PROTEIN ORIGAMI - A PROGRAM FOR THE CREATION OF 3D PAPER MODELS OF FOLDED PEPTIDES

MANUAL

Protein ORIGAMI is a browser-based web application that allows the user to create straightforward 3D paper models of folded peptides for research, teaching and presentations. An amino acid sequence can be turned into α-helices, β-strands and random coils that can be printed out and folded into properly scaled models, with a colour code denoting the biophysical characteristics of each amino acid residue (hydrophobicity, charge, etc.). These models provide an intuitive visual and tactile understanding of peptide interactions with other partners, such as helix-helix assembly, oligomerization, membrane binding, or pore formation. Helices can also be displayed as a helical wheel or helical mesh in 2D graphics, to be used in publications or presentations. The highly versatile programme Protein ORIGAMI is also suited to create less conventional helices with arbitrary pitch (e.g. 3_{10}-helix, π-helix, or left-handed helices). Non-canonical amino acids, labels and different terminal modifications can be defined and displayed at will, and different protonation states can be shown.

CITATION

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ACCESS

Protein ORIGAMI is recommended to be used via the web interface on http://ibg.kit.edu/protein_origami.

A command-line version is also available, installation instructions below.

INSTALLATION FOR USE ON THE COMMAND LINE

The *python* source code for use on the command line can be found on github: https://github.com/sabinereisser/protein_origami. For installation, follow these three steps:

1) Download the package

    git:

    ```
    git clone https://github.com/sabinereisser/protein_origami
    cd protein_origami
    ```

    OR

    wget

    ```
    wget https://github.com/sabinereisser/protein_origami
    /archive/master.zip

    unzip master.zip

    cd protein_origami-master
    ```

2) Run install script and source executable
    ```
    bash install.sh
    . ~/.bashrc
    ```

3) Run program
    ```
    protein_ORIGAMI
    ```

INPUT

WEB INTERFACE

Figure 1: Web interface http://ibg.kit.edu/protein_origami, subpage "Submit sequence". Fields are explained below. Hovering over the blue question mark signs shows help information. Fields are explained below according to the numbers in thre grey circles.

AMINO ACID SEQUENCE (1)

Type the one-letter code of the amino acid sequence. Use capital letters (default) for L-form, small letters for D-form (Caps Lock/Shift key). For use of non-canonical amino acids, use one of the letters B, J, U, X or Z.

Command line option: -s, e.g. `-s "MNLVDIAILILKLIVAALQLLDAVLKYLK"`

N-TERMINAL MODIFICATIONS (2)

Choose N-terminal modification: NH_3^+, formyl (HCO), acyl (R-CO), or None. Default is NH_3^+.

Command line option: -nter NH3/FOR/ACY, e.g. `-nter FOR`

C-TERMINAL MODIFICATIONS (3)

Choose C-terminal modification: COO^- (COO), NH_2 (amidated, NHE), NH-R (lipidated, LIP), or None. Default is COO^-.

Command line option: -cter COO/NHE/LIP, e.g. `-cter NHE`

PH-VALUE (4)

Choose pH range: <=7 (le7) or >=8 (ge8), affects charges of NH_3^+ terminus and histidine. pH <= 7: NH_3^+ charge +1, His charge +1. pH >= 8: NH_3^+ charge 0 (becomes NH_2), His charge 0. Default pH <= 7.

Command line option: -pH le7/ge8, e.g. `-pH le7`

HELIX PITCH (5)

Choose angular pitch in degrees for helix representations. Any value is possible, e.g. α-helix 100°, 3_{10}-helix 120°, π-helix ≈ 87°. Default value is 100°.

Command line option: -pitch VALUE, e.g. `-pitch 100`

REPRESENTATION (6)

Graphical representation of the amino acid sequence.

For 3D paper models, choose "Helix Origami" (helix_origami), "β-sheet" (beta_sheet), or "random coil" (random_coil). Default is "Helix Origami".

For 2D graphics for use in articles or presentations, choose "Helical wheel" (helical_wheel), "Helical mesh horizontal" (helical_mesh_horiz), or "Helical mesh vertical" (helical_mesh_vert).

Command line option: -repres helix_origami/helical_wheel/helical_mesh_vert/helical_mesh_horiz/beta_sheet/ random_coil, e.g. `-repres helical_wheel`

3 OR 1 LETTER CODE (7)

Show amino acid name in standard one or three letter code. Default: 3.

Command line option: -c 1/3, e.g. `-c 3`

COLOR / BLACK AND WHITE (8)

Use colored or uncolored amino acid representations: color or black/white. Default is color.

Colors are:

- yellow - hydrophobic (Ala, Ile, Leu, Met, Phe, Trp, Tyr, Val)
- red - anionic (Asp, Glu, free C-term)
- dark blue - cationic (Arg, Lys, Orn, protonated His, free N-term)
- light blue - polar (Asn, Gln, Ser, Thr, deprotonated His)
- green - structurally special (Cys, Gly, Pro)

Command line option: -cl color/bw, e.g. `-cl bw`

START INDEX (9)

If the peptide is a fragment of a bigger protein, the residue numbering can be adusted by setting a start index. Default 1.

Command line option: -b NUMBER, e.g. `-b 10`

SHIFT GEOMETRY (10)

In the helix representations, the start position can be shifted, e.g. in order to center a region of interest, by setting an integer value. Default is 0. See Figure 5.

Command line option: -sh NUMBER, e.g. `-sh 2`

NAME (11)

The output name of the peptide. It can contain numbers.

Command line option: -n NAME, e.g. `-n mypeptide`

NON-CANONICAL AMINO ACIDS

If the sequence contains non-canonical amino acids, use B, J, U, X or Z in the sequence. If "code" is set to three letters, the three-letter code is asked in a pop-up dialogue. If "color" is set to color, the color is asked in a pop-up dialogue, see Figure 2.
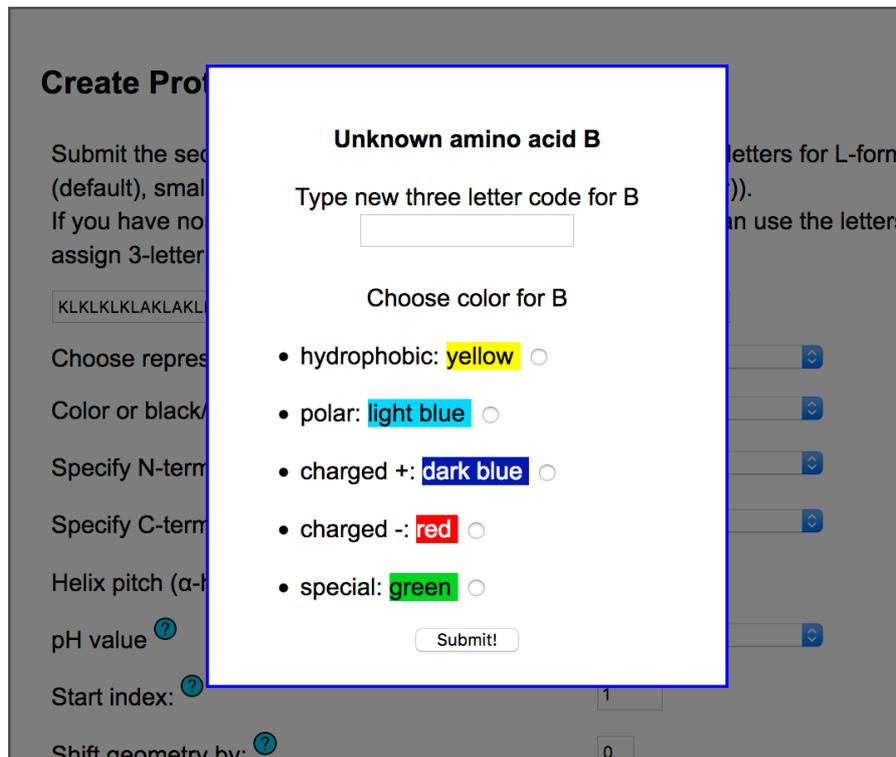

Figure 2: Dialogue for specifiaction of non-canonical amino-acids.

On the command line, the user is prompted to provide information about three-letter code and color.

OUTPUT

Output intendend for 3D paper models ("Helix Origami", "β-sheet", or "random coil") is produced in PDF format. "Helical wheel", "Helical mesh horizontal", or "Helical mesh vertical" are additionally produced in EPS and PNG format.

COMMAND LINE VERSION: CONVERSION WITH INKSCAPE

The command line application produces SVG files, which can be converted with *inkscape* (inkscape.org) to PDF or PNG

- via the graphical interface:

    File -> Save as (Select PDF; always for 3D paper models)

    File -> Export PNG Image

- via the command line:

    PDF fromat (seperately for each *_1.svg *_2.svg etc., when creating 3D paper models):

    ```
    inkscape name_1.svg -A name_1.pdf
    ```

    PNG format

    ```
    inkscape name.svg -e name.png -D -b white -d 300
    ```

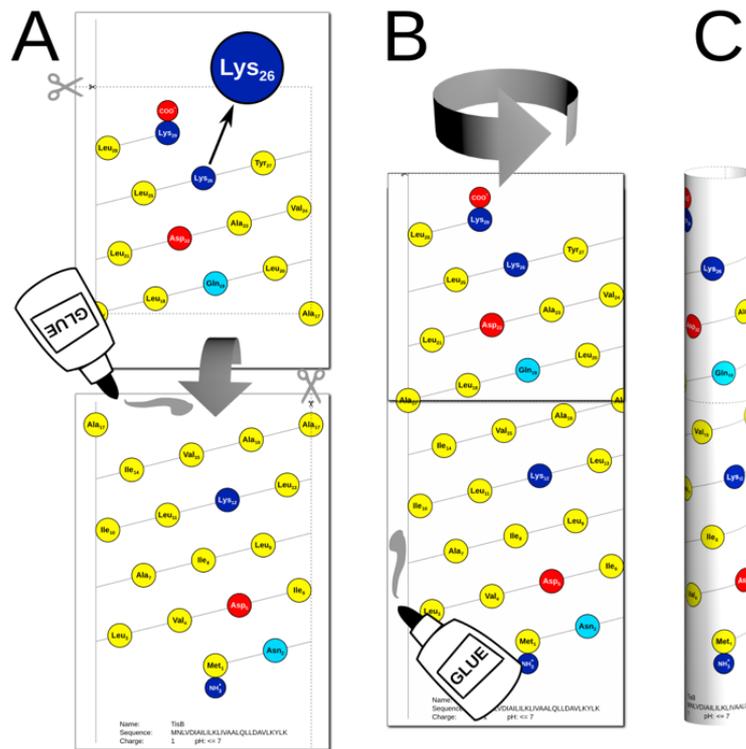   -d is the option for dpi, if you want higher quality, increase

Figure 3: Assembly of 3D Protein ORIGAMI model of an α-helix, as illustrated here for the amphipathic peptide TisB (1). First, the helix mesh representation is printed out on paper (Lys-26 is zoomed in to illustrate the 3-letter code and numbering). If the peptide is too long to fit on one page, additional pages have to be cut and glued together (A). Rolling up the sheet(s) along the long axis and gluing (B), a 3D peptide model is created (C). Residues are represented by circles that are color-coded according to the type of side chain: yellow - hydrophobic, red - anionic, dark blue - cationic, light blue - polar, green - special.

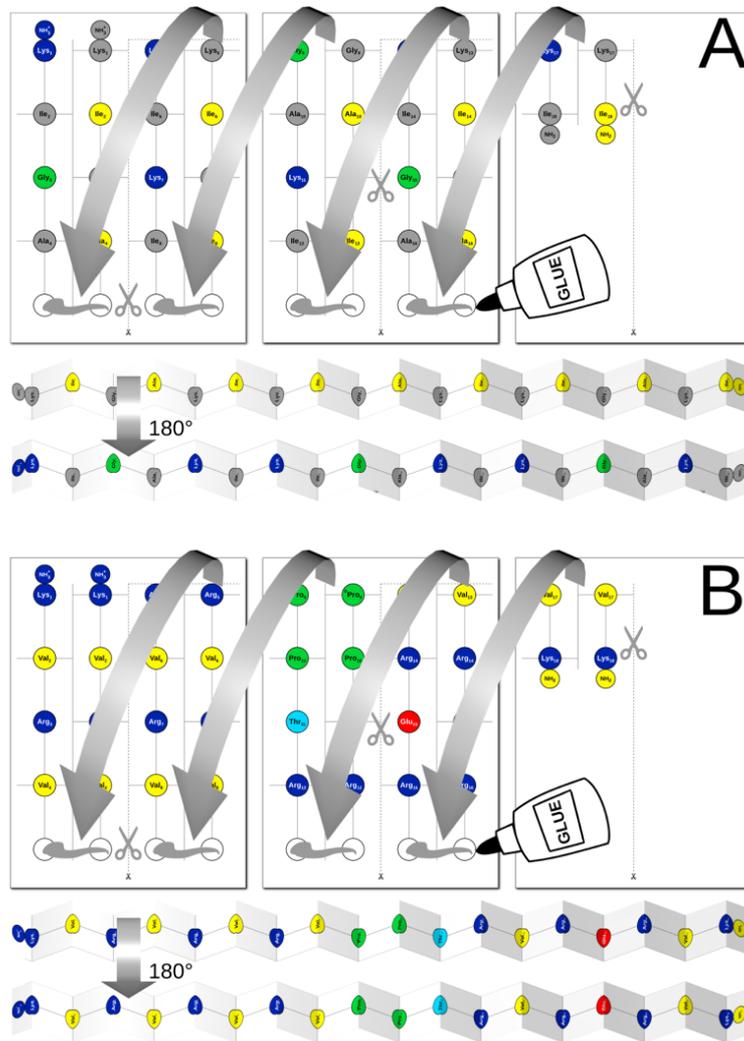Command line: `protein_ORIGAMI -n TisB -s "MNLVDIAILILKLIVAALQLLDAVLKYLK" -sh 2`

Figure 4: (A) Building a 3D Protein ORIGAMI model of a β-strand, as illustrated here for the amphiphilic peptide [KIGAKI]$_3$ (2–4). Upon gluing and folding into a double-sided zig-zag ribbon, all hydrophobic side chains are seen in yellow on one side (upper 3D model), while all charged side chains point to the other face in their respective color (bottom 3D model). On each face of the extended β-strand, every second "invisible" amino acid is indicated in grey. Several such β-strands can be assembled side-by-side into a β-sheet (not shown). (B) Random coil representation of an intrinsically disordered sequence, as illustrated here for the cell-penetrating peptide CLIP6 (5). In this case, the flexible chain of amino acids is represented in color on both sides of the extended paper strip.

Command line (A): `protein_ORIGAMI -s "KIGAKIKIGAKIKIGAKI" -cter NHE -repres beta_sheet -n KIGAKI`

Command line (B): `protein_ORIGAMI -s "KVRVRVRVpP TRVRERVK" -cter NHE -repres random_coil -n CLIP6`
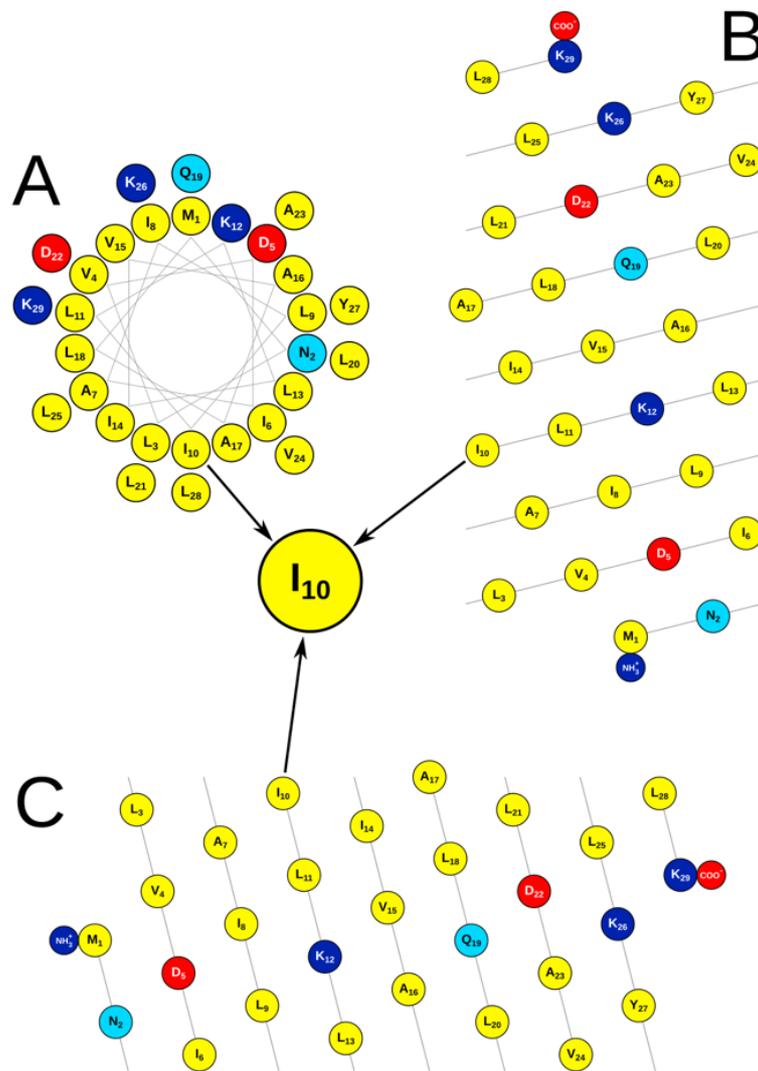
Figure 5: 2D graphics are used to illustrate helical peptides, as shown for the amphipathic peptide TisB (1). Ile-10 is zoomed in to illustrate the standard 1-letter code and numbering. (A) Helical wheel representation, (B) helix mesh vertical, (C) helix mesh horizontal. Residues are represented by circles that are color-coded according to the type of side chain: yellow - hydrophobic, red - anionic, dark blue - cationic, light blue - polar, green - special. (B) and (C) are generated with *shift geometry = 2* to move the polar strip (red, light blue and dark blue amino acids) into the figure center.

Command line (A): `protein_ORIGAMI -n TisB -s "MNLVDIAILILKLIVAALQLLDAVLKYLK" -c 1 -repres helical_wheel`

Command line (B): `protein_ORIGAMI -n TisB -s "MNLVDIAILILKLIVAALQLLDAVLKYLK" -c 1 -repres helical_mesh_vert -sh 2`

Command line (C): `protein_ORIGAMI -n TisB -s "MNLVDIAILILKLIVAALQLLDAVLKYLK" -c 1 -repres helical_mesh_horiz -sh 2`

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