```
#@title Drug Design
```

Drug Design

```
# from google.colab import drive
# drive.mount("/content/drive")
```

```
# Import Libraries
import pandas as pd
import numpy as np
import matplotlib.pyplot as plt
import keras
from keras import layers
from keras.models import Model
from keras import metrics
from keras import backend as K
import tensorflow as tf
from tensorflow.keras.optimizers import Adam
import warnings
import matplotlib.pyplot as plt
from tqdm import tqdm
import random
```

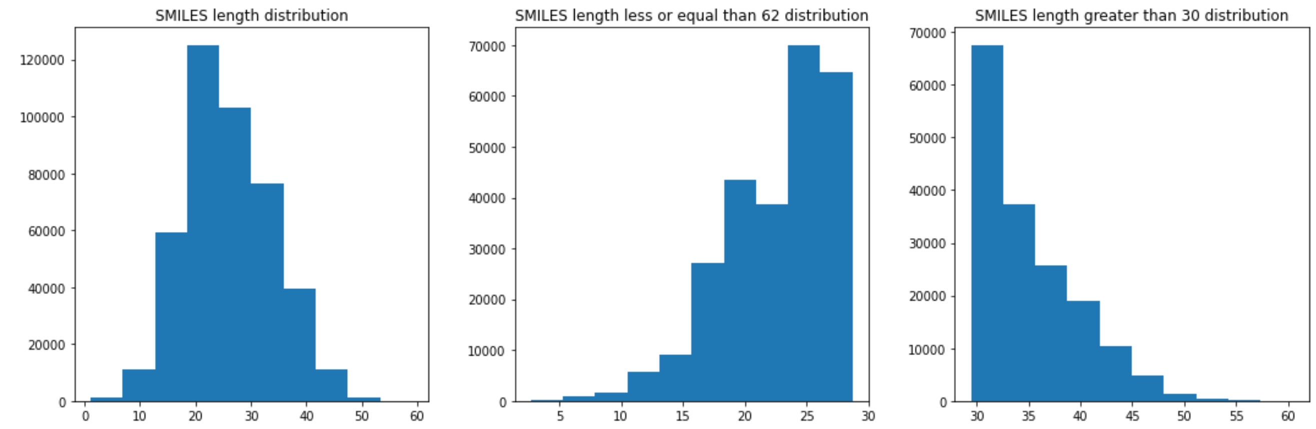
```
# Set environment variables and clear sessions
K.clear_session()
np.random.seed(237)
warnings.filterwarnings("ignore")
tf.compat.v1.disable_eager_execution()
%matplotlib inline
```

```
## Import Dataset from drive for Smile representation of drug molecules:
## Source for data: https://zinc.docking.org/substances/subsets/AA/
data = pd.read_csv('/content/drive/MyDrive/Dataset/MoleculeSythesis/dataset/AA.csv'
data.head()
```

	zinc_id	smiles
0	ZINC000000008151	C[C@H]1[C@@H](O)[C@H](CO)O[C@@H](O)[C@@H]1N
1	ZINC000000008153	CC[C@@H]1[C@@H](N)[C@@H](O)O[C@@H](CO)[C@@H]1O
2	ZINC000000008155	CC1(C)[C@@H](N)[C@@H](O)O[C@@H](CO)[C@@H]1O
3	ZINC000000018276	CS[C@@H]1CN[C@@H](CO)[C@H](O)[C@H]1O
4	ZINC000000018279	CS[C@@H]1[C@@H](O)CN[C@@H](CO)[C@@H]1O

```
#### Plot distribution of smile molecules vs the molecule length
fig, axes = plt.subplots(nrows = 1, ncols = 3, figsize = (15, 5))
axes[0].set_title("SMILES length distribution")
axes[0].hist(data['smiles'].str.len(), align = 'left')
axes[1].set_title("SMILES length less or equal than 62 distribution")
axes[1].hist(data[data['smiles'].str.len() <= 30]['smiles'].str.len(), align = 'lef
```

```
axes[2].set_title("SMILES length greater than 30 distribution")
axes[2].hist(data[data['smiles'].str.len() > 30]['smiles'].str.len(), align = 'left
fig.tight_layout()
plt.show()
```




```
# Super set of characters used for smile generations
SMILES_CHARS = [' ',
                '#', '%', '(', ')', '+', '-', '.', '/',
                '0', '1', '2', '3', '4', '5', '6', '7', '8', '9',
                '=', '@',
                'A', 'B', 'C', 'F', 'H', 'I', 'K', 'L', 'M', 'N', 'O', 'P',
                'R', 'S', 'T', 'V', 'X', 'Z',
                '[', '\\', ']',
                'a', 'b', 'c', 'e', 'g', 'i', 'l', 'n', 'o', 'p', 'r', 's',
                't', 'u'
]
```

```
#### Create dictionaries from character set for encoding and decoding smiles
encoder_dict = dict( (c,i) for i,c in enumerate( SMILES_CHARS ) )
decoder_dict = dict( (i,c) for i,c in enumerate( SMILES_CHARS ) )
print(encoder_dict)
print(decoder_dict)
```

```
{' ': 0, '#': 1, '%': 2, '(': 3, ')': 4, '+': 5, '-': 6, '.': 7, '/': 8, '0':
{0: ' ', 1: '#', 2: '%', 3: '(', 4: ')', 5: '+', 6: '-', 7: '.', 8: '/', 9: '0
```

```
smiles_data = data['smiles'][:250000]
smiles_data = np.array(smiles_data).reshape(-1)
print('Number of mols: '+str(len(smiles_data)))
idx = [i for i, x in enumerate(smiles_data) if len(x)<=120]
print('Number of valid mols: '+str(len(idx)))
smiles_data = smiles_data[idx]
print('Getting a unique character set...')
```

```
Number of mols: 250000
Number of valid mols: 250000
Getting a unique character set...
```

```
char_set = set()
for i in tqdm(range(len(smiles_data))):
    smiles_data[i] = smiles_data[i].ljust(62)
    char_set = char_set.union(set(smiles_data[i]))
char_set_list = sorted(list(char_set))
print('Number of characters: '+str(len(char_set_list)))
```

```
100%|██████████| 250000/250000 [00:00<00:00, 396205.17it/s]Number of character
```

```
def one_hot_encoder( smiles ):
    X = np.zeros( ( 62, len( SMILES_CHARS ) ) )
    for i, c in enumerate( smiles ):
        X[i, encoder_dict[c]] = 1
    return X

def one_hot_decoder( X ):
    smi = ''
    X = X.argmax( axis=-1 )
    for i in X:
        smi += decoder_dict[i]
    return smi
```

```
x = []
for i in data['smiles'][:500]:
    x.append(one_hot_encoder(i))
arr = np.array(x)
```

```
arr = arr.reshape(-1,62,56,1)
arr.shape
```

```
(500, 62, 56, 1)
```

```
#### Basic VAE Keras implementatin used as reference for encoder and decoder layer
#### Link: https://zinc.docking.org/substances/subsets/AA/

img_shape = (62, 56,1)
latent_dim = 2

input_img = keras.Input(shape=img_shape)

x = layers.Conv1D(32, 7,
                  padding='same',
                  activation='relu',
                  )(input_img)

x = layers.Conv2D(128, 3,
                  padding='same',
```

```
                  padding='same',
                  activation='relu',
                  strides=(2, 2))(x)

x = layers.Conv2D(128, 3,
                  padding='same',
                  activation='relu')(x)

x = layers.Conv2D(128, 3,
                  padding='same',
                  activation='relu')(x)

shape_before_flattening = K.int_shape(x)

x = layers.Flatten()(x)
x = layers.Dense(32, activation='relu')(x)

z_mu = layers.Dense(latent_dim)(x)
z_log_sigma = layers.Dense(latent_dim)(x)


def sampling(args):
  z_mu, z_log_sigma = args
  epsilon = K.random_normal(shape=(K.shape(z_mu)[0], latent_dim),
  mean=0., stddev=1.)
  return z_mu + K.exp(z_log_sigma) * epsilon

z = layers.Lambda(sampling)([z_mu, z_log_sigma])


decoder_input = layers.Input(K.int_shape(z)[1:])

x = layers.Dense(np.prod(shape_before_flattening[1:]),
                 activation='relu')(decoder_input)

x = layers.Reshape(shape_before_flattening[1:])(x)

x = layers.Conv2DTranspose(32, 3,
                           padding='same',
                           activation='relu',
                           strides=(2, 2))(x)

x = layers.Conv2D(1, 3,
                  padding='same',
                  activation='sigmoid')(x)

decoder = Model(decoder_input, x)

z_decoded = decoder(z)


class CustomVariationalLayer(keras.layers.Layer):
    def vae_loss(self, x, z_decoded):
        x = K.flatten(x)
        z_decoded = K.flatten(z_decoded)
        xent_loss = keras.metrics.binary_crossentropy(x, z_decoded) #Recin loss
        kl_loss = -5e-4 * K.mean(1 + z_log_sigma - K.square(z_mu) - K.exp(z_log_sig
```

```
        return K.mean(xent_loss + kl_loss)

    def call(self, inputs):
        x = inputs[0]
        z_decoded = inputs[1]
        loss = self.vae_loss(x, z_decoded)
        self.add_loss(loss, inputs=inputs)
        return x

y = CustomVariationalLayer()([input_img, z_decoded])


# VAE model statement
vae = Model(input_img, y)

vae.compile(optimizer='rmsprop', loss=None)

vae.summary()
```

```
WARNING:tensorflow:Output custom_variational_layer missing from loss dictionar
Model: "model_1"
________________________________________________________________________________
Layer (type)                    Output Shape         Param #     Connected to
================================================================================
input_1 (InputLayer)            [(None, 62, 56, 1)]  0
________________________________________________________________________________
conv1d (Conv1D)                 (None, 62, 56, 32)   256         input_1[0][0]
________________________________________________________________________________
conv2d (Conv2D)                 (None, 31, 28, 128)  36992       conv1d[0][0]
________________________________________________________________________________
conv2d_1 (Conv2D)               (None, 31, 28, 128)  147584      conv2d[0][0]
________________________________________________________________________________
conv2d_2 (Conv2D)               (None, 31, 28, 128)  147584      conv2d_1[0][C
________________________________________________________________________________
flatten (Flatten)               (None, 111104)       0           conv2d_2[0][C
________________________________________________________________________________
dense (Dense)                   (None, 32)           3555360     flatten[0][0]
________________________________________________________________________________
dense_1 (Dense)                 (None, 2)            66          dense[0][0]
________________________________________________________________________________
dense_2 (Dense)                 (None, 2)            66          dense[0][0]
________________________________________________________________________________
lambda (Lambda)                 (None, 2)            0           dense_1[0][0]
                                                                 dense_2[0][0]
________________________________________________________________________________
model (Functional)              (None, 62, 56, 1)    370497      lambda[0][0]
________________________________________________________________________________
custom_variational_layer (Custo (None, 62, 56, 1)    0           input_1[0][0]
                                                                 model[0][0]
================================================================================
Total params: 4,258,405
Trainable params: 4,258,405
Non-trainable params: 0
________________________________________________________________________________
```

```
vae.fit(x=arr, y=None,
        shuffle=False,
        epochs=120,
```

```
        batch_size=16
    )
```

```
Train on 500 samples
Epoch 1/120
500/500 [==============================] - 1s 2ms/sample - loss: 1568276.3942
Epoch 2/120
500/500 [==============================] - 0s 613us/sample - loss: 0.0442
Epoch 3/120
500/500 [==============================] - 0s 611us/sample - loss: 0.0378
Epoch 4/120
500/500 [==============================] - 0s 605us/sample - loss: 0.0358
Epoch 5/120
500/500 [==============================] - 0s 618us/sample - loss: 0.0348
Epoch 6/120
500/500 [==============================] - 0s 618us/sample - loss: 0.0342
Epoch 7/120
500/500 [==============================] - 0s 615us/sample - loss: 0.0338
Epoch 8/120
500/500 [==============================] - 0s 621us/sample - loss: 0.0335
Epoch 9/120
500/500 [==============================] - 0s 618us/sample - loss: 0.0333
Epoch 10/120
500/500 [==============================] - 0s 627us/sample - loss: 0.0330
Epoch 11/120
500/500 [==============================] - 0s 637us/sample - loss: 0.0326
Epoch 12/120
500/500 [==============================] - 0s 618us/sample - loss: 0.0325
Epoch 13/120
500/500 [==============================] - 0s 625us/sample - loss: 0.0322
Epoch 14/120
500/500 [==============================] - 0s 639us/sample - loss: 0.0324
Epoch 15/120
500/500 [==============================] - 0s 625us/sample - loss: 0.0320
Epoch 16/120
500/500 [==============================] - 0s 615us/sample - loss: 0.0322
Epoch 17/120
500/500 [==============================] - 0s 611us/sample - loss: 0.0319
Epoch 18/120
500/500 [==============================] - 0s 617us/sample - loss: 0.0316
Epoch 19/120
500/500 [==============================] - 0s 612us/sample - loss: 0.0314
Epoch 20/120
500/500 [==============================] - 0s 609us/sample - loss: 0.0313
Epoch 21/120
500/500 [==============================] - 0s 611us/sample - loss: 0.0312
Epoch 22/120
500/500 [==============================] - 0s 610us/sample - loss: 0.0310
Epoch 23/120
500/500 [==============================] - 0s 608us/sample - loss: 0.0309
Epoch 24/120
500/500 [==============================] - 0s 633us/sample - loss: 0.0307
Epoch 25/120
500/500 [==============================] - 0s 621us/sample - loss: 0.0306
Epoch 26/120
500/500 [==============================] - 0s 615us/sample - loss: 0.0305
Epoch 27/120
500/500 [==============================] - 0s 618us/sample - loss: 0.0303
Epoch 28/120
500/500 [==============================] - 0s 614us/sample - loss: 0.0304
Epoch 29/120
```

```
500/500 [==============================] - 0s 613us/sample - loss: 0.0299
```

```
result = []

for i in random.sample(range(1, 10000000), 100):
  for j in random.sample(range(1, 10000000), 100):
    sample_vector = np.array([[i,j]])
    res = decoder.predict(sample_vector)
    res = res[0].reshape(62,56)
    result.append(one_hot_decoder(res).replace(' ',''))

set(result)
```

```
{'C%//@1/17@@@H(()O)[C@H5(5TC6.6.(O)/C@#]1OT6TT%-8%I%1%)I)',
 'C%//@1/17@@@H(()O)[C@H5(5TC6.6.(O)/C@#]1OT6TT%-86I%1%)I)',
 'C%//@1/17@@@H(()O)[C@H5(5TC6.6.(O)/C@#]1OT6TT%-87I%1%)I)',
 'C%//@1/17[@@@H(()O)[C@H5(5TC6.6.(O)/C@#]1.T6TT%-7%1%)I)',
 'C%//@1/17[@@@H(()O)[C@H5(5TC6.6.(O)/C@#]1.T6TT%-7I%1%)I)',
 'C%//@1/17[@@@H(()O)[C@H5(5TC6.6.(O)/C@#]1OT6TT%-7I%1%)I)',
 'C%//@1/17[@@@H(()O)[C@H5(5TC6.6.(O)/C@#]1OT6TT%-87I%1%)I)',
 'C%//@1/17[@@@H((CO)[C@H5(5TC6.6.(O)/C@#]1.T6TT%-7I%1%)I)',
 'C%//@1/17[@@@H((CO)[C@H5(5TC6.6.(O)/C@#]1.T6TT%67I%1%)I)',
 'C%//@1/17[@@@H((CO)[C@H5(5TC6.6.(O)/C@#]1.T6TT%67I%\\%)I)',
 'C%//@1/17[@@@H((CO)[C@H5(5TC666.(O)/C@#]1.T6TT%6#I%\\%)I)',
 'C%//@1/17[@@@H((CO)[C@H5(5TC666.(O)/C@#]1.T6TT%67I%\\%)I)',
 'C%//@1/17[@@@H((CO)[C@H5(5TC666.(O)/C@#]1.T6TT%M#I%\\%)I)',
 'C%//@1/17[C@@H((CN)[C@H5(OTC666.(O)/C@#]1.T6T8%M8#I%\\%)I)',
 'C%//@1/17[C@@H((CO)[C@H5(5TC666.(O)/C@#]1.T6TT%M#I%\\%)I)',
 'C%//@1/17[C@@H((CO)[C@H5(OTC666.(O)/C@#]1.T6T8%M#I%\\%)I)',
 'C%//@1/17[C@@H((CO)[C@H5(OTC666.(O)/C@#]1.T6T8%M8#I%\\%)I)',
 'C%//@1/17[C@@H((CO)[C@H5(OTC666.(O)/C@#]1.T6TT%M#I%\\%)I)',
 'C//@1/17[C@@H((CN)[C@H5(O)TC666.(O)/C@#]1.T6T8%M8#I%\\%)I)',
 'C//@1/17[C@@H((CN)[C@H5(OTC666.(O)/C@#]1.T6T8%M8#I%\\%)I)',
 'C//@1/17[C@@HB(CN)[C@H5(O)TC666.(O)/C@#]1.T6T8%M8#I%\\%)I)',
 'C//@1/17[C@@HB(CN)[C@H5(O)TC666.(O)/C@HT1.T6T8%M8#I%\\%)I)',
 'C//@1/17[C@@HB(CN)[C@H5(O)TC666.(O)/C@H]1.T6T8%M8#I%\\%)I)',
 'C//@7/11[C@@HB(CN)[C@H5(O)TC666.(O)/C@HT1.T6T7%M8#I1\\%)I)',
 'C//@7/17[C@@HB(CN)[C@H5(O)TC666.(O)/C@HT1.T6T7%M8#I%\\%)I)',
 'C//@7/17[C@@HB(CN)[C@H5(O)TC666.(O)/C@HT1.T6T7%M8#I1\\%)I)',
 'C//@7/17[C@@HB(CN)[C@H5(O)TC666.(O)/C@HT1.T6T8%M8#I%\\%)I)',
 'C5//@7/11[C@@HB(CN)[C@H5(O)TC666.(O)/C@HT1.T6T7%M8#I1\\%)I)',
 'C5//@7/11[C@@HB(CO)[C@H5(O)TC666.(O)/C@HT1.T6T7%M8#I1\\%)I)',
 'N%//@1/17@@@H(()O)[C@H5(5TC6.6.(O)/C@#]1OT69T%-8%I%1%)I)',
 'N%//@1/17@@@H(()O)[C@H5(5TC6.6.(O)/C@#]1OT6TT%-8%I%1%)I)',
 'N%//@1/17@@@s(()O)C@H5(5TC6.6.(O)/C@#.1OT69T%-8%I%1))I)',
 'N%//@1/17@@@s(()O)C@H5(5TC6.6.(O)/C@#.1OT69T%-8%I%\\))I)',
 'N%//@1/17@@@s(()O)C@H5(5TC6.6.(O)/C@#]1OT69T%-8%I%1%)I)',
 'N%//@1/17@@@s(()O)C@H5(5TC6.6.(O)/C@#]1OT69T%-8%I%1))I)',
 'N%//@1/17@@@s(()O)[C@H5(5TC6.6.(O)/C@#]1OT69T%-8%I%1%)I)',
 'N%//@1/17@@@s(()s)C@H5(5TC6.6.(O)/C@#.1OT69T%-8%I%\\))I)',
 'N%//@7/17@@@s(()s)C@H5(5TC6.6.(O)/C@#.1OT69T%-8%I%\\))I)',
 'N%/C@7/17@@@s(()s)C@H5(5TC6.6.(O)/C@#.1OT69T%-8%I%\\))I)',
 'N%/C@H/17@@@s(()s)C@H5(5TC6.6.(O)/C@#.1OT69T%-8%I%\\))I)',
 'N%/C@H/17@@@s(()ssC@H5(5TC6.6.(O)/C@#.1O69T%-8%I%\\))I)',
 'N%/C@H/17@@@s(()ssC@H5(5TC6.6.(O)/C@#.1OT69T%-8%I%\\))I)',
 'N%/C@H/17@@@s(()ssC@H5(OTC6.6.(O)/C@#.1O69T%-8%I%\\))I)',
 'N%/C@H/17@@@s()s@H](OTC6.6.(O)/C@#.1O69T%-8%IMg))I)',
 'N%/C@H/17@@@s()s@H](OTC6.6.(O)/C@..1O69T%-8%IM))I)',
 'N%/C@H/17@@@s()s@H](OTC6.6.(O)/C@..1O69T%-8%IMg))I)',
 'N%/C@H/17@@@s()sC@H5(OTC6.6.(O)/C@#.1O69T%-8%I%g))I)',
```

```
'N%/C@H/17@@@s()sC@H](OTC6.6.(O)/C@#.1O69T%-8%I%g))I)',
'N%/C@H/17@@@s()sC@H](OTC6.6.(O)/C@#.1O69T%-8%IMg))I)',
'N%/C@H/17@@@s()ssC@H5(OTC6.6.(O)/C@#.1O69T%-8%I%\\))I)',
'N%/C@H/17@@@s()ssC@H5(OTC6.6.(O)/C@#.1O69T%-8%I%g))I)',
'N%/C@H/17@@@s(u)s@H](OTC6.6.(O)/C@..1O69T%-8%IM))I)',
'N%/C@H/17@@@s(u)s@H](OTC6.6.(O)/C@.1O69T%-8%IM))I)',
'N/@N/1CC@H](())]iO[C@@H](O)CC@@.11OI5',
'N/@N/1CC@H](())]ii[C@@H](O)CC@@.11OI5',
'N/@N/1CC@H](())iO[C@@H9(O)CC@@.116I5',
'N/@N/1CC@H](())iO[C@@H](O)CC@@.116I5',
'N/@N/1CC@H](())iO[C@@H](O)CC@@.11O6I5',
'N/@N/1CC@H](())iO[C@@H](O)CC@@.11OI5',
```