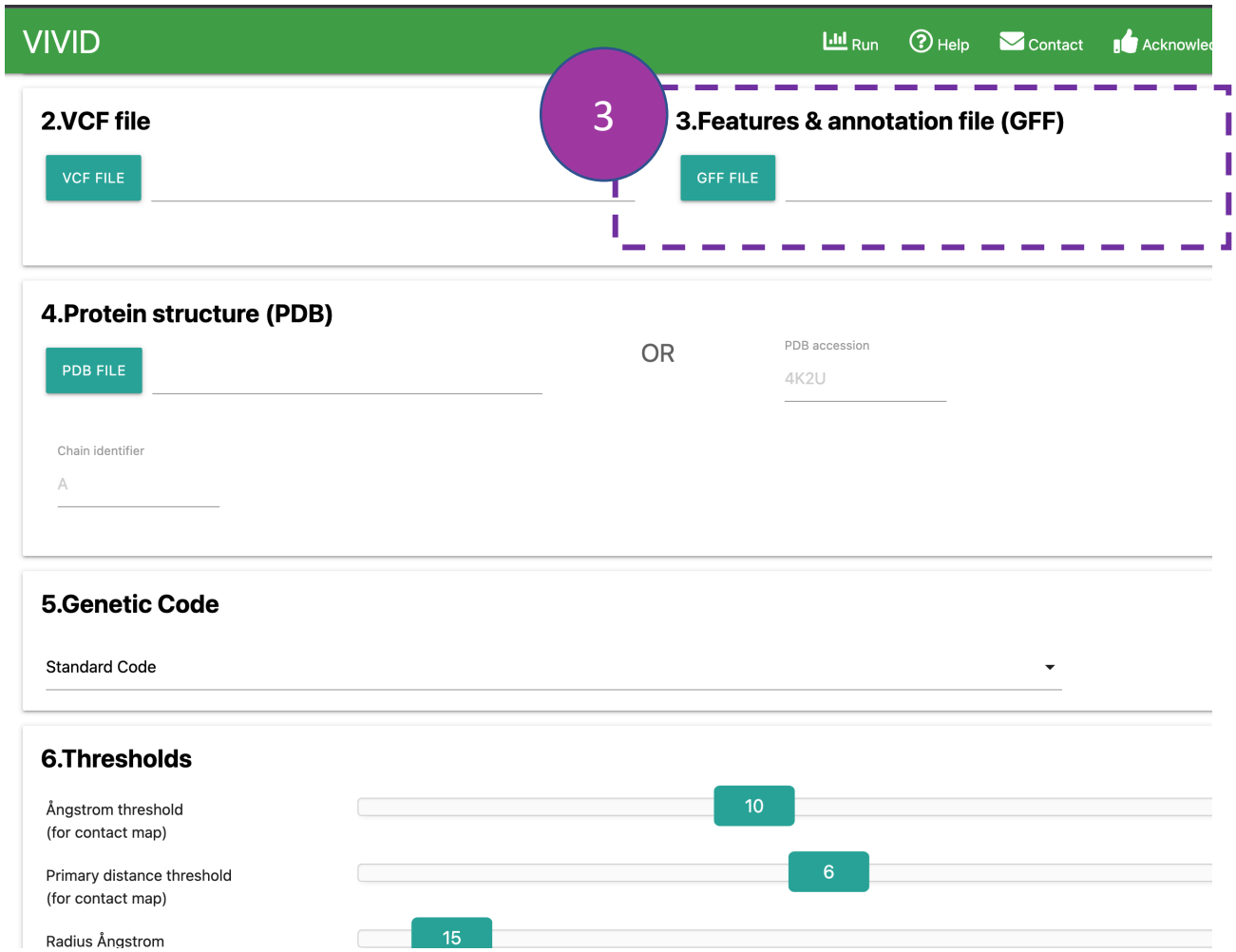
# Run Analysis




## VCF file

Provide a VCF file that contains only bi-allelic SNPs. If the VCF file size is large (>500 Mb), we suggest users reduce the file size by selecting/keeping SNPs specific to the coding region of the query sequence to avoid lengthy processing times. If the VCF file is unavailable, SNP information can also be provided in a tabular format (download example).

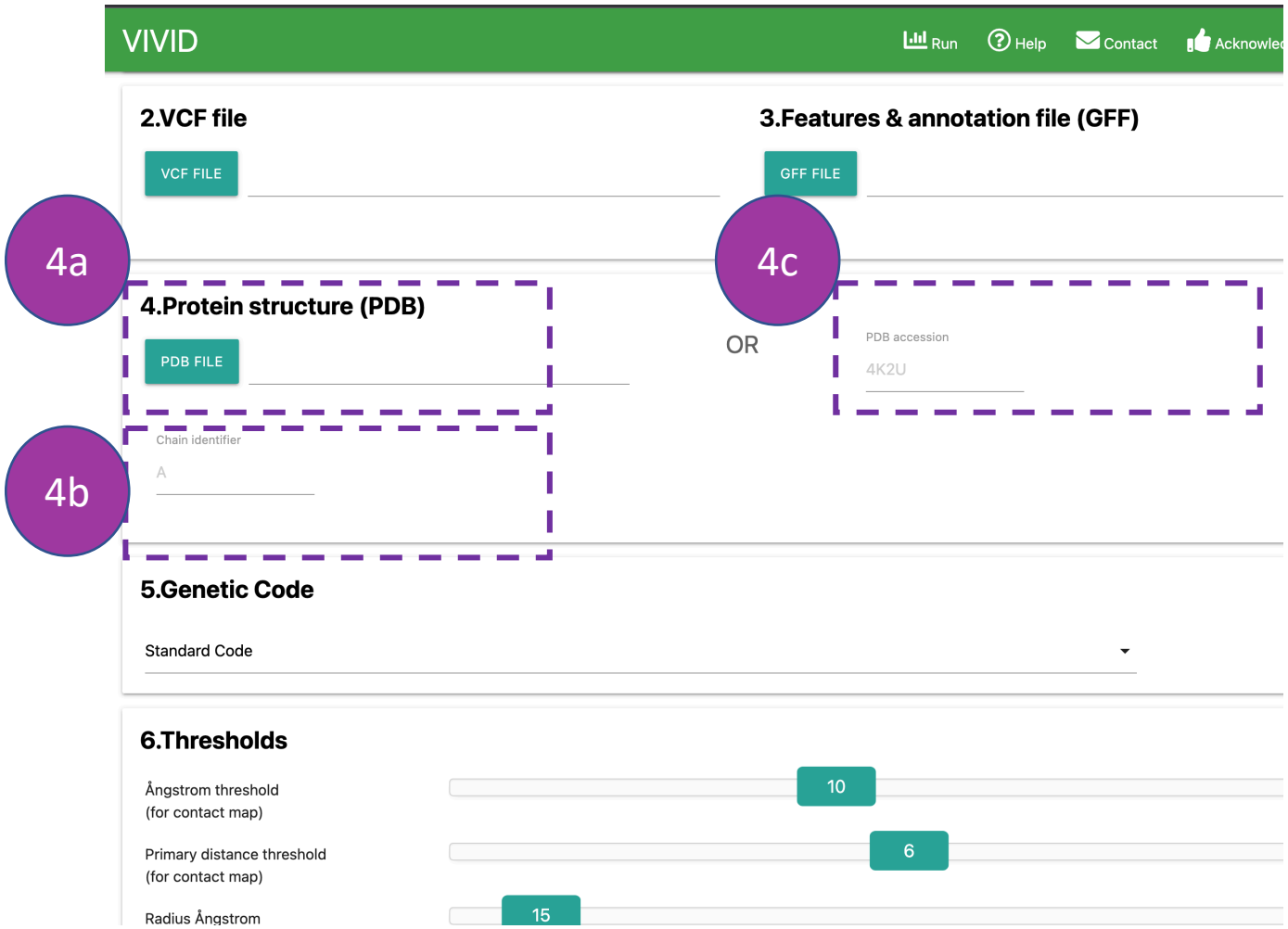
**Please note:**
The nucleotide coding sequence should be from the same version of the reference genome used to call SNPs.




# Run Analysis

## GFF file

Provide a GFF annotation file that should contain the "CDS" feature. If the GFF file is unavailable, CDS coordinates can also be provided in tabular format (download example).

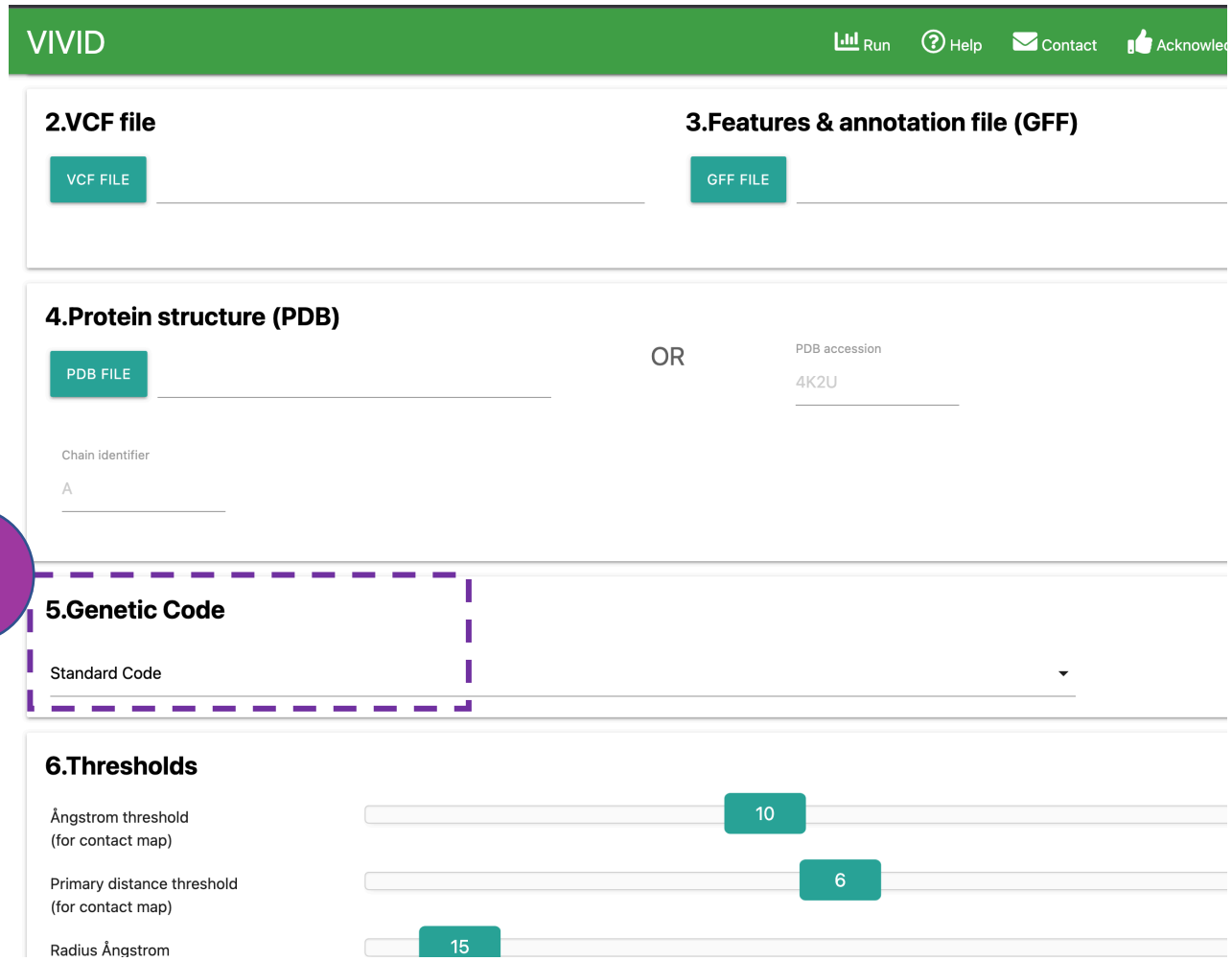



# Run Analysis

## Protein structure (PDB)

Provide a protein structure file **(4a or 4c)** and chain ID **(4b)** if you have your PDB structure. This can be provided by either uploading a PDB file from the local system **(4a)** or accessing it via the RCSB PDB by providing a PDB ID **(4c)**. These details will be auto-filled if AlphaFold models are selected at the beginning.

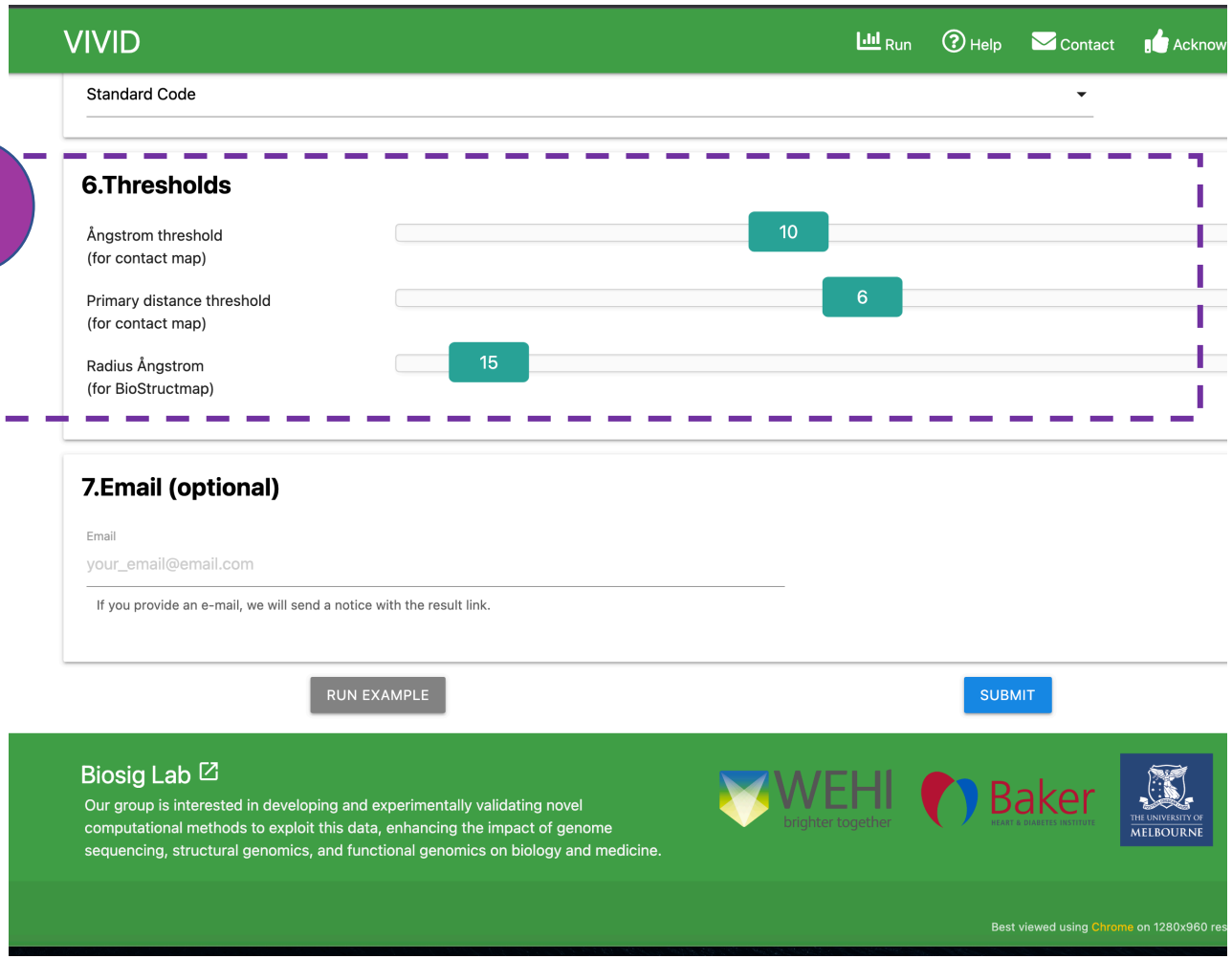
# Run Analysis




## Genetic code

Select the appropriate genetic code (default: ‘Standard Code’) from the drop-down menu used to translate queried coding sequence into amino acids.

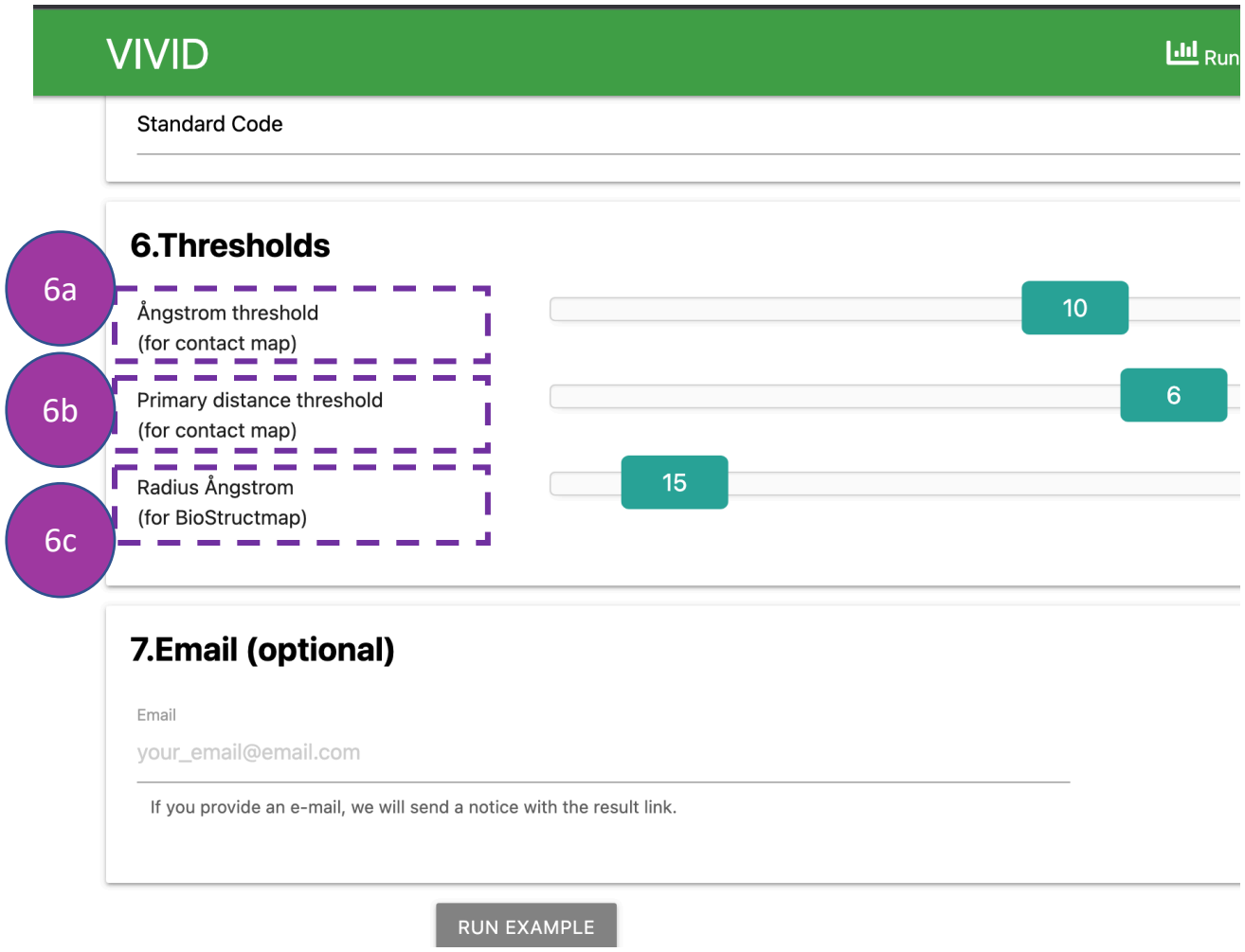
# Run Analysis




## Thresholds

These inputs are optional and are associated with “Contact Map” and “BioStructmap” analyses that display pairwise residue interactions and perform 3D sliding window population genetics analyses. Ångstrom (0.1 nanometres) is the standard unit of measurement for protein crystal structures.

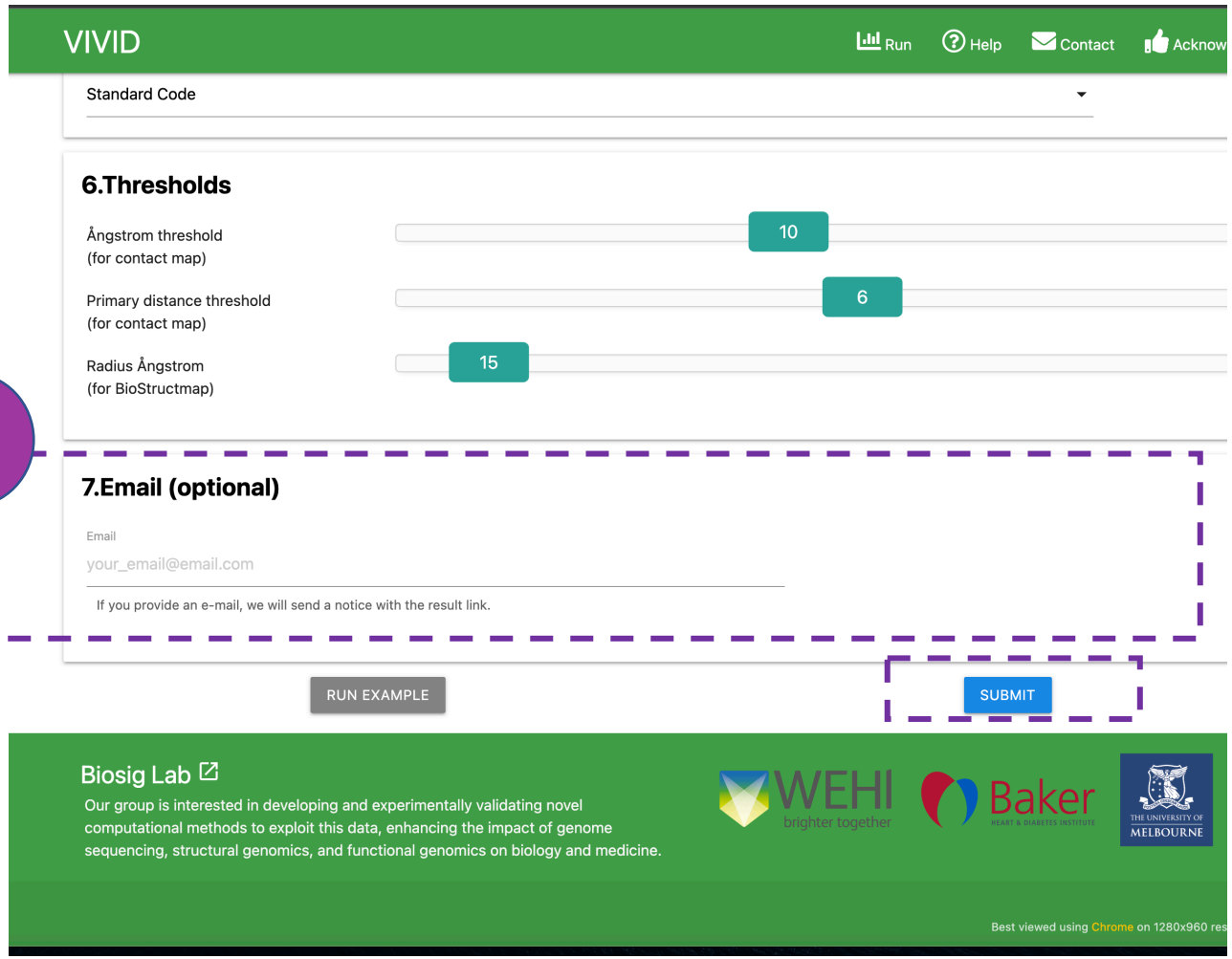
# Run Analysis




## Thresholds

Here, the **Ångstrom threshold (6a)** indicates the Euclidian distance in 3-dimensional space between alpha carbon atoms of amino acids (default: 10 Ångstrom) in the contact map. The **primary distance threshold (6b)** represents the number of amino acids apart in the primary sequence (default: 6 AA) in the contact map. **Radius Ångstrom (6c)** represents Euclidean distance from the alpha carbon atoms of the mutated residues (default: 15 Ångstrom), for which 3D sliding window population genetic analyses will be performed.

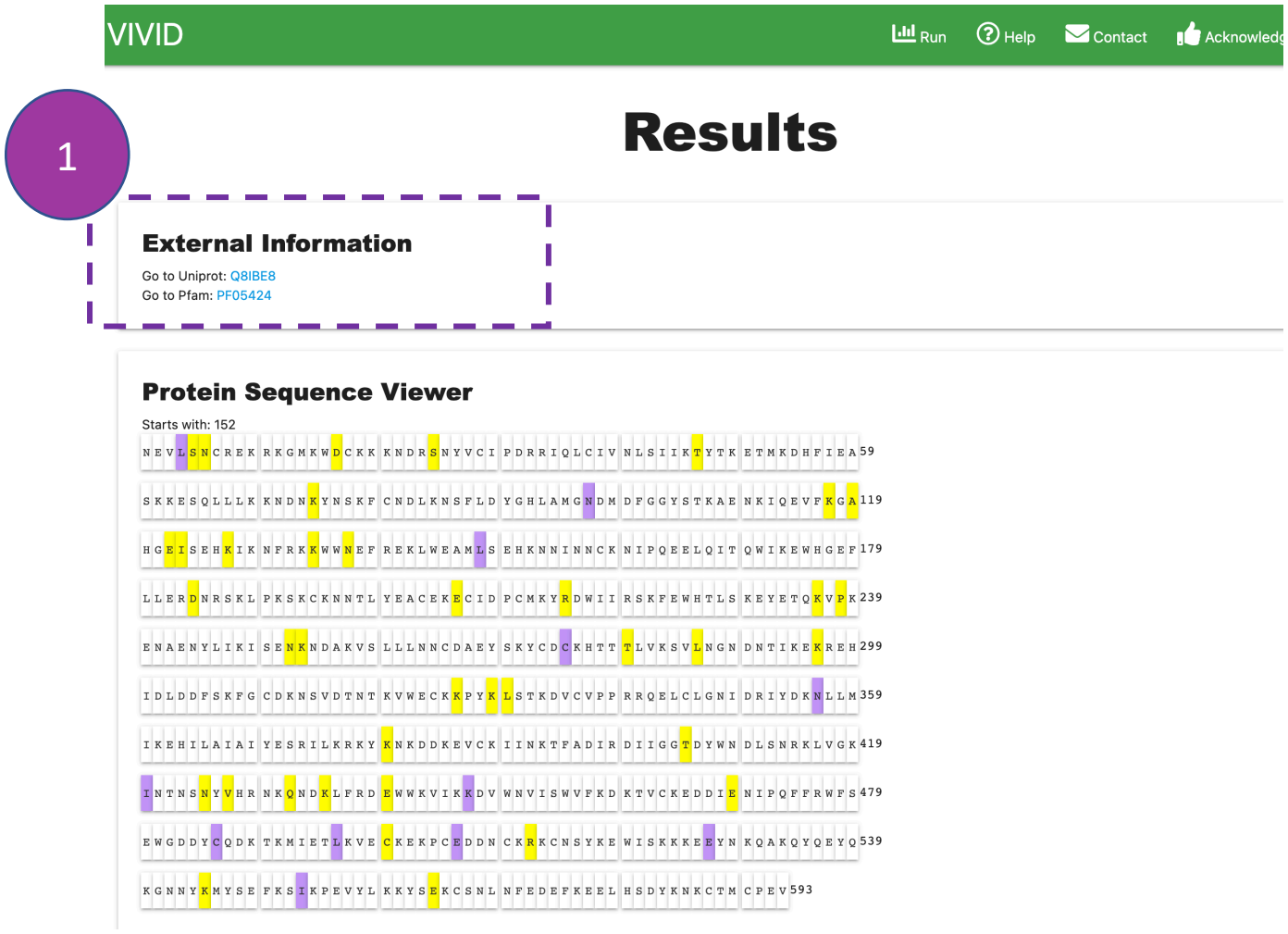
# Run Analysis




## Email

By providing an **Email** address, the user can receive a notification email after job completion.

Click **SUBMIT** to get your results




# Results

## External Information

Provides a link for UniProt and Pfam databases to obtain additional biological information where users can render structural and functional domain information (e.g., conserved structural domains, active sites, etc.) on protein sequence and structure to identify mutational hotspots.

**Please note:**

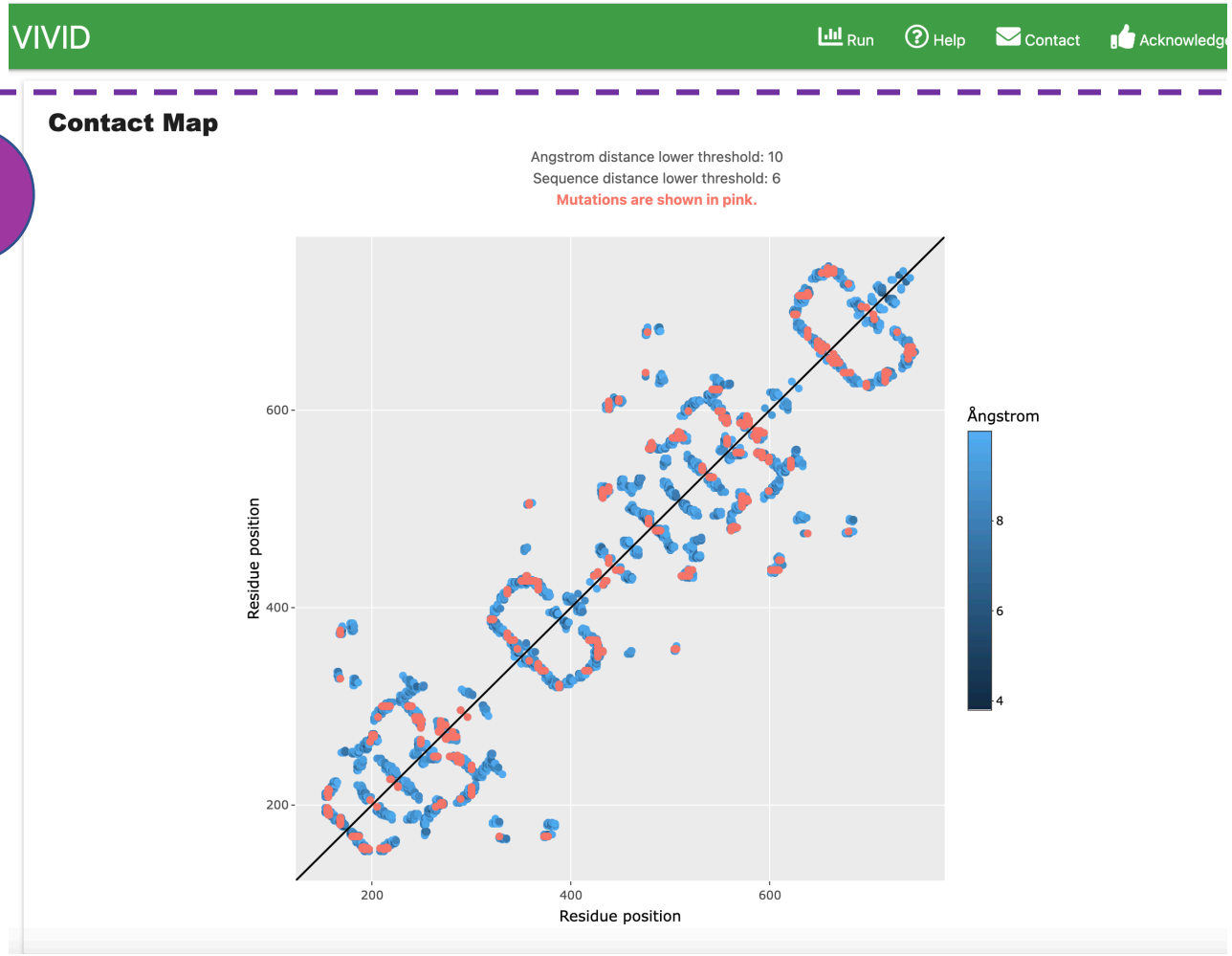
The UniProt and Pfam IDs are obtained by performing a BLAST search of the nucleotide query sequence against the SWISSPROT database


# Results

## Protein Sequence Viewer

The nucleotide coding sequence of a gene is encoded into amino acid residues of a protein where synonymous (purple) and non-synonymous (yellow) mutations are highlighted by default. Only residues present in the PDB file are represented in the primary sequence. This interactive panel can be used to select and highlight **External Information** from above, in primary sequence and 3D Visualisation.

# Results



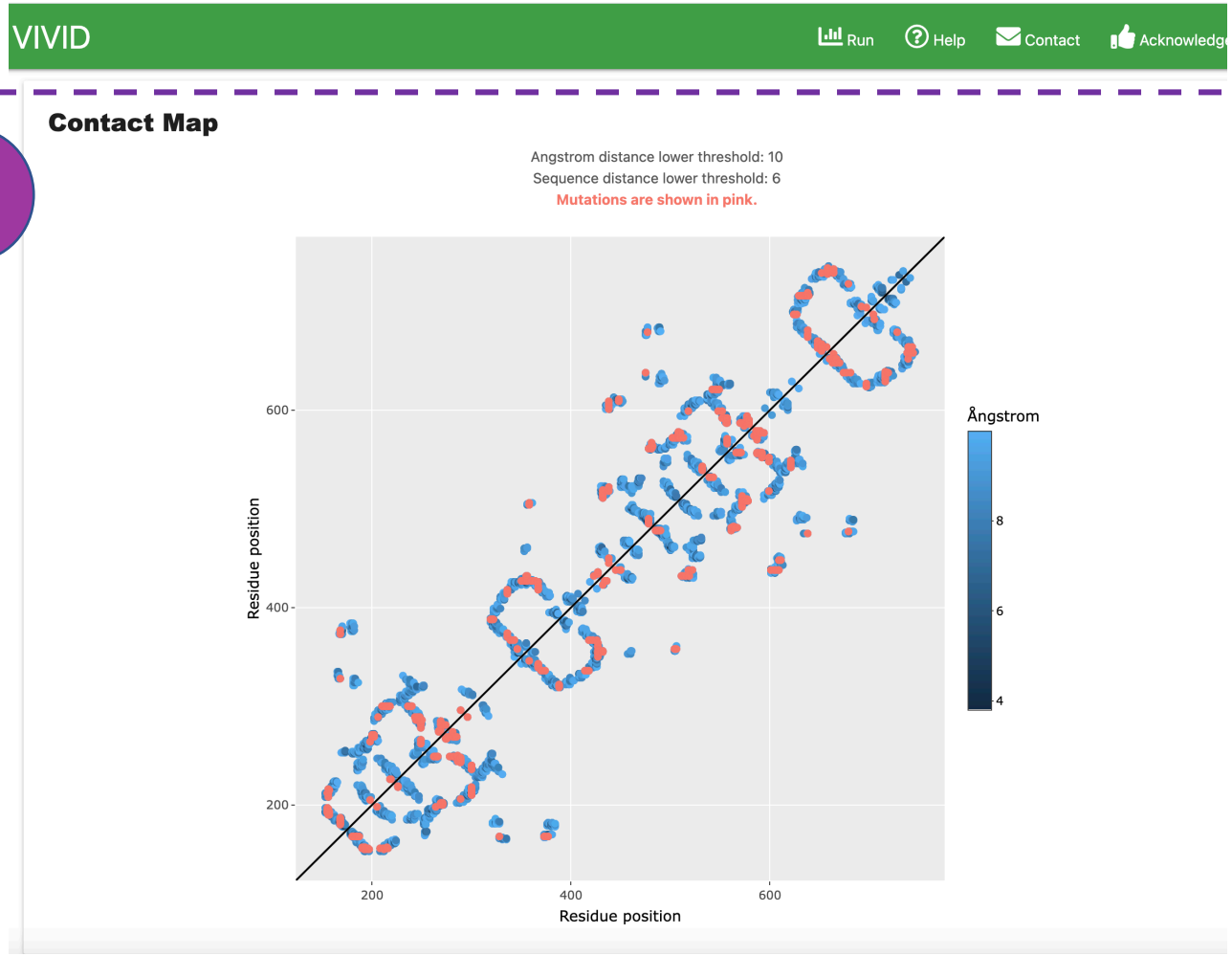

3

## Contact Map

This represents pairwise residue-residue interactions. Interactions within user-defined *Angular threshold* in 3D-space and found more than the *primary distance threshold* are shown in blue, where interactions involving mutated residues are highlighted in pink. This interactive panel allows users to *zoom in* by selecting a box. Also, users can *hover over* interactions to display details of interacting residues.

# Results

3

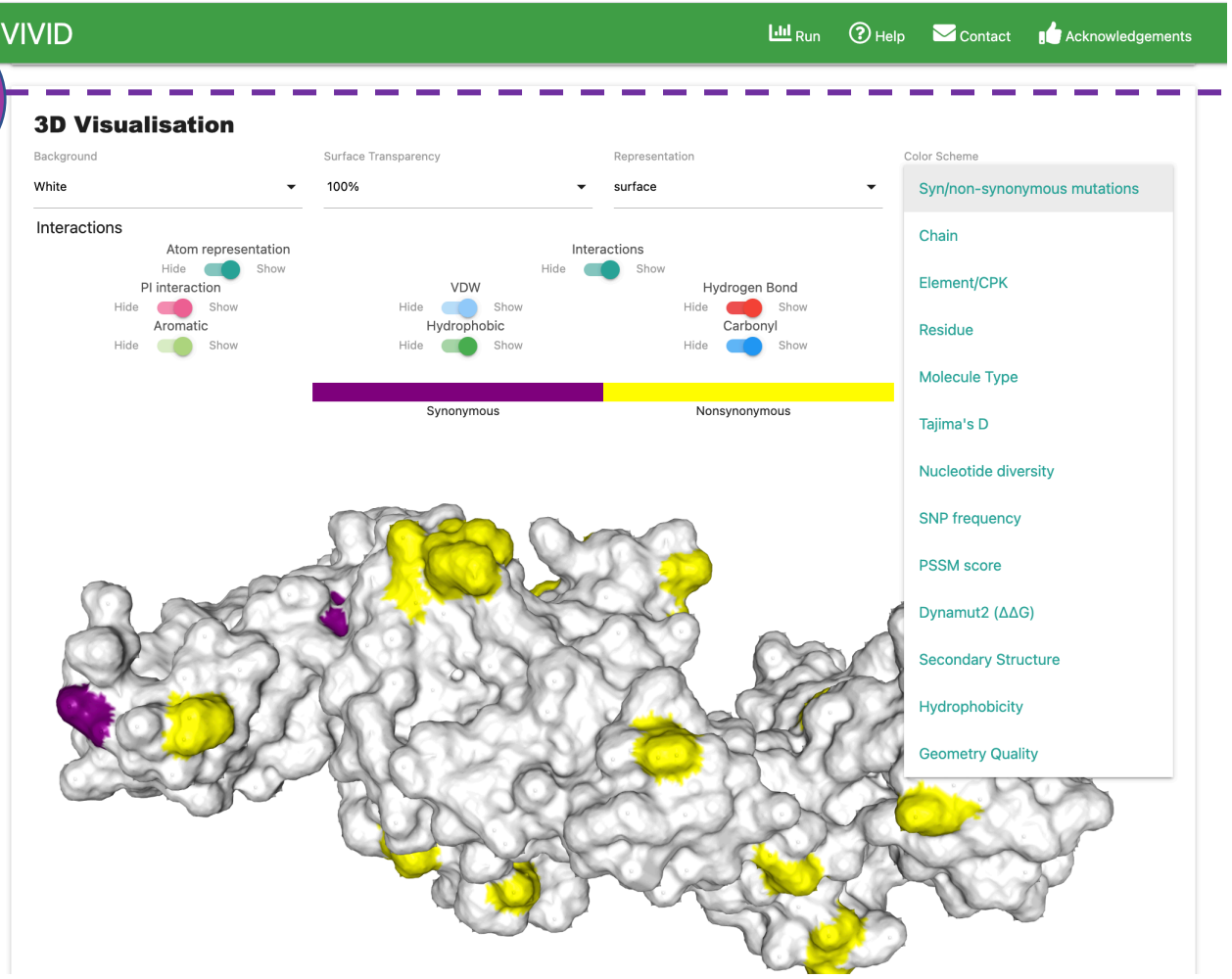



## Contact Map

**Please note:**

If users want to display more long-range interactions in 2D space and avoid closely associated residues in the primary sequence, they can go back to the submission page and increase the Ångstrom threshold and Primary distance threshold.

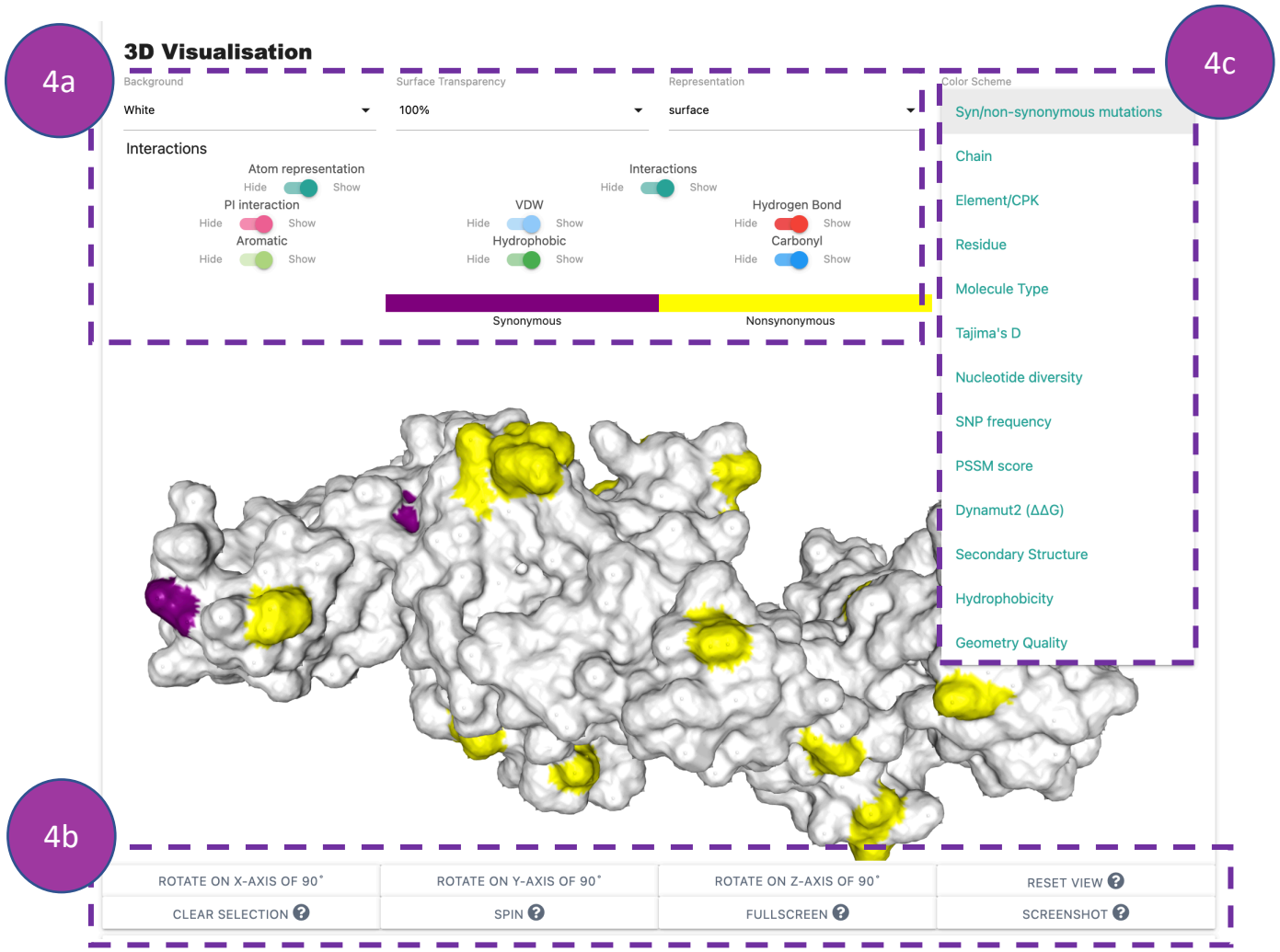
4




# Results

## 3D Visualisation

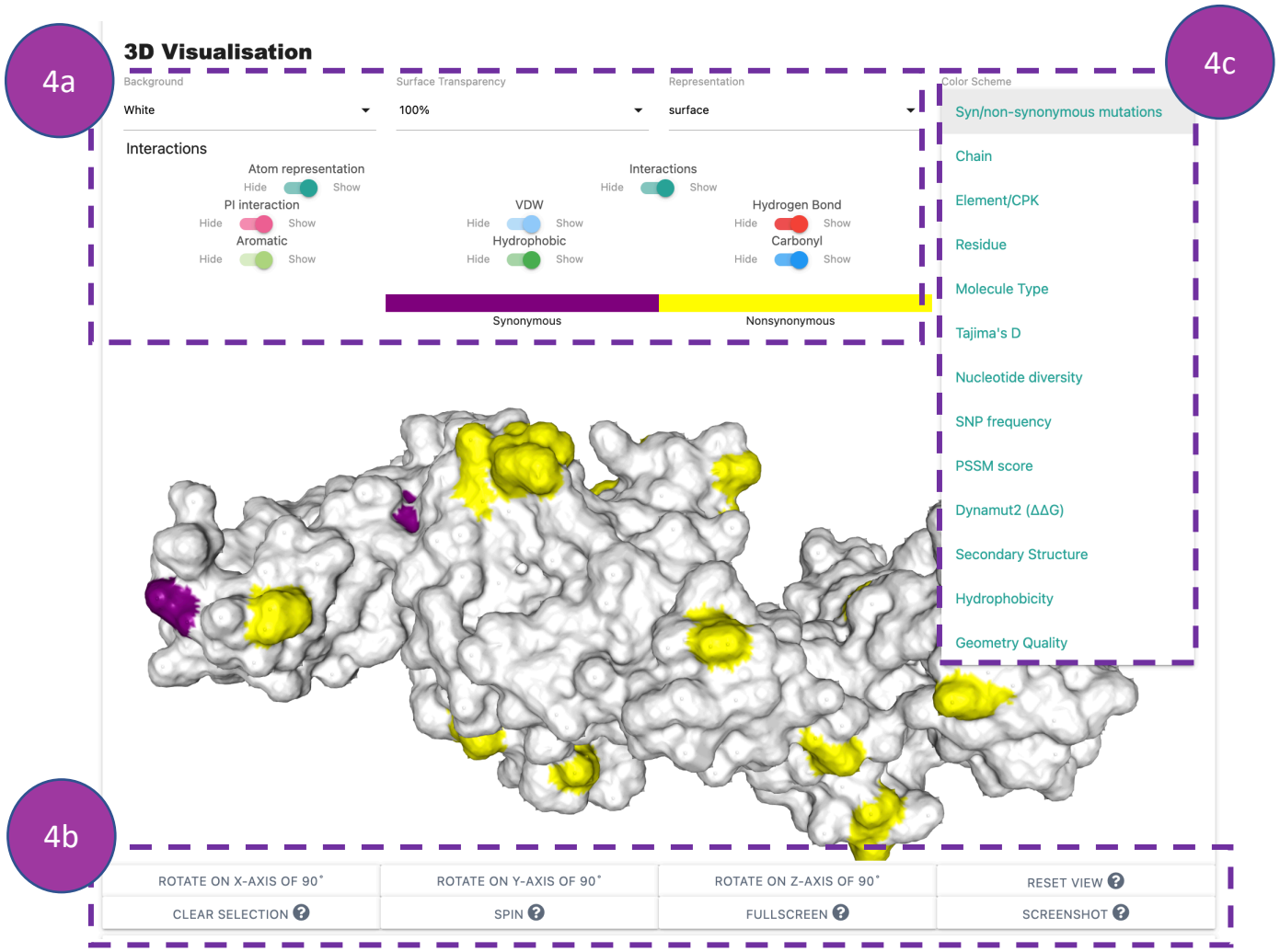
This panel shows interactive 3D viewer. Default view displays interatomic interactions between the wild-type residue and nearby residues.




# Results

## 3D Visualisation

Interactions can be hidden or displayed using the controls provided **(4a)**. The viewer can be manipulated using buttons at the bottom of the panel **(4b).** VIVID allows users to perform multiple 3D renderings using the control panel by selecting options from the 'colour scheme' drop-down menu **(4c).** The default colour scheme is synonymous and non-synonymous mutations. Some interesting, informative visualisation in the 'colour scheme' could be Tajima's D, Nucleotide diversity, SNP frequency, PSSM score and Dynamut2 (ΔΔG).




# Results

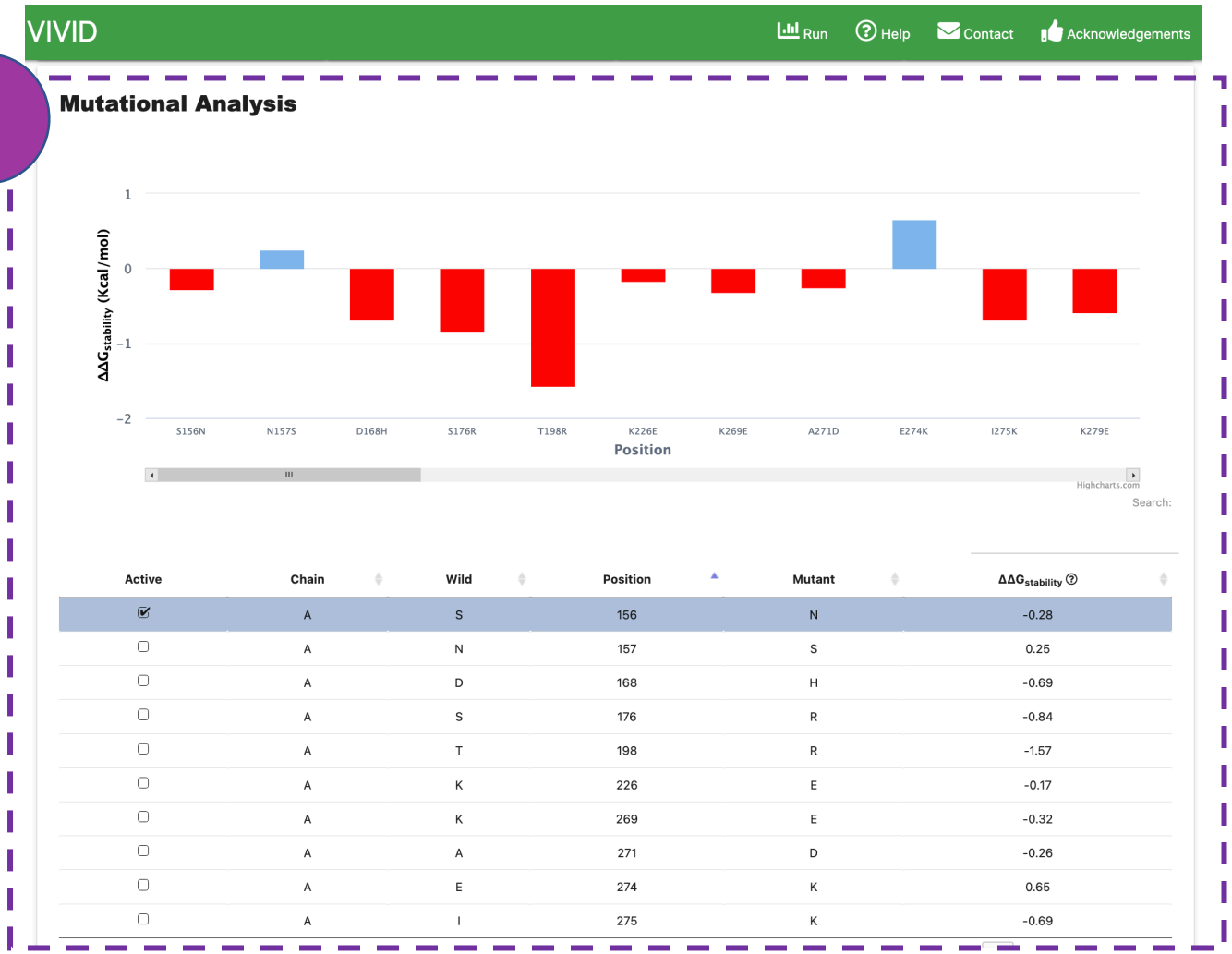
## 3D Visualisation

**Please note:**

Population genetics indices such as Tajima's D and Nucleotide diversity are calculated with a 3D sliding window (default Radius Ångstrom = 15) analysis in the BioStructmap program. Depending on the size of the protein, the default value of Radius Ångstrom might not be sufficient; hence the user can go back to the submission page and increase/decrease the Radius Ångstrom threshold. For more details, please refer to the BioStructmap publication [1].

[1] Guy AJ, Irani V, Richards JS, Ramsland PA. 2018. BioStructMap: a Python tool for integration of protein structure and sequence-based features. Bioinformatics 34:3942-3944.

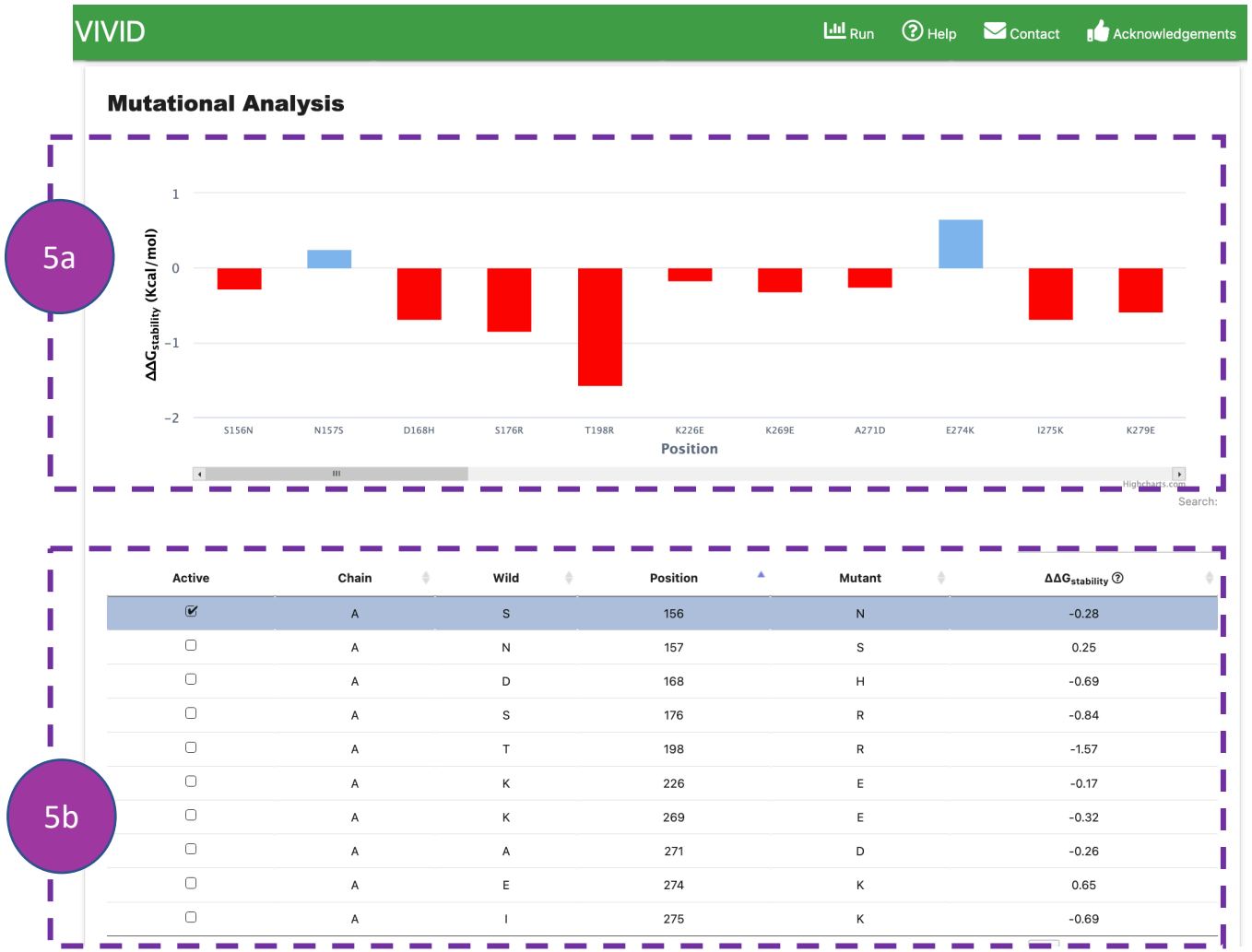
# Results




## Mutational Analysis

This panel will be shown once Dynamut2 computations are completed. It displays predicted changes of folding free energy ($\Delta\Delta G$) of substituted amino acids on protein structure stability and flexibility using the Dynamut2 program.

# Results

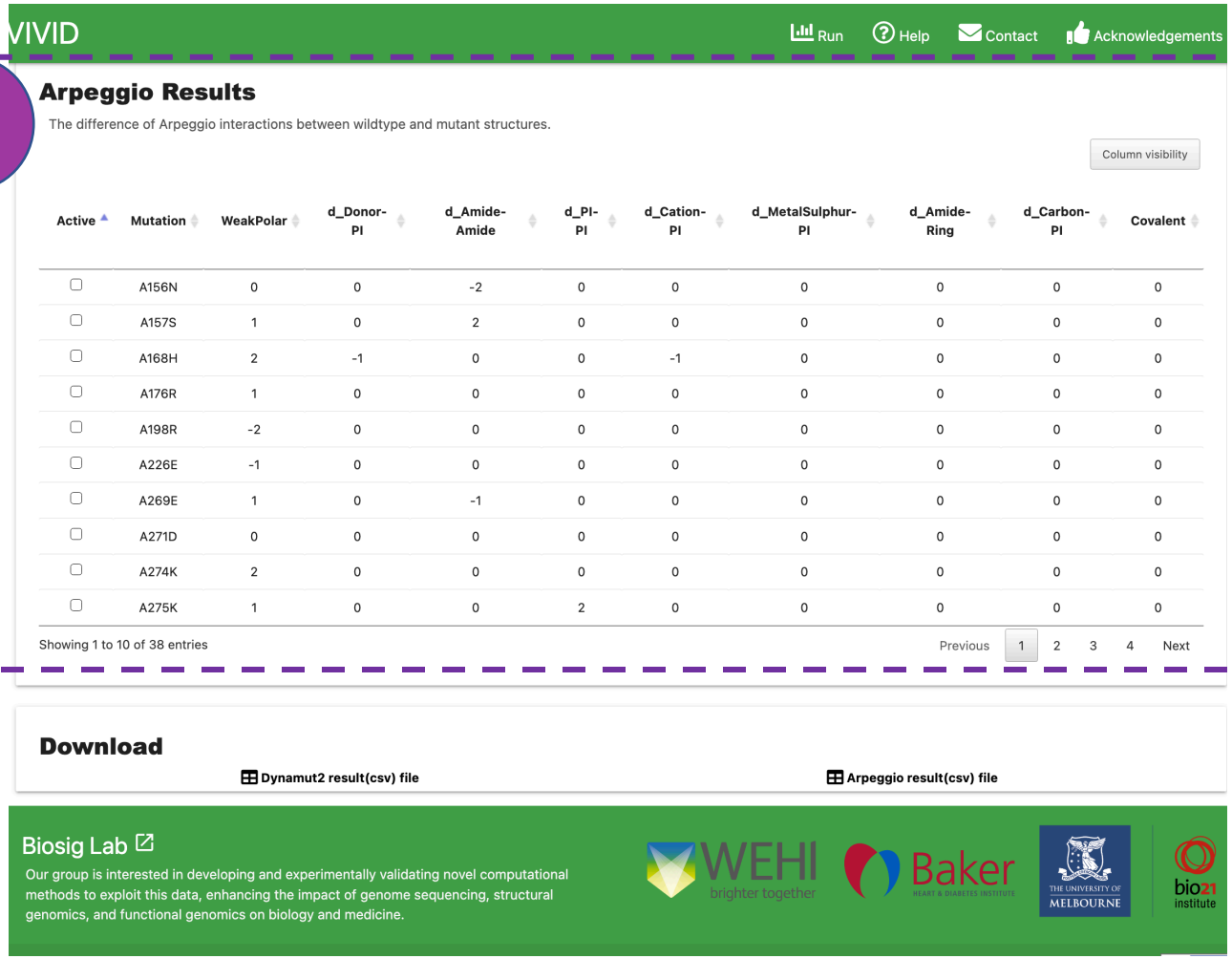



## Mutational Analysis

ΔΔ*G* values are represented in a bar chart **(5a)** and tabular format **(5b).** ΔΔ*G* values can also be visualised in the 3D visualisation panel by clicking on a drop-down menu of 'colour scheme'. For more details about ΔΔ*G* calculation, please refer to the Dynamut2 publication [2].

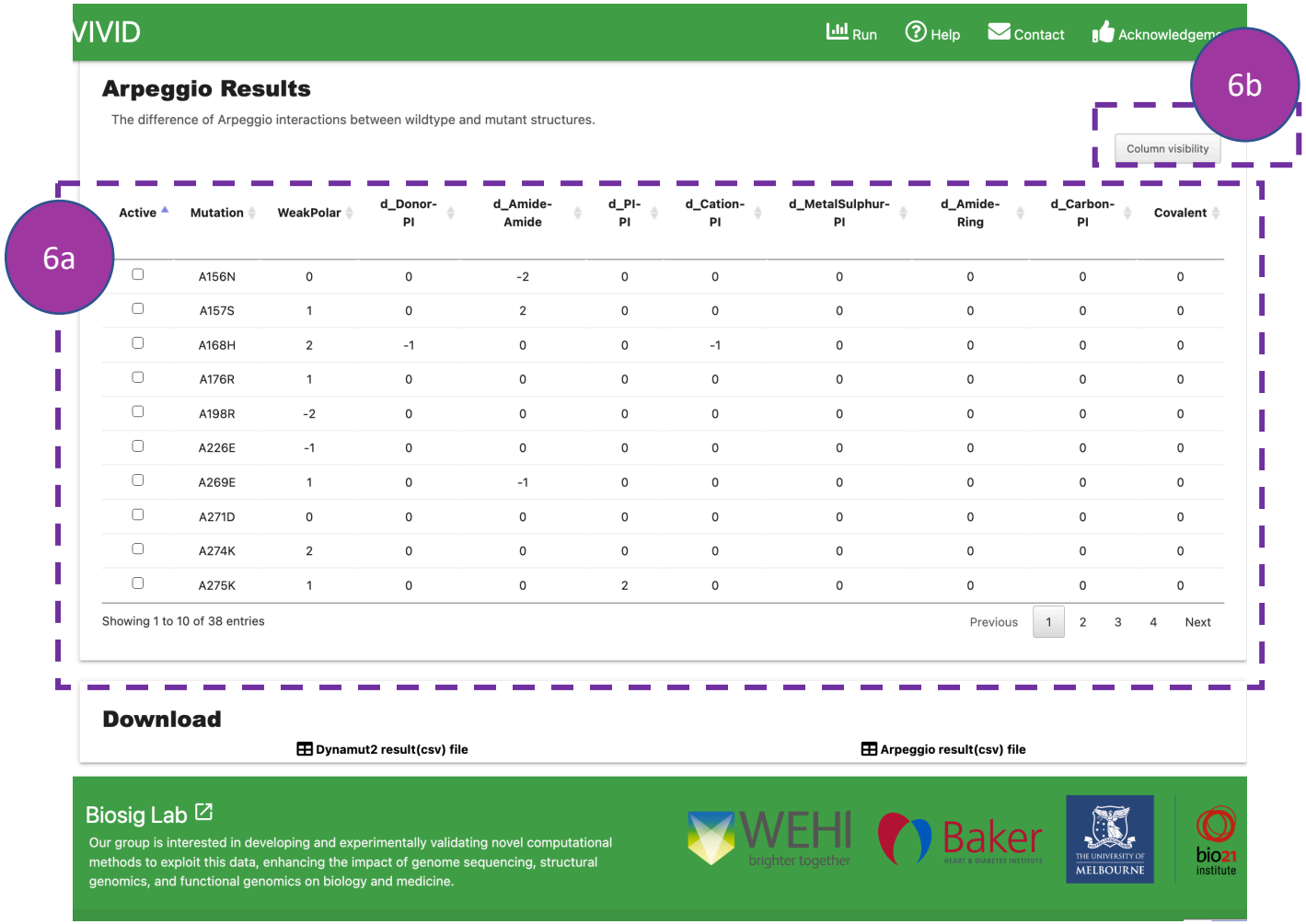
[2] Rodrigues CHM, Pires DEV, Ascher DB. 2020. DynaMut2: Assessing changes in stability and flexibility upon single and multiple point missense mutations. Protein Science : A Publication of the Protein Society 30:60 - 69.

# Results




## Arpeggio Results

This panel displays information about interatomic interactions between the substituted residue and nearby residues in in protein structures. Mainly, it reports changes among 20 interatomic interactions when compared wildtype and mutant residues. Users can use this table to get information about lost and gained interaction after substitution in a protein structure.

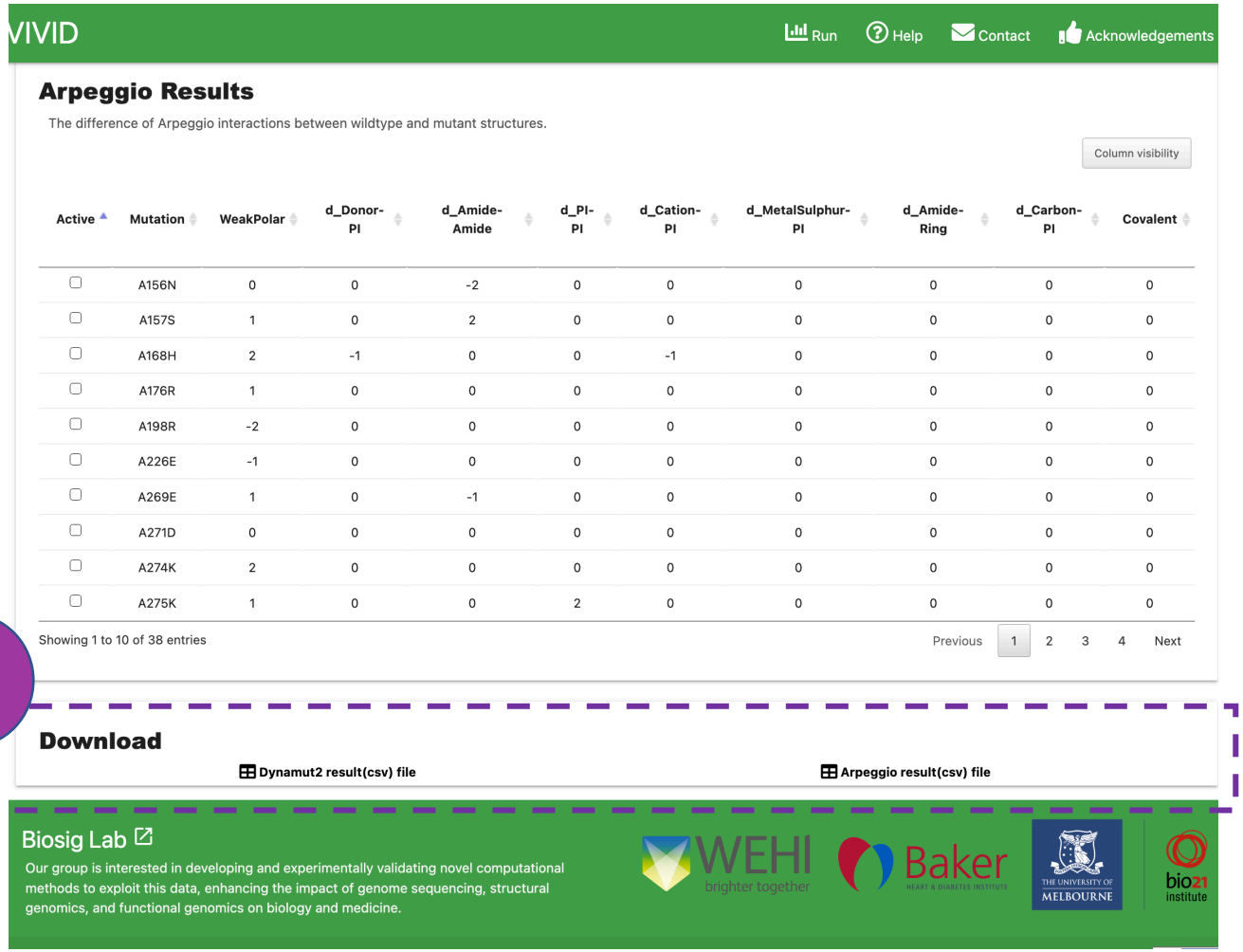



# Results

## Arpeggio Results

By default, information about nine types of interactions is shown in the table **(6a).** Users can click on 'column visibility' **(6b)** to display additional interactions. For more details, please refer to the Arpeggio publication [3].

[3] Jubb HC, Higueruelo AP, Ochoa-Montaño B, Pitt WR, Ascher DB, Blundell TL. 2017. Arpeggio: A Web Server for Calculating and Visualising Interatomic Interactions in Protein Structures. J Mol Biol 429:365-371.

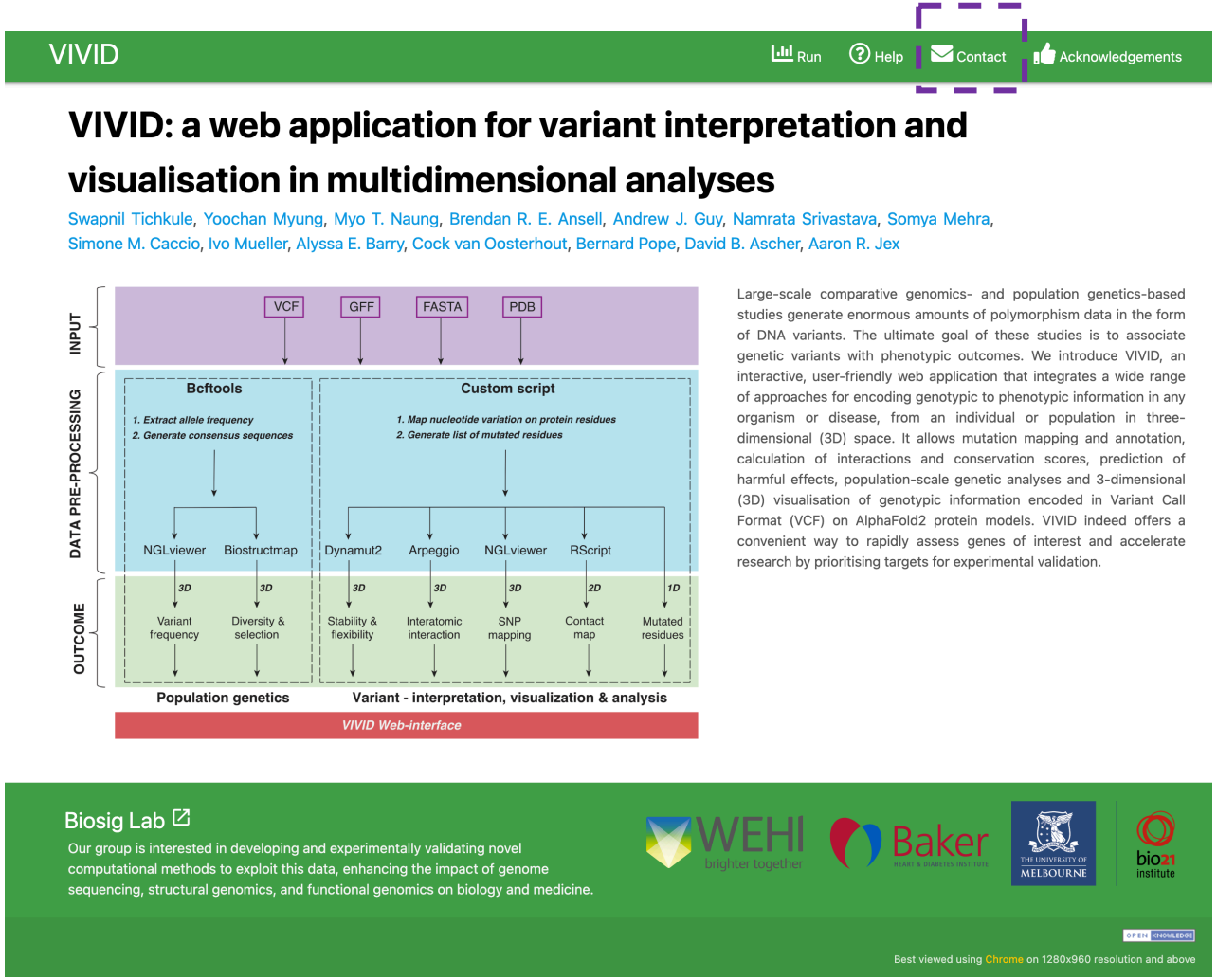



7

# Results

## Download

Users can download results of Dynamut2 $\Delta\Delta G$ values and Arpeggio interactions of substituted protein residues.




# Contact Us

In case you experience any trouble using VIVID or if you have any suggestions or comments, please do not hesitate in contacting us either via **email** or via our **Group website**.

If you are are contacting regarding a job submission, please include details such as input information and the job identifier.