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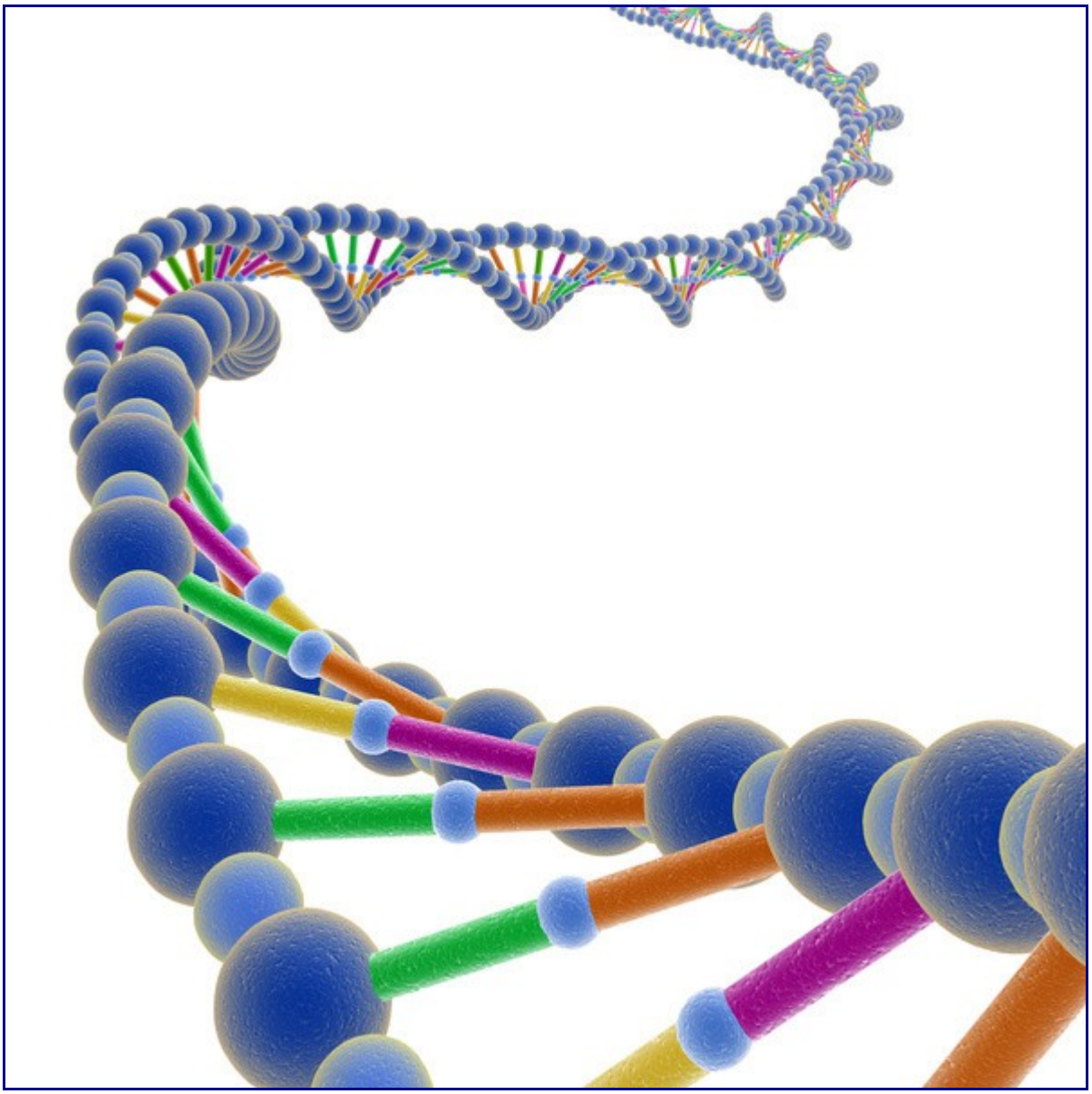
The Brix refers to a database that contains data which refers to protein fragments that may be derived from the residue of the 4-14 placements of non-homologous proteins. This data will be incorporated into the growing peptide spectral library as organization and search data on the topic improves. Currently the Brix database contains 7290 proteins that have been derived from the Astral40 set.

These have been fragmented to different lengths that can range from 4-14 amino acids. These amino acids may also be clustered in six different thresholds that note their distance and/or similarity from the protein backbone where they were derived.

There are very few loops registered in Brix, so to address this issue, Loop Brix was added to the system to help structure non-regular elements. These are organized with clustering of end to end elements and their distance between residues that flank the top of the peptide. Currently the system also encourages user submitted structures to be uploaded so long as they match Brix classes.

This allows for further representation of the variation within this protein. You may also note low confidence regions or gaps in structures that could possibly be matches with other fragments.



Purpose and Analysis

The ability to review high-resolution structures of proteins is considered essential for researchers that are hoping to understand the function of these chemicals.

- An availability of a database which outlines the protein structures of these elements will help researchers to categorize their discoveries regarding the peptide's function within the cell so a path can be paved for future drug design.
- There are several peptide databases available online, including the peptide spectral library, but these venues focus largely on providing a text-based format for peptide analysis while the Brix system will provide interactive three-dimensional models of each fragment. The Brix system also focuses on a specific database which means the data set will be somewhat contained. Other systems have noted issues with slow processing or crashing during function because there is simply too much data to support on one server.
- Currently technology lacks the ability to create sufficient protein structures that would be necessary to replicate backbone moves, so research focuses on using protein fragments within these backbone structures. The Brix database has been specifically designed to categorize the information on these fragments so researchers can determine how best to employ them.

While thousands of these fragments have been established within the Brix system, there is still a great deal of research that must be done to fully establish these peptides as well as noting their functionality. Some researchers are also noting processes where these fragments could be chemically replicated for medical use.

This information can all be loaded to the Brix system so researchers may collaborate on these efforts and avoid wasting resources on portions of a study or studies which have already been successfully accomplished.

The Brix Browsing Interface

In order to maintain a semblance of organization within the database, the Brix library has been developed with two levels where users can collect or deposit data.

- Each portion of the database is filed according to the fragment level or the class level of the given piece of data.
- Fragment levels throughout the system may be sorted by secondary structure, PDB ID or the sequence.
- Classes will be sorted based on the fragment length within the 4-14 residue structure, the class size and the clustering threshold that describes the compactness of this class. The regular expressions of this amino acid sequence, secondary structures that are determined by the DSSP, the sheet, turn, loop and helix content within the structure, may also be used to organize classifications within the class search system.

The class of each fragment also supplied an image of each element with superposed fragments supplied via Chimera. Logos of the structure and sequence and their distributions are also showcased via the Web logo.

The Loop Brix Browsing Interface

To further establish order within this system, the Loop Brix interface will be divided into an additional

three levels.

- Structures may be located given the subclass level of their fragments, noting those that have a similar backbone pattern or length of the structure within the backbone.
- Items are organized via the superclass level noting fragments that have similar end to end distance or contain matching end residues.
- Finally fragments can simply be organized by the fragment level of the structure.

To encourage an easier search mechanism, the Loop Brix database allows the subclass and super classes within the structure to be queried with the same parameters used to organize the Brix database as well as noting the end to end distance of all peptides listed.

This encourages all users to search for structures based on the information that was noted during an experimental session with the understanding that these figures can be very difficult to replicate and the data provided for a given search may be incomplete.

Applying Brix Technology in Research

Any large scale DNA processing will rely heavily on a researcher's ability to sequence large amounts of protein data which means it is essential to have a full understanding of this makeup.

- To understand how a protein functions, it is absolutely essential to develop a full scale 3D model of its performance and structure. Efforts to create such maps have been taken on at a worldwide level, but the experimental protein structures are being determined at a very slow pace, resulting in the need for computational methods for these protein structures.
- Much of the difficulties here lie with the fact that there is simply an issue with size, as proteins appear to have an infinite number of existing size and developmental patterns.
- Research has begun to focus on protein fragments as building blocks to construct the necessary proteins for research. Previous research had indicated that these fragments were unrelated to the final protein structure, but science has further indicated that this was never the case.
- All items that are being used in this field are being loaded into the Brix system, both at the fragmental level and as a shape within the full protein structure.

All items entered into the Brix system can be viewed from any direction in high levels of detail. This encourages scientists to view fragments as individual building blocks or as they react to fragments that interconnect within this structure.

Researchers have already found great use for these mechanisms in determining how to better form protein backbones by taking advantage of this research.

Establishing the Need for a Database

Much like the larger peptide spectral library, there has been a great calling for an interactive database which would allow users to share data regarding protein fragments that are regularly being applied and used in research settings.

- It is generally theorized that peptide based protein interactions constitute as much as 40 percent of total protein interactions. Within the body, there is precious little information concerning the structural details that take place within these interactions.
- Drug designs are beginning to highly focus on the development of peptide mediated interactions with a great deal of research being solely dedicated to this field of study. This is due to the fact that these peptide mediated interactions are predominantly the structures which are present when managing regulatory networks or signaling processes within the body, processes which many therapeutic drugs are designed to interact with.
- The Brix can be used to provide a reliable set of data regarding the non-redundant processes within these complexes and can be designed with increased accuracy.
- Most current models of peptide sequences are based on specific types of interactions that have been noted for a limited protein base with small ligands.
- A recent program, PepX was designed to provide exhaustive data of these protein peptide complexes with unbiased science. This included a data bank that includes lengths stretching to 35 residues. These complexes were also clustered via their binding interfaces while similar peptide databases based their structuring on sequence homology. This allows for the creation of a diverse set of protein peptide interactions that can be widely examined.
- Annotation for these complexes includes a structural and biological information set that will encourage browsing and searching for clusters as well as individual complexes. This will also provide a wider design data set for those that are working with fragment clusters that have been outlined via the Brix database which works alongside the PepX structure.

While these peptides and fragments have long been in use for research and medical applications, technology has only recently grown to the point where it could provide a significant source for an interactive multi-dimensional view of the peptide, which has increased the practicality of such an application.

This makes it significantly more likely that users would be able to apply this data and replicate the

structure of a given protein from its base elements with increased accuracy, thus increasing the likelihood that synthesized versions of such proteins would react in the same biological manner as their naturally produced counterparts.

Direct Application

Analysis of the system has revealed that the Brix is capable of revealing an average of 99 percent of the structural coverage of protein structures with a mean square distance at 1 angstrom.

- At the global level it was revealed that proteins could be reconstructed using this information with accuracy around .48 angstrom. The main structures within these proteins were covered well during replication but loop regions appeared irregular at first. It was later found that there was a reoccurring motif in their structure that offered a lower frequency than those in the regular secondary structures.
- Small elements recurring within the backbone could be used to restructure larger loop regions that were between 4 and 8 residues in length with much success.

Several short sequences have a great deal of structural ambiguity between extended conformations and the alpha helix. As the length of these sequences increases the sequence plasticity could no longer be observed by scientists monitoring this progress. This helps to illustrate the theory that there is context dependency within polypeptide structures.

Bridging and Protein Covering Online

Two algorithms have been applied to the Brix system in order to encourage simplicity for those looking to explore the full size of the library.

- The Loop Brix or Brix system may be analyzed with the bridging or covering system, which will be determined based on the nature of the given query.
- A bridging algorithm search will allow the user to search for fragments using the distance between the pairs of anchoring residues. This can be applied regardless of the backbone coordinates that might be applied to these fragments.
- The covering algorithm is designed to search the backbone coordinates of the input structure so that the user may be paired with any similar fragments that have been noted in the Brix database.

These search mechanisms have been developed for the online version of the database to make it easier for users to coordinate information through a partial search. In many circumstances, the backbone coordinates of a fragment being used or established in a research setting may be unavailable or poorly defined given the parameters of the research at the time.

Loops may also be difficult to derive during research tasks, but these searches would allow users to confirm plausible loops even if the information presented was not accurate enough to sustain a full search within the Brix database.

In addition to providing a high-level browsing interface, the Brix system also contains services that allow for the automation of high querying throughout the database. All information stored within the Brix system or the Loop Brix library may be downloaded through the comma-separated values (CSV) loaded within the system.

This will generally be applied for those searching the system via a specific URL that was provided via

a link from an additional source. However, search queries can also lead to this specific link structure which can be cited or shared with others that may require access to this portion of the database for further collaboration. Regional portions of the Brix database are also available via the SQL portal.

Click here to view our entire PDF research library