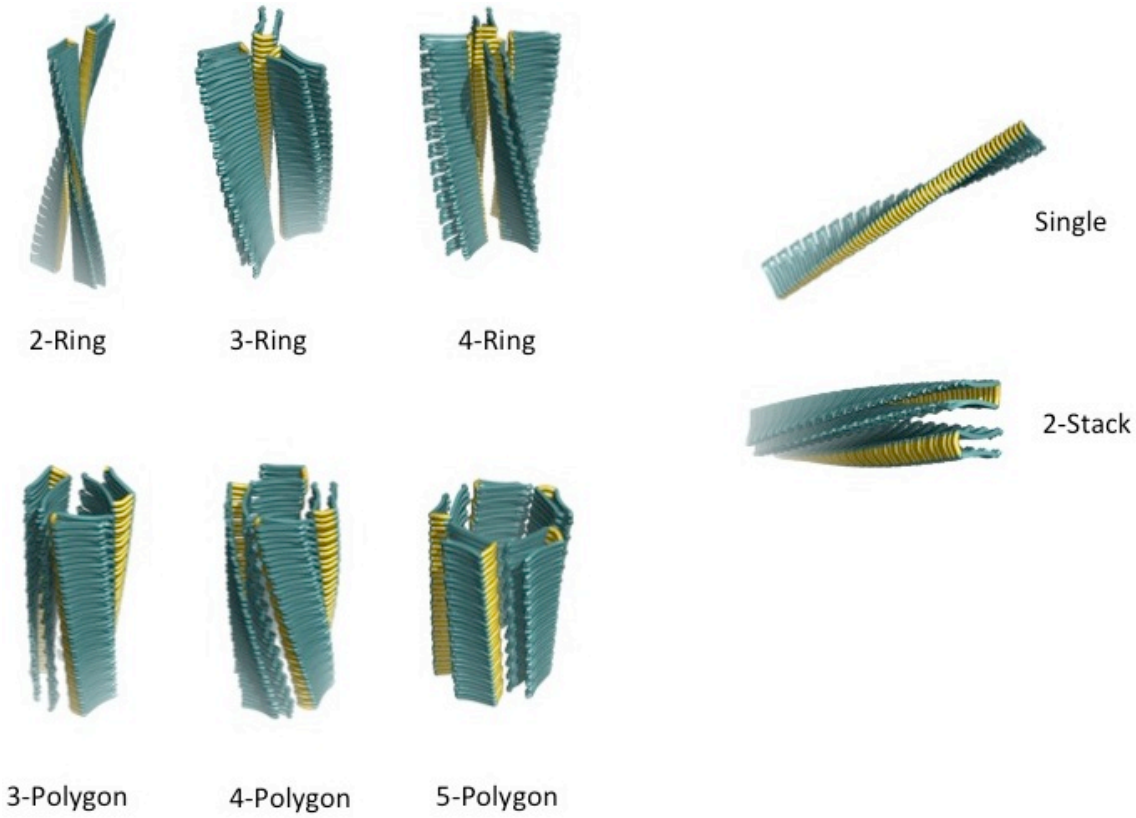
CreateFibril v 2.5 (released on Feb. 11th, 2015)

About

CreateFibril is a tool to build atomic resolution models of protein fibrils. Starting with the PDB file of an amyloid structure, one can specify the structural parameters needed to build polymorphic fibrils. H-bond distances specify the distances in angstroms between aggregated monomers on a fibril, rotation angels specifies the fibril twist in degrees, and the polymorphism type selects the number and orientation of the filaments making up the fibril. The tool helps you create amyloid structures that belong to the Single, Stack and Ring classes in the figure below:



Citation:

When citing this tool in any scientific publication please refer to it as:

Smaoui, Mohamed Raef, et al. "Computational Assembly of Polymorphic Amyloid Fibrils Reveals Stable Aggregates." *Biophysical journal* 104.3 (2013): 683-693.

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Usage & Examples

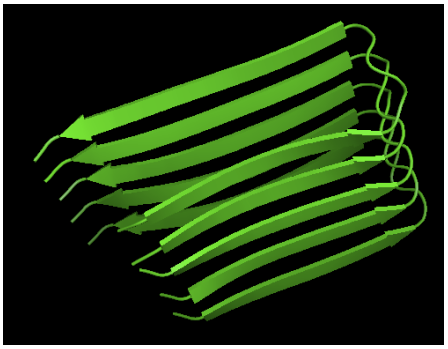
CreateFibril is written in python. Download the CreateFibril.zip file and unzip it anywhere in your file system.

EXAMPLE 1: Single Fibrils

Use the 2BEG.pdb file to create a long amyloid fibril of 15 monomers in length

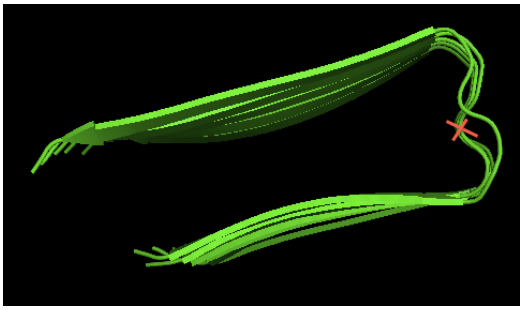
Step 1:

Dowload the 2BEG.pdb file from http://pdb.org. The 2BEG.pdb file contains 10 models of the protein. We only need 1 model. Delete models 2-10 from the file and delete all records that do not start with ATOM. The following image is the 2BEG.pdb file viewed in PyMOL



Step 2:

We are now left with a PDB file that contains an amyloid of 5 monomers. We will extend this to the required 15 monomers of length. To do this, we first need to find a fibril axis that the amyloids would extend on. Viewing the 2BEG.pdb file in a tool like PyMOL suggests that the fibril axis could be somewhere close to point X in the following image:



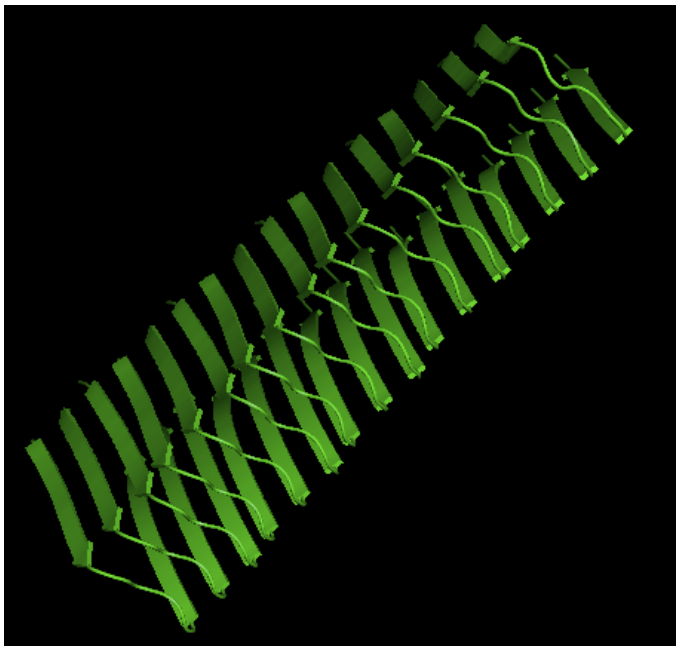
This point is located on the CA atom of residue 28 and has the following x,y,z coordinates: 14.389,-1.077,-4.250

STEP 3:

We know that amyloid structures rotate slightly about the fibril axis as they aggregate, and we know that they aggregate roughly 4 angstroms apart. We will use this knowledge to build our structure. To that we will call CreateFibril with the following parameters:

```
python ./CreateFibril.py -f 2BEG.pdb -c 2,4 -r 5 -d 4 -a 5 -fp 14.389,-
1.077,-4.250,28 -nr 26
```

This would create a file in the CreateFibril directory called: 2BEGr5c24d4.0a5.0.pdb and produces the following aggregate structure:



The **–f** parameter is the input filename, -**c 2,4** selects chains B,C,D from the PDB file to replicate and extend the aggregation of the amyloid. **–r 5** tells the program to replicate the selected chains (in this case B,C,D) 5 times, **-a 5** is the rotation angle of the monomers as they aggregate (5 degrees), **-nr 26** is the total number of residues (amino acids) in the 2BEG protein. Finally, the **-fp 14.389,-1.077,-4.250,28** is the x,y,z,residue point where the fibril axis passes (we found this in Step 2).

EXAMPLE 2: Building Ring Structures

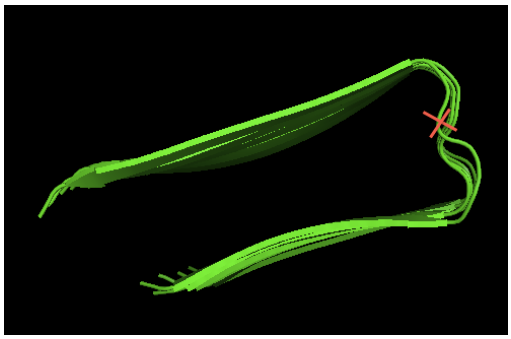
We will use the same 2BEG.pdb file that we experimented with in Example 1. We will create 2-Ring, 3-Ring and 4-Ring structures in this example

STEP 1:

We will use the same fibril axis that we explored in Example 1 Step 2: The point where the fibril axis passes through is located on the CA atom of residue 28 and has the following x,y,z coordinates: 14.389,-1.077,-4.250

STEP 2:

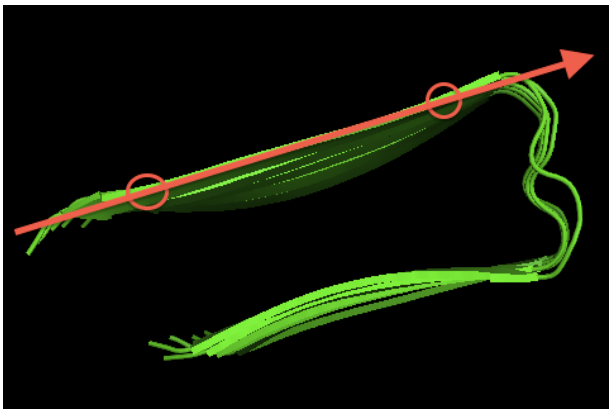
We need to specify the Head Point of a ring structure. This is the point that is located on the center of the ring region in an amyloid. It is marked with a red X in the image below:



The x,y,z coordinates of this point are 14.834,0.339,1.376

STEP 3:

We need to specify a strand vector that determines the direction of the Ring structures as they aggregate. We can pick 2 points to specify this strand, as shown in the following image:



These 2 points are 10.818,5.058,0.948 and -11.850,5.695,2.729

STEP 4

We can now call the CreateFibril program by the following command:

```
python ./CreateFibril.py -f 2BEG.pdb -c 2,4 -r 5 -d 4 -a 5 -fp 14.389,-
1.077,-4.250,28 -Ring 2 -Radius 6 -nr 26
```

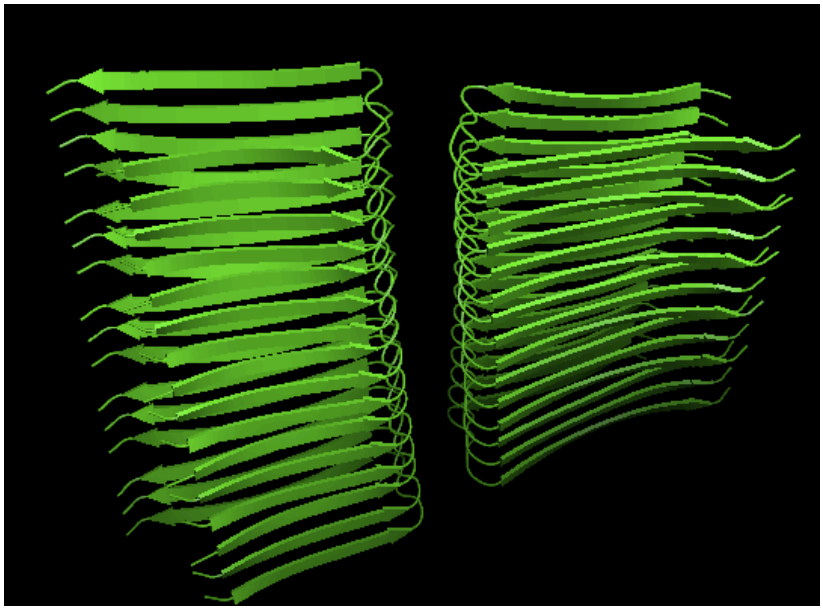
This now specifies that we want to create a Ring structure with 2 protofilaments that are 6 angstroms apart from one another (Radius). The program will then ask for 3 additional fields:

```
python ./CreateFibril.py -f 2BEG.pdb -c 2,4 -r 5 -d 4 -a 5 -fp 14.389,-1.077,-4.250,28 -Ring 2 -Radius 6 -nr 26

*******************************
CreateFibril will build a Ring structure. Please specify the following parameters:

Enter head point of ring structure (Point on the curve of the amyloid) x,y,z: 14.834,0.339,1.376
Enter point1 of strand vector x,y,z: 10.818,5.058,0.948
Enter point2 of strand vector x,y,z: -11.850,5.695,2.729
```

This creates the following PDB file:



STEP 5:

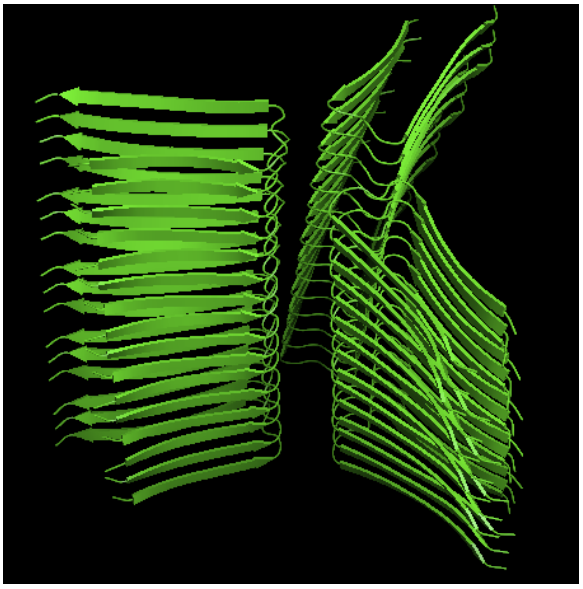
We can also create a Ring structure with 3 or 4 protofilaments. Following the same procedure as in STEP 4 we call:

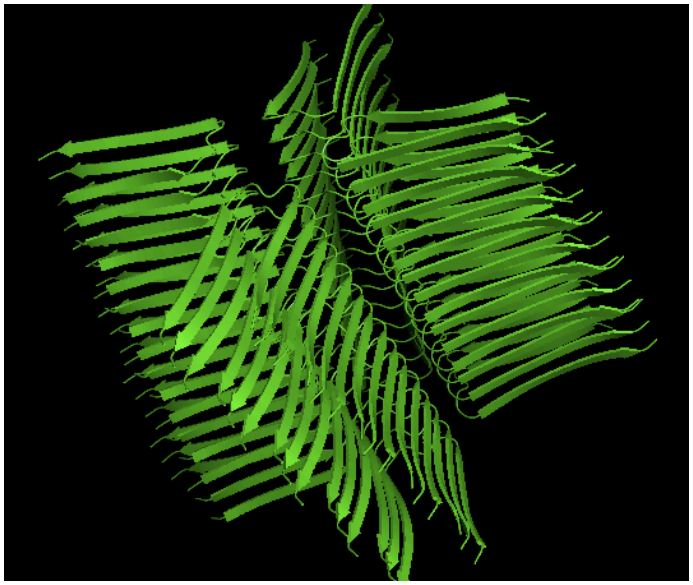
```
python ./CreateFibril.py -f 2BEG.pdb -c 2,4 -r 5 -d 4 -a 5 -fp 14.389,-
1.077,-4.250,28 -Ring 3 -Radius 10 -nr 26
```

and

```
python ./CreateFibril.py -f 2BEG.pdb -c 2,4 -r 5 -d 4 -a 5 -fp 14.389,-
1.077,-4.250,28 -Ring 4 -Radius 12 -nr 26
```

to produce the following 2 PDB structures





EXAMPLE 3: Building Polygon Structures

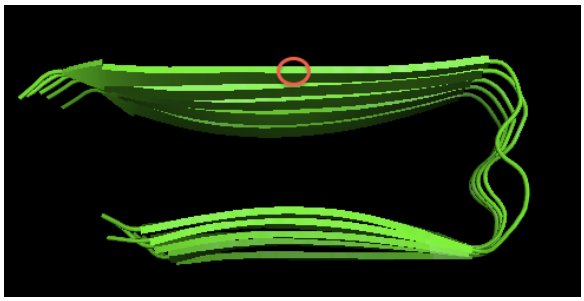
We will use the same 2BEG.pdb file that we experimented with in Examples 1 and 2. We will create 2-Polygon, 3-Polygon and 4-Polygon structures in this example.

STEP 1:

We will use the same fibril axis that we explored in Example 1 and 2: The point where the fibril axis passes through is located on the CA atom of residue 28 and has the following x,y,z coordinates: 14.389,-1.077,-4.250

STEP 2:

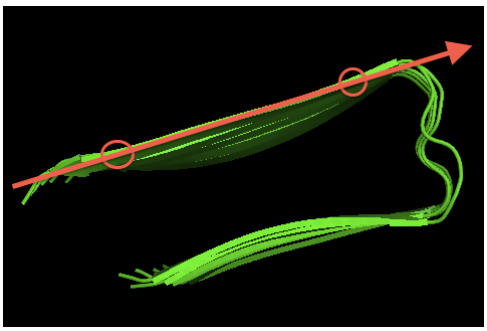
We need to specify the mid Point of a beta strand that will face other strands in the Polygon structure. It is marked with a red oval in the image below:



The x,y,z coordinates of this point are -2.010,4.594,1.850

STEP 3:

As in Example 2, we need to specify a strand vector that determines the direction of the Polygon beta strands. This will be used to in a vector cross product to determine how to place the other protofilaments (It is not necessary that you understand what it does, it's only necessary to provide it to the program). We can pick 2 points to specify this strand, as shown in the following image:



These 2 points are 10.818,5.058,0.948 and -11.850,5.695,2.729

STEP 4

We can now call the CreateFibril program by the following command:

```
python ./CreateFibril.py -f 2BEG.pdb -c 2,4 -r 5 -d 4 -a 5 -fp 14.389,-
1.077,-4.250,28 -Polygon 2 -Radius 15 -nr 26
```

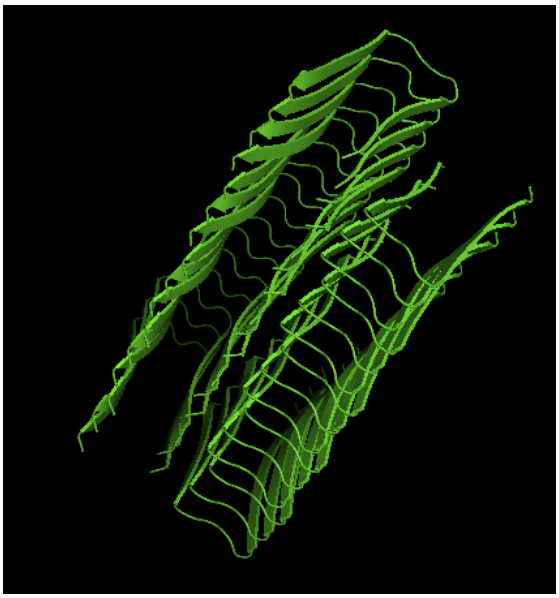
This now specifies that we want to create a Polygon structure with 2 protofilaments that are roughly 15 angstroms apart from one another (Radius). The program will then ask for 3 additional fields:

```
python ./CreateFibril.py -f 2BEG.pdb -c 2,4 -r 5 -d 4 -a 5 -fp 14.389,-1.077,-4.250,28 -Polygon 2 -Radius 15 -nr 26

******************************
CreateFibril will build a Polygon structure. Please specify the following parameters:

Enter mid point of polygon structure (Point on the center of the facing strand) x,y,z: -2.010,4.594,1.850
Enter point1 of strand vector x,y,z: 10.818,5.058,0.948
Enter point2 of strand vector x,y,z: -11.850,5.695,2.729
```

This creates the following PDB file:



STEP 5:

We can also create a Polygon structure with 3 or 4 protofilaments. Following the same procedure as in STEP 4 we call:

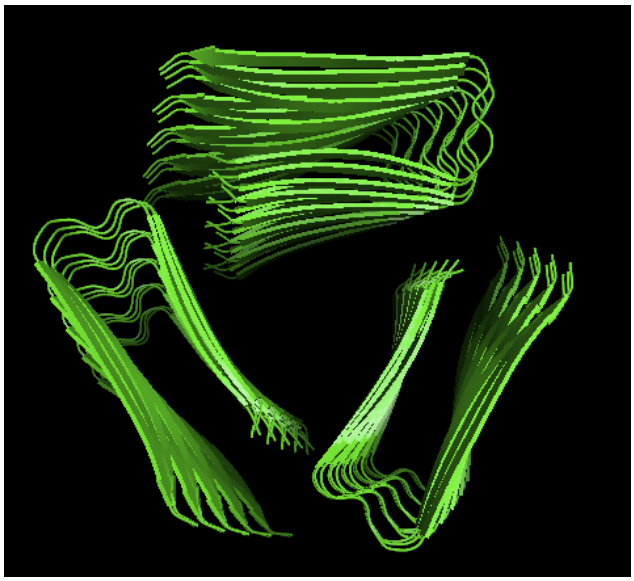
```
python ./CreateFibril.py -f 2BEG.pdb -c 2,4 -r 5 -d 4 -a 5 -fp 14.389,-
1.077,-4.250,28 -Polygon 3 -Radius 25 -nr 26
```

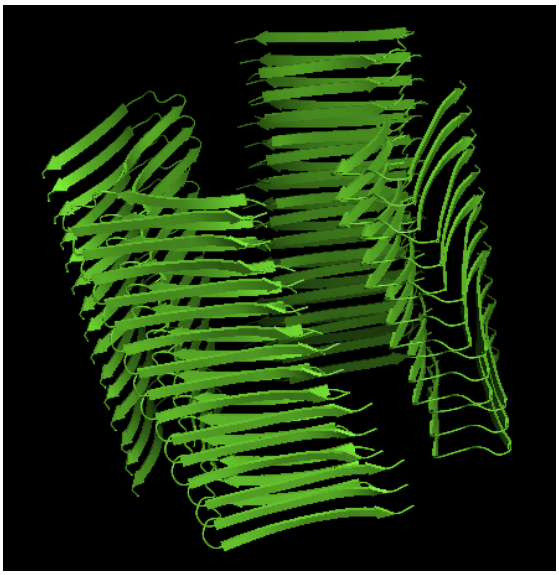
and

```
python ./CreateFibril.py -f 2BEG.pdb -c 2,4 -r 5 -d 4 -a 5 -fp 14.389,-
```

```
1.077,-4.250,28 -Polygon 4 -Radius 15 -nr 26
```

to produce the following 2 PDB structures





Keep in mind that the distance (-d) and rotation angle (-a) parameters might need to be tweaked for different polymorphs to build more accurate structures.