Contents

Introduction:

The Bioreactor handbook is a supplement to the software that we made. Most iGEMers may not be familiar with Reactor design term and this handbook was curated to be quick guide to reactor design. To the best of our capabilities, we have described various parts of a reactor like impellers, tanks and more so that future iGEM teams can design their own reactor without experience with Mechanical design.

Modelling Software

CAD Modelling:

CAD modelling enables the user to generate, create and visualize their Designs. In this handbook we're going to be using CAD softwares to design and simulate the Bioreactor. The Choice of modelling softwares we can use is fairly abundant.

Most Softwares are free for students to use for the term of their Education, under an education/student license, The software we'll be using here are Fusion360, but you're free to use whatever software you're comfortable with, The CAD software just needs to be able to export the model in the format of an .STEP or .STP file, For those who require a free or open-source CAD software, FreeCAD is an excellent Alternative.

Design Rules

Types of Reactors

- **Batch Reactor**
  It is the simplest type of reactor where the materials are loaded in and the reaction/fermentation/growth proceeds over time. The construction of the batch reactor (agitator/mixing tank) includes a tank, an impeller for mixing, a

shaft and a few baffles to promote better mixing characteristics. This type of reactor is generally used for small-scale production.

- **CSTR (Continuous Stirred Tank Reactor)**
  While following a similar construction of a typical batch reactor, this reactor includes an additional feature. This type of reactor allows for a continuous operation in place of a transient operation like we see in a batch reactor. This allows for a larger production volume and easier scalability.

- **PFR (Plug Flow Reactor)**
  PFRs are generally used in enzymatic reactions. The reaction mixture is generally pumped into the reactor on one end and the reaction proceeds as a function of distance from the entry, hence forming a gradient of concentrations across the length of the reactor. This type of reactor is generally not used as bioreactors, but can be adapted to function in certain cases.

- **Semi-Batch or Fed-Batch reactor**
  This type of reactor follows similar construction to the Batch Reactor, but allows a continuous input or output of material. It is generally used to feed the reaction mixture with fresh material or to purge unwanted or inert reactants (like Carbon Dioxide).
  It has all the added benefits of a Batch reactor but has expanded capabilities due to the ability to add or remove materials whenever necessary.

- **Catalytic reactor**
  A derivative of the PFR, it follows similar construction rules, while including catalysts to facilitate the reaction. This reactor is designed with surface area and flow rate to ensure maximum residence time in the reactor to facilitate maximum contact and time for the reaction to proceed in the presence of a catalyst. Naturally, due to the added functionality, this type of reactor is highly specific to the reaction and requires extensive design.

Types of Tanks

- **Flat bottom**
  It is the most common type of reactor bottom, due to its ease of design and manufacturing. Although quite simple to make and use, the design might lead to poor drainage at the end of the reaction cycle. In a CSTR, it might lead to dead spots (locations where the flow velocity is zero).

- **Dished Bottom**
  Dished bottom are rounded tank bottoms. They are generally used in pressurised mixing tanks. There are 3 common types of dished bottom tanks:

  1) 2:1 Elliptical
  2) ASME 80:10
  3) Standard Flanged or dished bottom

  Tanks with dished bottoms generally improve on the structural rigidity, hence allowing for pressurized operation of the mixing tank. The rounded bottom improves drainage capability and also offers higher solid suspension performance when compared to a cone bottom (with the exception of a 2:1 elliptical design).
  This type of tank bottom increases the tank height, hence requiring a longer shaft for the impeller. The 2:1 Elliptical type decreases solid suspension characteristics, hence might require a complex impeller design (kicker or tickler impeller).

- **Sloped Bottom**
  As the name suggests, this tank features a sloped bottom, allowing for a good drainage performance without the large tradeoffs of a cone bottom.
  Although it's easier to construct compared to a Dished bottom or Cone bottom, it suffers from poor solid suspension capabilities as the depth increases due to the slope. This type of tank also complicates impeller and shaft design due to the slope bottom.

- **Cone Bottom**
  As the name implies, this tank uses a cone bottom to provide excellent drainage for high solid content slurries. The loss of product during drainage is miniscule. With all its perks, this design suffers from a lot of complications, starting with poor solid suspension performance, increased fluid stall, higher chances of stratification, large temperature gradients and radial flow. The increased shaft length due to the bottom type also adds to the total cost and design complications of this tank. Typically, this tank is not used for solid concentration above 5%.

Impeller Design

- **Flow Characteristics**

The impellers are also classified according to the flow pattern i.e. axial flow and radial flow. Axial flow discharge coincides with the axis of the impeller shaft, so when the impeller operates in a down pumping mode, the flow impinges on the bottom of the tank and spreads out in all directions toward the wall. The flow rises along the walls up the liquid surface and is pulled back to the impeller. Since axial flow impellers produce only one loop, fluids mix faster and blend time is reduced compared to radial flow impellers. The fluid does not take sharp turns near impellers and because of this, power consumption is less than that of radial flow impellers at the same speed and same diameter.
Radial Flow Radial Flow discharge is parallel to the impeller radius toward the vessel wall. If a radial impeller is not positioned close to the surface or the tank bottom, the flow will split into two streams upon impinging on the tank wall. Each flow loop will continue along the wall and then return to the impeller.

Once you've made the choice use these particular equations to figure out the values.

$$\frac{Z_L}{D_T} = 1 \qquad \frac{D_I}{D_T} = \frac{1}{3}$$

$$\frac{W}{D_T} = \frac{1}{10} \qquad \frac{Z_I}{D_I} = 1$$

$$\frac{D_d}{D_I} = \frac{3}{4} \qquad \frac{I}{D_I} = \frac{1}{4}$$

$$\frac{b}{D_I} = \frac{1}{5} \qquad \frac{m}{D_T} = \frac{1}{5}$$

where:

Z_L = Static liquid depth
D_T = Tank diameter
D_I = Impeller diameter
Z_I = Impeller distance from tank bottom
W = Baffle width
D_d = Impeller disc diameter
I = Impeller blade length
b = Impeller blade width
H_T = Tank height
m = Baffle tip distance from tank bottom

- % of Diameter
  Typically Around 30% of the tank diameter, This value is just enough for agitation of the fluid.
  - Rushton
    This type of impeller is typically used for Radial flow in Microbial applications

  - Pitch Blade
    If your use case is Shear sensitive then Pitch blade impellers are a great choice,promoting Axial Flow

  - Helical
    For High viscosity applications a Helical blade works best promoting distributed flow

Tank Design

- **AERATION SYSTEM (SPARGER)**

Sparger is a device for introducing air into the fermenter. Aeration provides sufficient oxygen for organisms in the fermenter. Fine bubble aerators must be used. Large bubbles will have less surface area than smaller bubbles which will facilitate oxygen transfer to a greater extent. Agitation is not required when aeration provides enough agitation which is the case with the Air lift fermenter. But this is possible only for mediums with low viscosity and low total solids. For aeration to provide agitation the vessel height/diameter ratio (aspect ratio) should be 5:1. Air supply to sparger should be supplied through a filter.

The sparger's function is to provide proper aeration to the media for optimum growth of microorganisms. There are mainly three kinds of spargers and one type combining features of all three.
1. Porous sparger
2. Orifice sparger
3. Nozzle sparger

1. Porous sparger: made of sintered glass, ceramics or metal. It is used only in lab scale-non agitated vessels. The size of the bubble formed is 10-100 times larger than pore size. There is a pressure drop across the sparger and the holes tend to be blocked by growth which is the limitation of porous sparger.
2. Orifice sparger: used in a small stirred fermenter. It is a perforated pipe kept below the impeller in the form of crosses or rings. The size should be ~ ¾ of impeller diameter. Air holes drilled on the under surfaces of the tubes and the holes should be atleast 6mm diameter. This type of sparger is used mostly with agitation. It is also used without agitation in some cases like yeast manufacture, effluent treatment and production of SCP.
3. Nozzle sparger: Mostly used on a large scale. It is a single open/partially closed pipe positioned centrally below the impeller. When air is passed through this pipe there is lower pressure loss and does not get blocked.
4. Combined sparger agitator: This is air supply via hollow agitator shaft. The air is emitted through holes in the disc or blades of the agitator.

Baffle Design/size

Baffles are metal strips that prevent vortex formation around the walls of the vessel. These metal strips attached radially to the wall for every 1/10th of vessel diameter. Usually 4 baffles are present but when the vessel diameter is over 3dm3 around 6-8 baffles are used. There should be enough gap between wall and baffle so that scouring action around the vessel is facilitated. This movement minimizes microbial growth on baffles and fermentation walls. If needed cooling coils may be attached to baffles.

- % of Diameter
- Flat Baffle
- Helical Baffle

Design equations of our agitator

1. Actual gas flow rate: Qg=(3.14/4)*D^2.0. (V_o)

2. Flooding condition :

$$Qg < 0.6 \left[\frac{N^2 D_i^5}{D_T^{1.5}} \right]$$

3. Reynolds Number

$$N\,Re = \frac{D_i^2 . \rho . N}{\mu}$$

4. Aeration number:

$$NA = \frac{Qg}{N D_i^3}$$

5. Power

$$P = 2 \times NP \times \rho \times N^3 \times D_i^5$$

6. Power Number

$$NP = 4 + \frac{1}{NRe}$$

7. Gassing Factor

$$\frac{Pg}{P} = 2.1\times10^{3}.NA^{4} - 1.1\times10^{3}.NA^{3} + 2.2\times10^{2}.NA^{2} - 19NA + 1$$

8. Hold-up:

$$\phi = \frac{V_G - V_L}{V_G} = 1.8\,[\tfrac{Pg}{\rho V}]^{0.14}\ V_0^{\ 0.75}$$

9. Gassed volume:

$$VG = V/(1 - \phi)$$

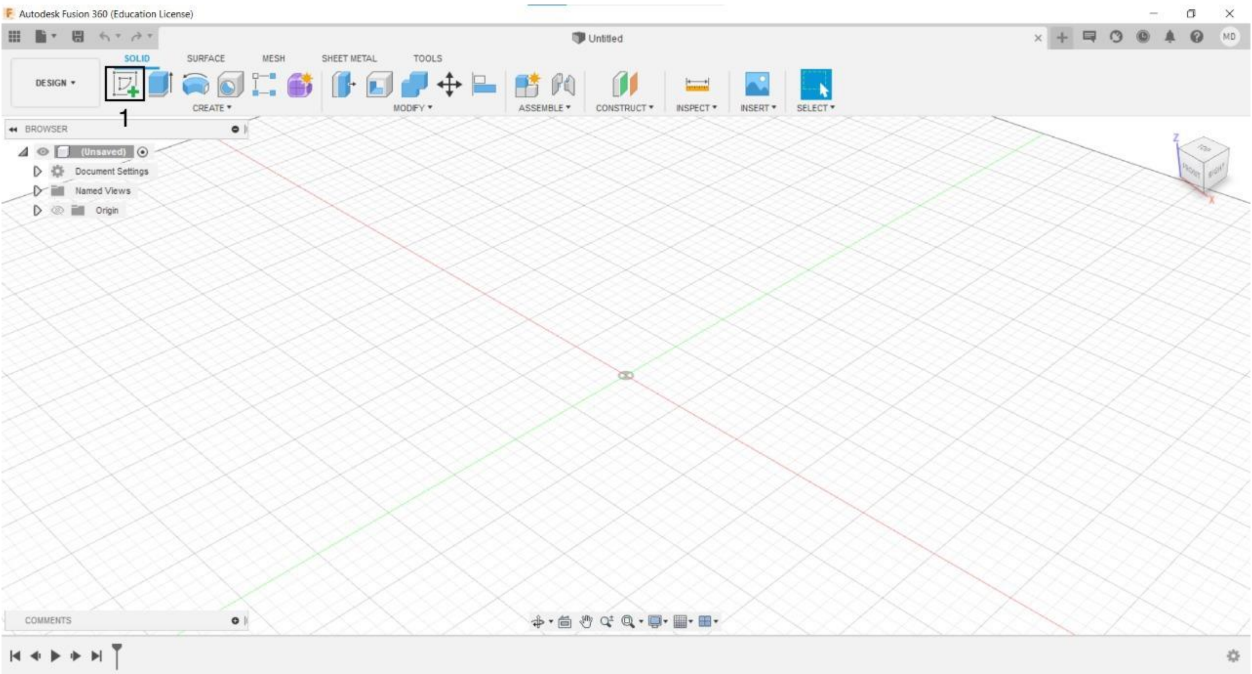
10. Height of the Bioreactor:

$$H^{*} = \frac{4V_G}{\pi D_T^2}$$

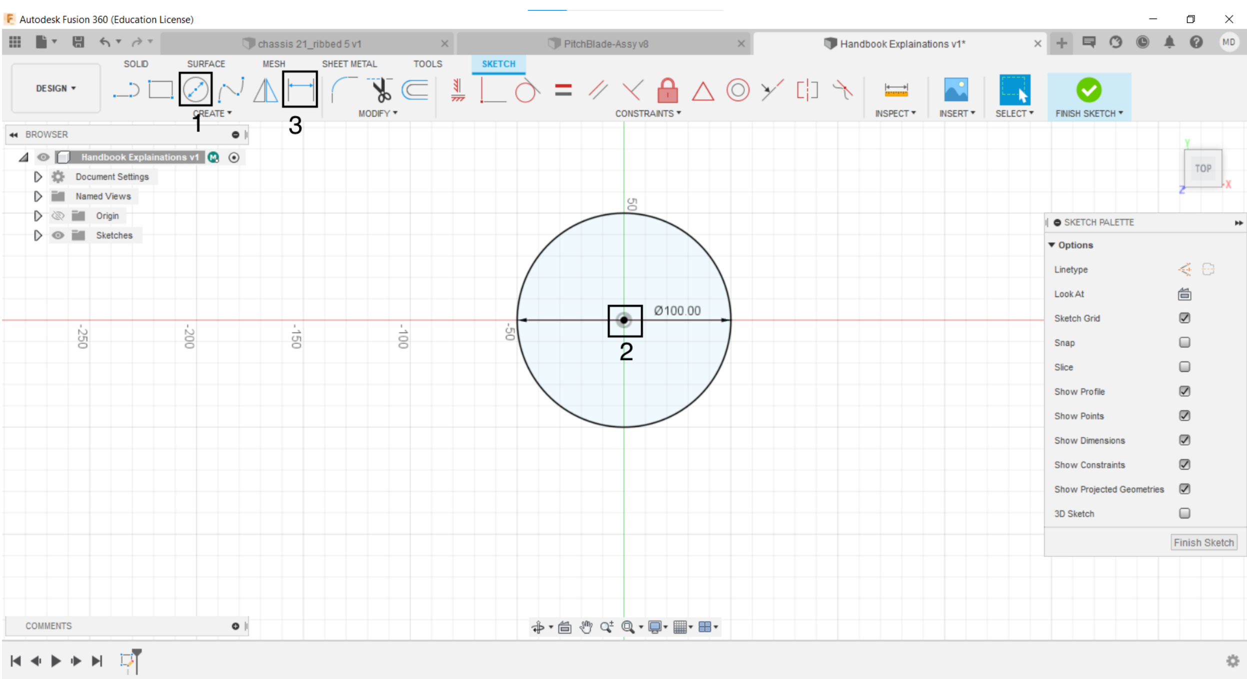
11. Height of the Bioreactor with 10% head space:

$$H_L^{11} = 1.1 \ \text{x}\ H^{*}$$

Making the Model:

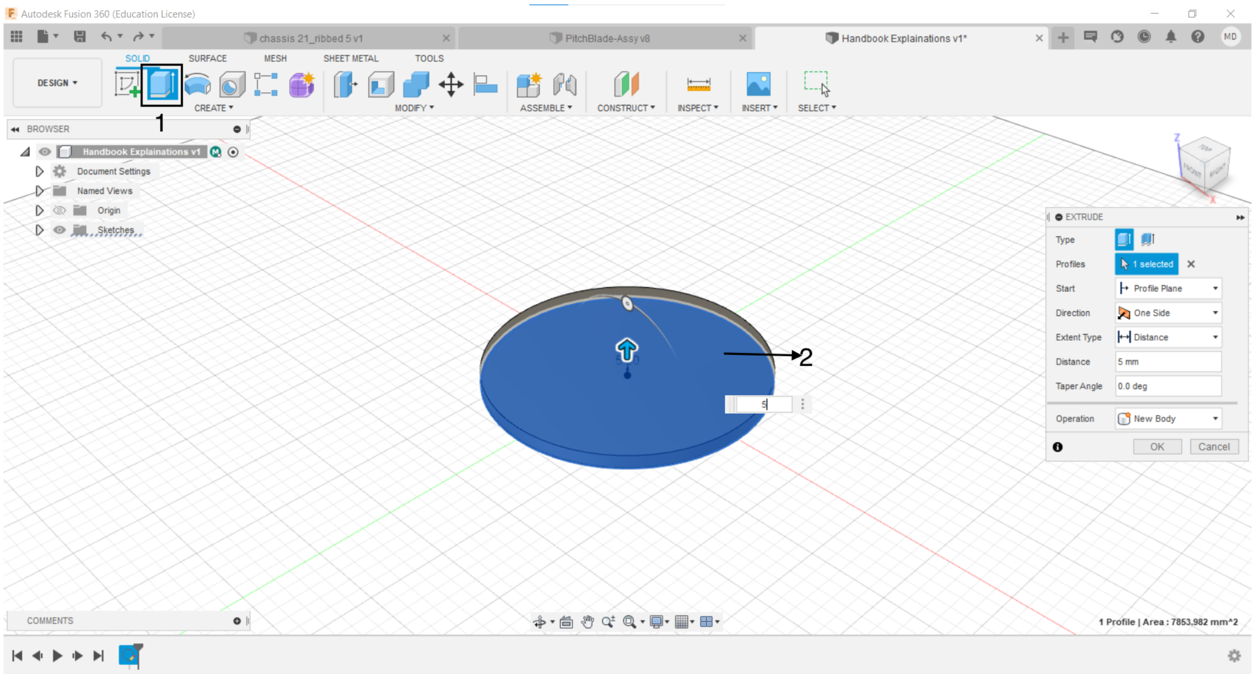


1 - Start off by clicking on the sketch option, this will give you the option of selecting a plane to sketch on



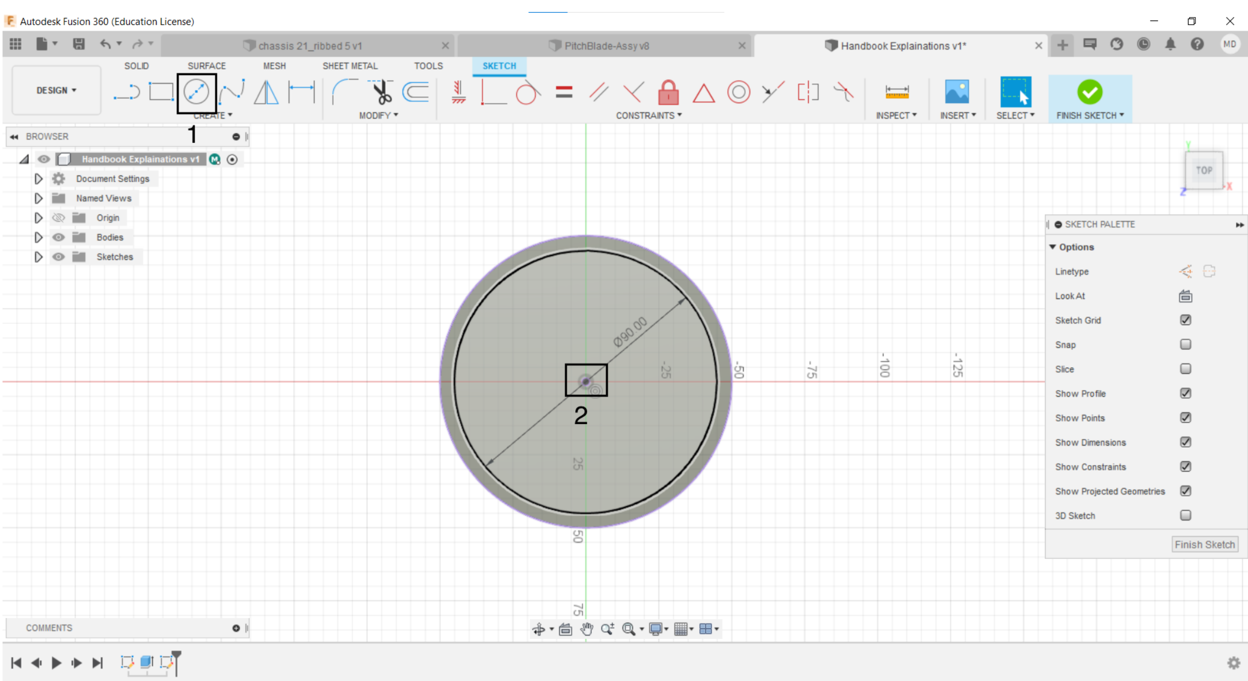
2 - Making a Circle

1. Click on the Circle Option labeled as 1 and select the center of the of the circle on the center of the page
2. Click on the dimension option and type in the value of radius or diameter of the circle



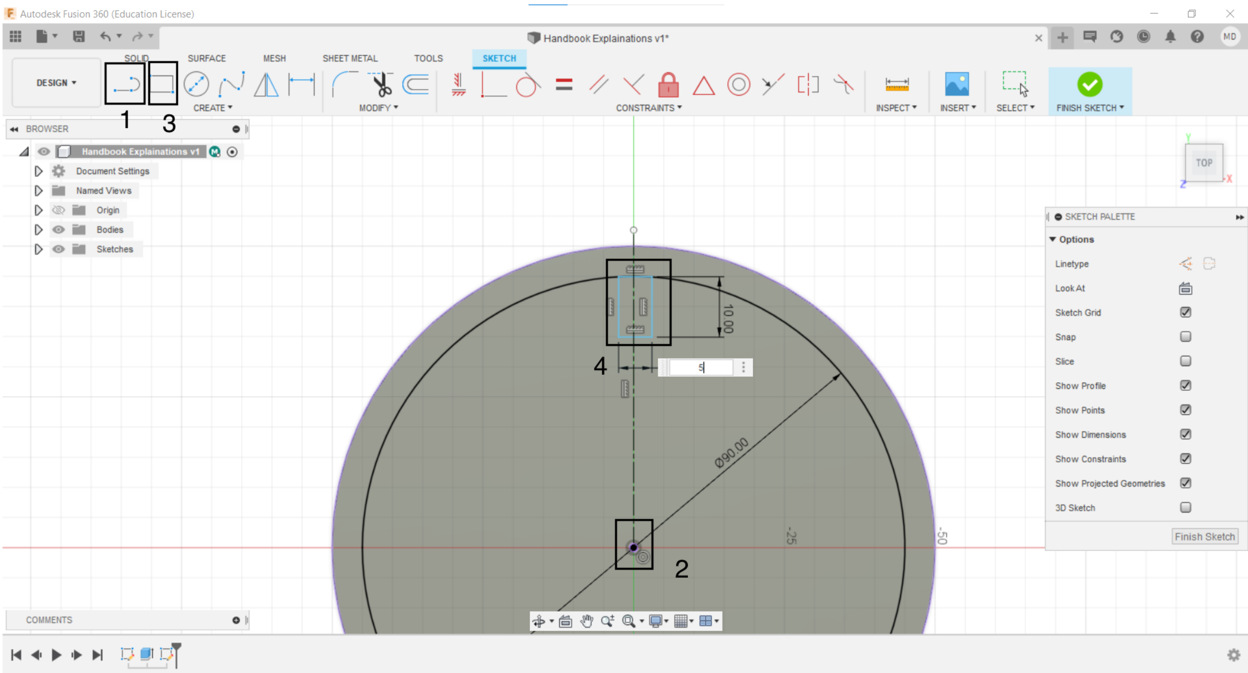
3 - Extruding a Disc

1. Click on the extrude function labeled as 1 and click on the circle, this should bring up a dialog box for giving the extrusion a height, this will be the thickness of the base



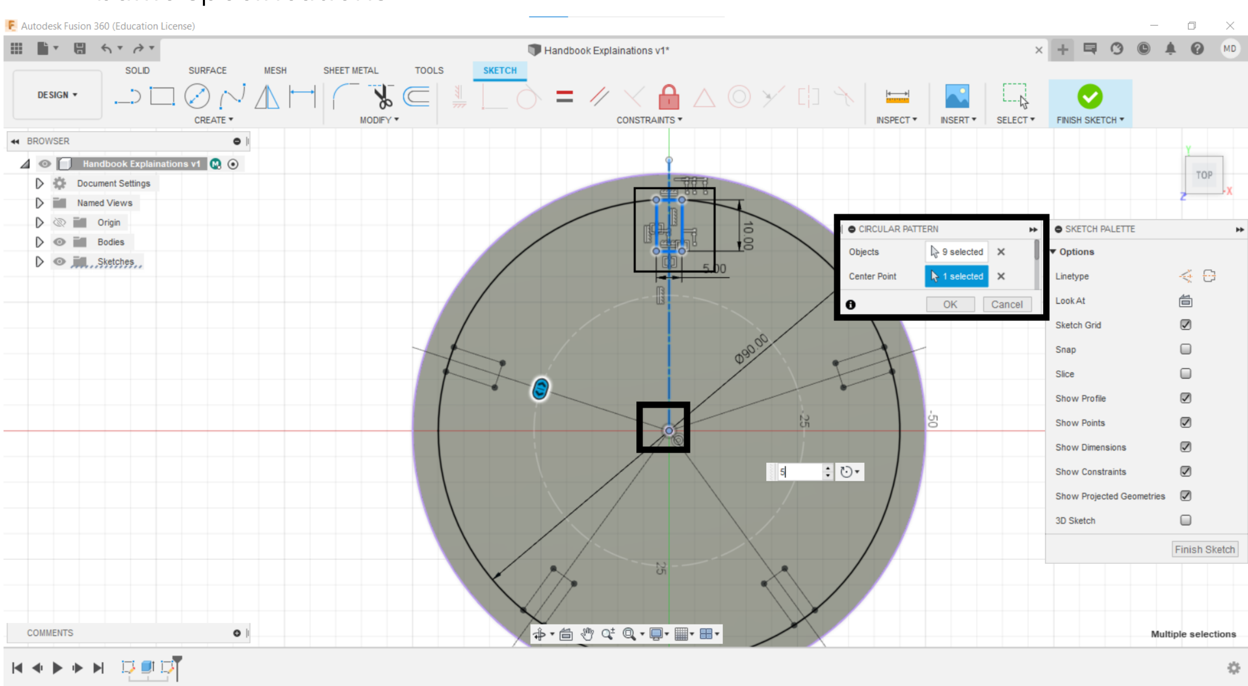
4 - Make the circle for the inner diameter

1. Click on the center of the circle and and set the value for the radius of the inner tank



5 - Make Baffles

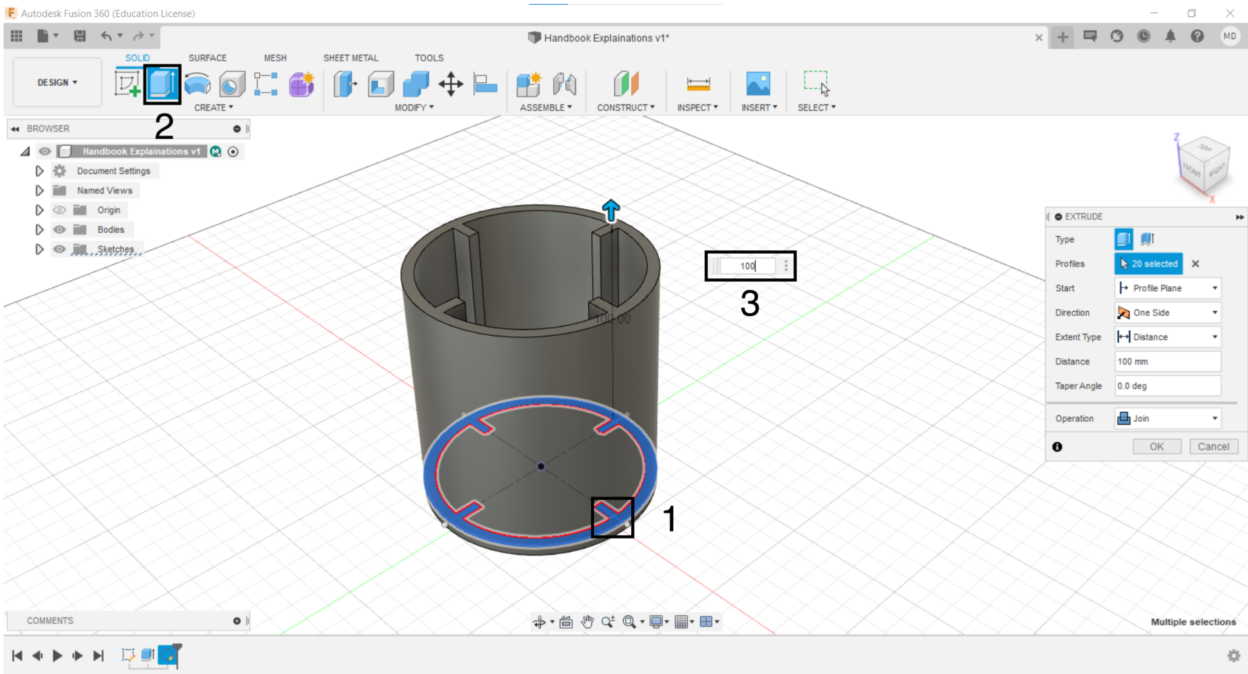
1. Click on the line function and make a line at 90° from the horizontal click on Construction element to make this one
2. Click on the rectangle function labeled 2 and dimension it according to your baffle specifications



6 - Making Multiple Baffles

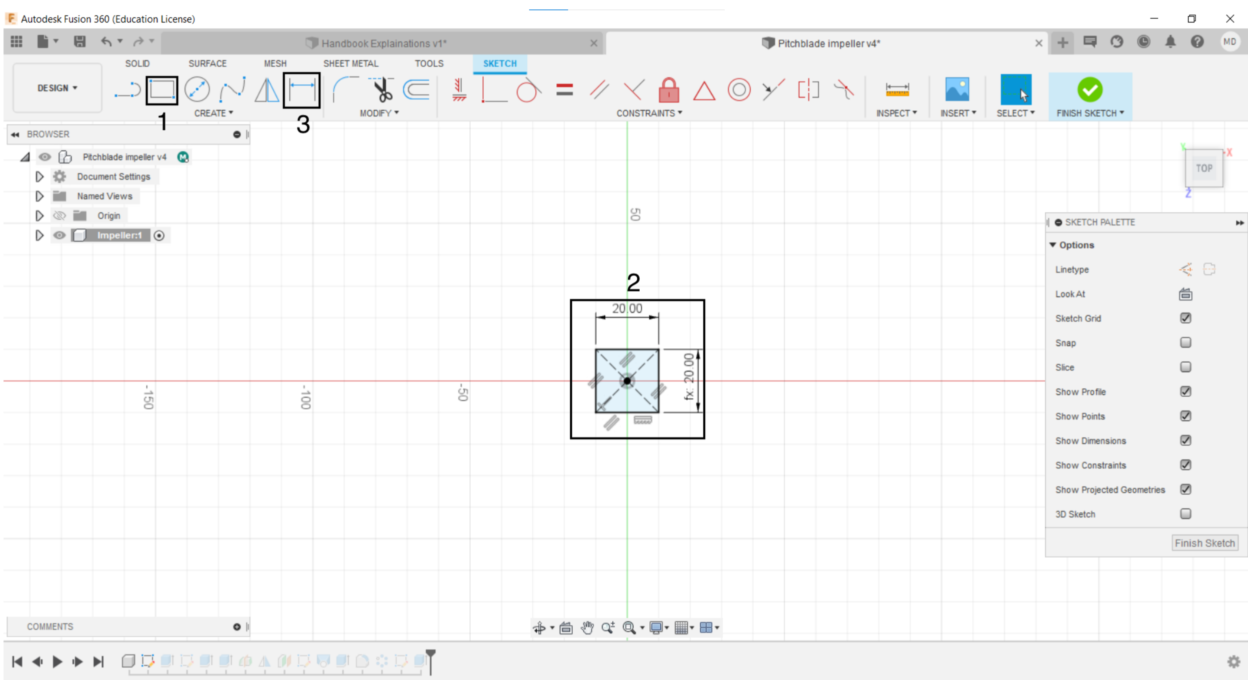
1. Click on the Circular Pattern Function under create
2. Select all the construction elements made earlier

3. Select the center point as the center of the circle
4. Choose the number of instances as the required number of baffles
5. Exit sketch



7 - Extrude the Tank with Baffles

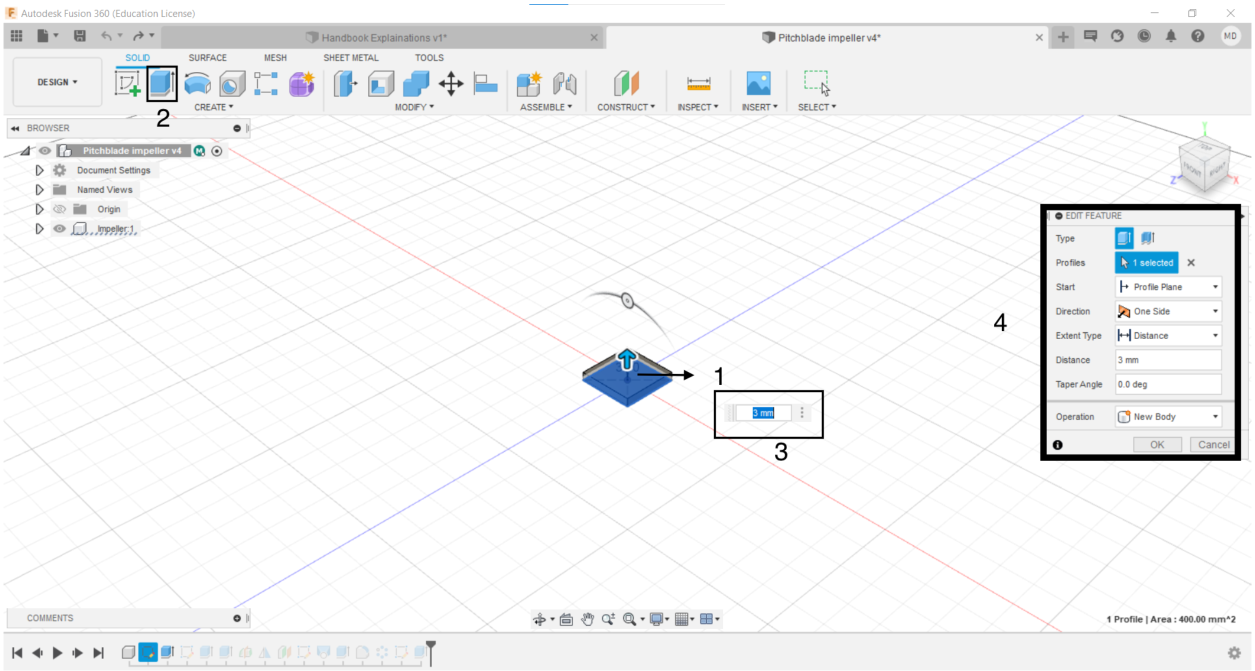
1. Select all the faces with the tank and Baffles
2. Choose extrude labeled 2 and specify the length to extrude



8 - Make the impeller

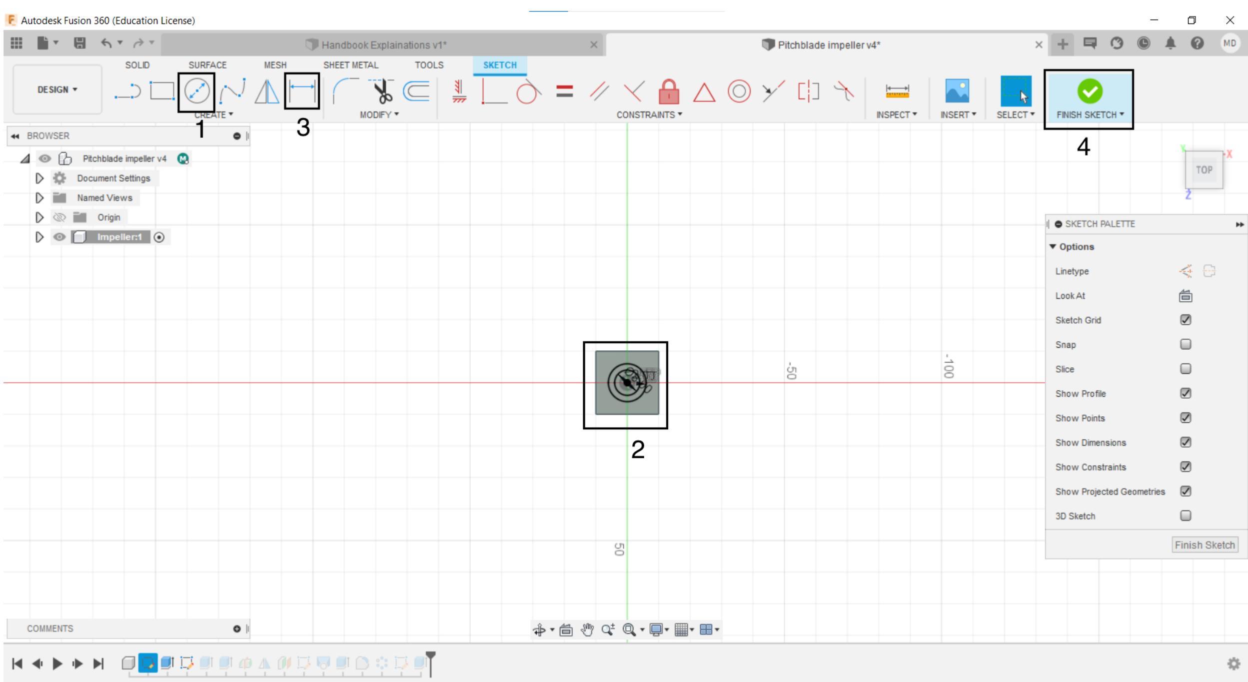
1. Select another plane for sketching

2. Click on rectangle labeled 1
3. Draw a rectangle and dimension it according to your specification
4. Exit out of sketch



9 - Extruding the Hub

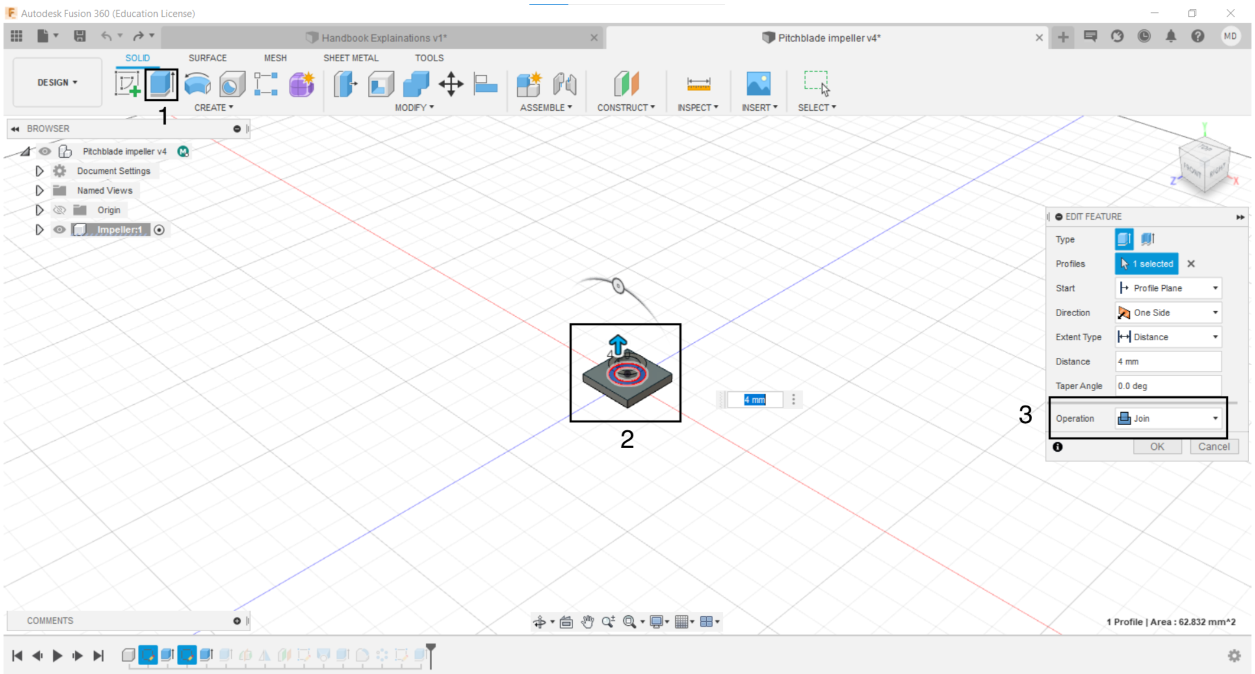
1. Select the face of the hub and select extrude, specify the dimension



10 - Making a hub for the shaft

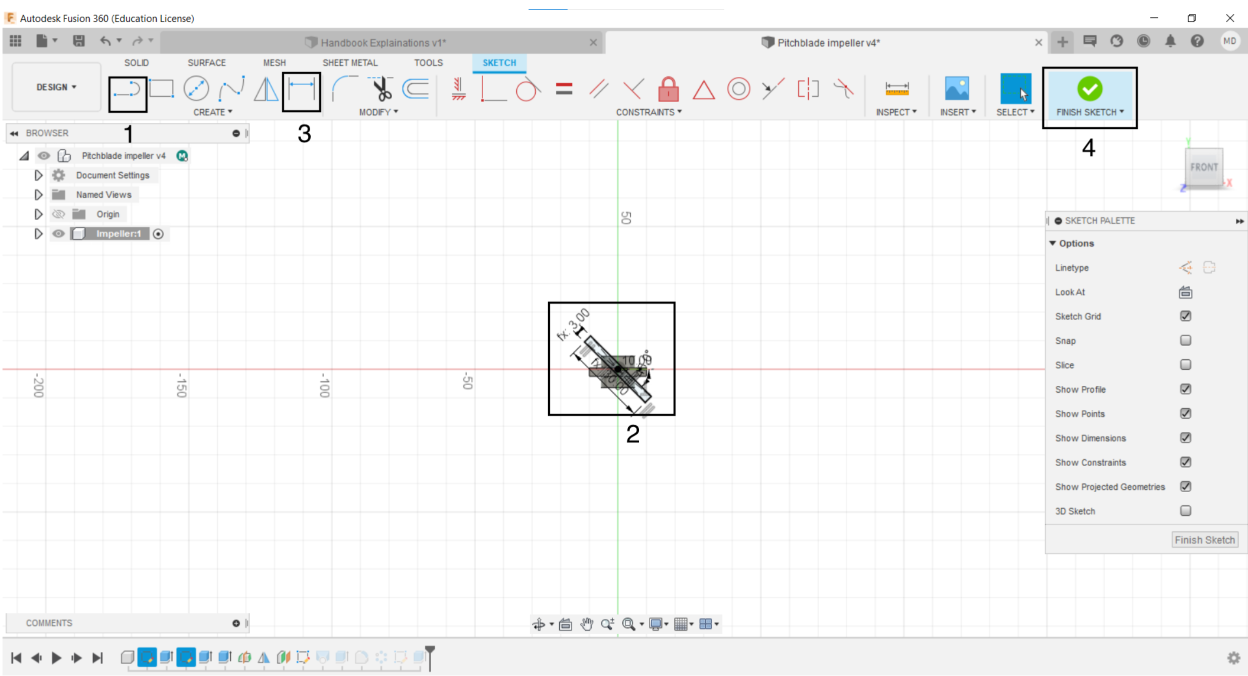
1. Select the circle option and make a circle similar to shaft diameter

2. Exit sketch



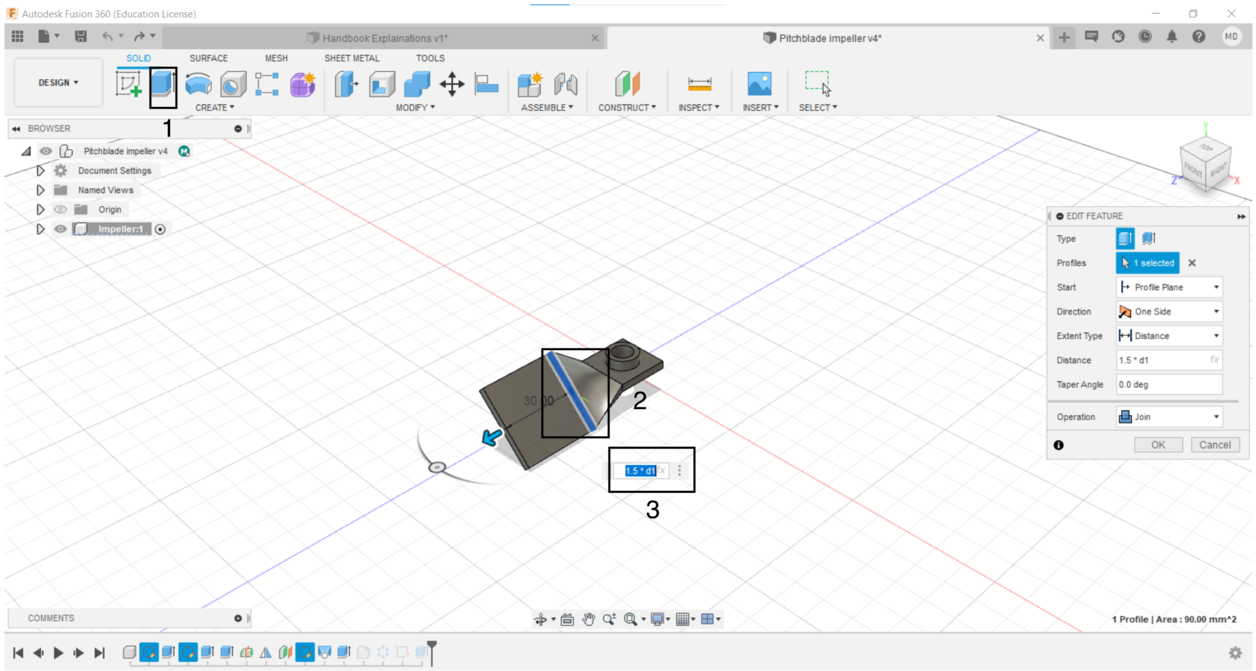
11 - Symmetrically extrude Hub on both sides

1. Select the extrude function labeled 1 and select the face
2. Click on extrude both sides and use the operation as join



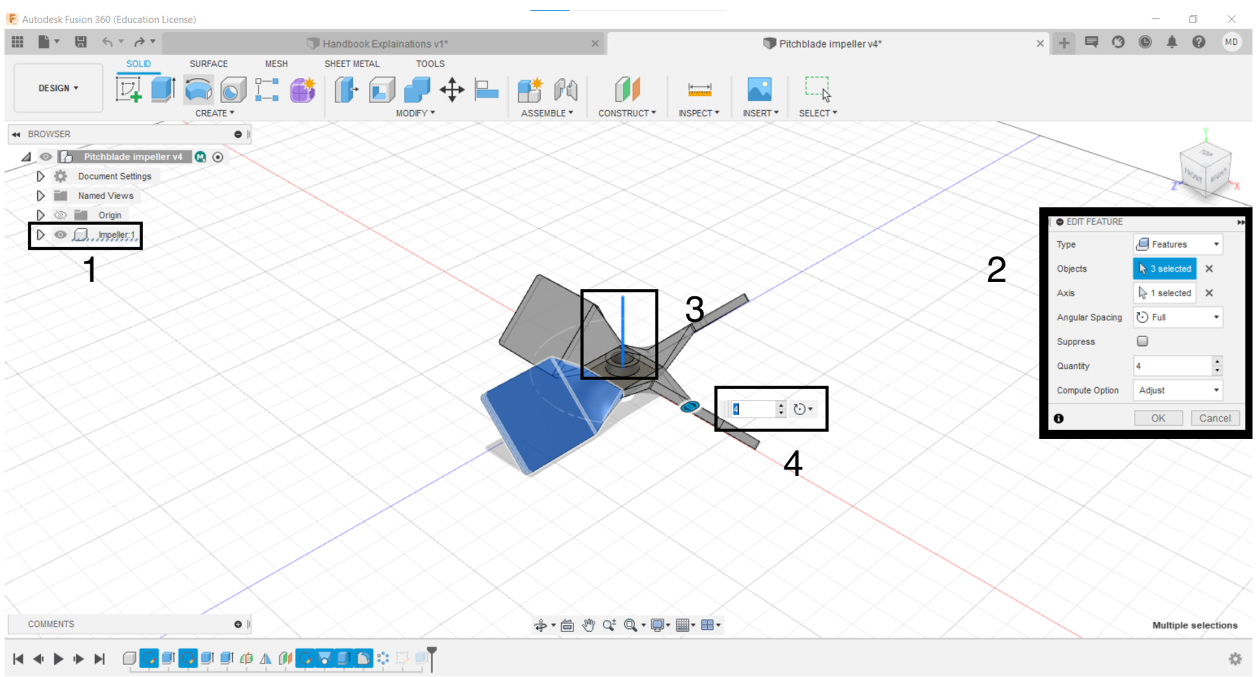
12 - Make the Profile for the impeller

1. Make your impeller profile using the line tool and dimension it accordingly



13 - Create Loft and Extrude

1. Use the loft function under Create to make a loft surface between the hub face and the profile made
2. Selecting the profile click extrude and specify the dimension



14 - Creating a Circular Pattern

1. Click on the impeller body on the tree and choose circular pattern under create, choose the number of impellers needed.

Congratulations with a new assembly file and moving these parts into their respective positions you have successfully Made and Designed a BioReactor.

Finishing up:
We hope this helps the teams in iGEM as a basis to get started with Bioreactor design.

Resources:

1) https://bioprocessing.weebly.com/fermentation.html
2) https://blog.craneengineering.net/mixing-tank-geometry-its-all-about-that-base
3) https://www.chemicalprocessing.com/articles/2003/take-mixing-to-the-max
4) https://www.chemicalprocessing.com/articles/2005/dont-get-mixed-up-by-scale-up/
5) https://www.pharmacalculations.com/2016/05/types-of-agitators.html
6) Principles of Fermentation Engineering by Peter Stanbury