```
!pip install torch torchvision
!pip3 install tqdm
```

In [1]:

```python
import pickle
from pathlib import Path
from collections import namedtuple
from itertools import chain
from copy import deepcopy

from tqdm import notebook, tqdm
from typing import List, Generator
```

In [2]:

```python
import numpy as np
import pandas as pd
import matplotlib.pyplot as plt
import seaborn as sns
```

In [3]:

```python
from sklearn.metrics import precision_recall_curve, average_precision_score, recall_score, precision_score

from sklearn.metrics import accuracy_score

from sklearn.metrics import roc_curve, auc, roc_auc_score
from sklearn.metrics import confusion_matrix, classification_report
```

In [4]:

```python
import torch
from torch import nn
from torch.optim import SGD, Adam
from torch.utils.data import Dataset, DataLoader
```

In [5]:

```python
from utils import plot_confusion_matrix, evaluate_model, load_pickle
```

In [6]:

```python
pd.set_option('max_colwidth', 800)
sns.set_context("notebook", font_scale=1.0, rc={"lines.linewidth": 3.0})
sns.set_style("darkgrid", {"axes.facecolor": ".89"})

# torch.manual_seed(170188)
# np.random.seed(170188)


%load_ext autoreload
%autoreload 2
%matplotlib inline
```

In [7]:

```python
device = torch.device('cuda' if torch.cuda.is_available() else 'cpu')
device
```

Out[7]:

```
device(type='cuda')
```

In [8]:

```python
class PatienstDataset(Dataset):
    """Emerson Patients dataset."""

    N = 80

    def __init__(self, root_dir, word2idx):
        self.df = PatienstDataset.collect_data(root_dir)

        self.data, self.target = self.__extract_info(word2idx)
        self.padded = list(map(lambda x: np.pad(x, (0, PatienstDataset.N - len(x)), 'constant', constant_values=0
), self.data))

    def __len__(self):
        return self.df.shape[0]

    def __getitem__(self, idx):
        sample = torch.LongTensor(self.padded[idx])
        target = torch.tensor(self.target[idx], dtype=torch.float32)

        return sample, target

    def __extract_info(self, word2idx):

        self.df['convert'] = self.df['amino_sequences'].apply(lambda x: PatienstDataset.despach(word2idx, x))
        self.df['target'] = self.df['target'].map({'positive': 1, 'negative': 0})

        return self.df['convert'].values, self.df['target'].values

    @staticmethod
    def despach(word2idx, x):
        return [word2idx[word] for word in x]

    @staticmethod
    def collect_data(path: Generator) -> object:

        patient_doent_include_sequences = []
        count = 0

        patients = []
        max_sequences = 0

        patient = namedtuple('patient', ['name', 'data', 'label'])

        for item in path.glob('*'):

            name, label = item.stem.split('_')

            try:

                df = pd.read_csv(item, usecols=['combined'])

#                 df.drop_duplicates(keep='first', inplace=True)
#                 df.reset_index(drop=True,inplace=True)

                max_sequences = df.shape[0] if df.shape[0] > max_sequences else max_sequences

                df = df['combined'].str.split('_', expand=True)

                df.rename(columns={0: 'v_gene', 1: 'amino_sequence', 2: 'j_gene'}, inplace=True)

                amino_acid = df['amino_sequence'].to_list()

                person = patient(name, amino_acid, label)

                patients.append(person)

            except KeyError:

                count += 1
                patient_doent_include_sequences.append(item.name)

        print(f"Maximum number of sequences is: {max_sequences}")
        print(f"The number of patients filtered due to centers is: {count}")
        print(f"Patient names/files is: {patient_doent_include_sequences}")

        names, train_text, labels = zip(*patients)
        data_frame = pd.DataFrame({'patient_name': names, 'amino_sequences': train_text, 'target': labels})

        return data_frame
```

In [9]:

```
ROOT = Path('data')
TRAIN = ROOT / 'lstm_train_256'
TEST = ROOT / 'lstm_test_256'
```

In [10]:

```
# Load golden TCRs
obj = load_pickle('256_centers.pkl')
```

In [11]:

```
# Provide an index for each sequence in the embedding layer
words = list(map(lambda x: x.split('_')[1], obj))
word2idx = {word: idx for idx, word in enumerate(sorted(words), 1)}
print(len(word2idx))
```

```
256
```

In [12]:

```
# Add padding to the sequence dictionary
word2idx['__Meaningless__'] = 0
word2idx = dict(sorted(word2idx.items(), key=lambda item: item[1]))
print(len(word2idx))
```

```
257
```

In [13]:

```
list(word2idx.items())[:5]
```

Out[13]:

```
[('__Meaningless__', 0),
 ('CAISEAQNTEAFF', 1),
 ('CAISESGTGGGYTF', 2),
 ('CAISESQDRGHEQYF', 3),
 ('CASASANYGYTF', 4)]
```

In [14]:

```
train_dataset = PatienstDataset(TRAIN, word2idx)

train_dataloader = DataLoader(train_dataset, batch_size=50,shuffle=True)
```

```
Maximum number of sequences is: 77
The number of patients filtered due to centers is: 3
Patient names/files is: ['HIP13945_negative.csv', 'HIP13465_negative.csv', 'HIP05763_negative.csv']
```

In [15]:

```
len(train_dataset)
```

Out[15]:

```
638
```

In [16]:

```
print(train_dataset.data[:2])
```

```
[list([26, 111, 171, 92, 201, 86, 135, 172, 182, 183, 28, 57, 8, 58, 61, 28, 87, 46, 84, 57, 174, 20
7, 39, 85, 52, 52, 8, 81, 45, 46, 45, 68, 46])
 list([117, 197, 120, 19, 93, 50, 209, 50, 12, 15, 78, 140, 50, 197, 237, 219, 2, 193, 245, 32, 85,
215, 153, 96, 219])]
```

In [17]:

```
test_dataset = PatienstDataset(TEST, word2idx)

test_dataloader = DataLoader(test_dataset, batch_size=1,shuffle=True)
```

```
Maximum number of sequences is: 63
The number of patients filtered due to centers is: 2
Patient names/files is: ['Keck0063_negative.csv', 'Keck0024_negative.csv']
```

In [18]:

```
class Net(nn.Module):
    def __init__(self, embeddings_shape=len(word2idx), embedding_dim=10, hidden_layer=10):
        super(Net,self).__init__()
        self.embedding_layer = nn.Embedding(num_embeddings=embeddings_shape, embedding_dim=embedding_dim)

        self.fc1 = nn.Linear(embedding_dim,hidden_layer)
        self.fc2 = nn.Linear(hidden_layer,1)

        self.bn1 = nn.BatchNorm1d(hidden_layer, affine=False)

        self.dropout = nn.Dropout(0.2)

    def forward(self,x):

        # (1) embeddings layer
#         self.embedding_layer.weight.data[0, :] = 0
        x = self.embedding_layer(x)
        x = torch.sum(x, 1)

#         output = open('person_embedding.pkl', 'wb')
#         pickle.dump(x.detach().numpy(), output)
#         output.close()


        # (1) hidden layer
        x = self.dropout(x)
        x = self.fc1(x)
        x = torch.relu(x)
        x = self.bn1(x)

        # (2) output layer
        x = self.dropout(x)
        x = self.fc2(x)
        x = torch.sigmoid(x)

        return x
```

In [19]:

```
#hyper parameters
learning_rate = 0.05
Epochs = 25
```

In [20]:

```
def init_weights(m):
    if type(m) == nn.Linear:
        torch.nn.init.xavier_uniform_(m.weight)
        m.bias.data.fill_(0.01)
```

In [21]:

```
model = Net(embeddings_shape=len(word2idx) , embedding_dim=7, hidden_layer=16)
model.apply(init_weights)
model
```

Out[21]:

```
Net(
  (embedding_layer): Embedding(257, 7)
  (fc1): Linear(in_features=7, out_features=16, bias=True)
  (fc2): Linear(in_features=16, out_features=1, bias=True)
  (bn1): BatchNorm1d(16, eps=1e-05, momentum=0.1, affine=False, track_running_stats=True)
  (dropout): Dropout(p=0.2, inplace=False)
)
```

In [22]:

```
# Optimizer, Loss
optimizer = Adam([p for p in model.parameters() if p.requires_grad],lr=learning_rate, weight_decay=0.005)
loss_fn = nn.BCELoss()
```

In [23]:

```
losses = []
accur = []

best_accuracy = 0
best_loss = 9E6
l1_regularization, l2_regularization = torch.tensor(0.), torch.tensor(0.)

for epoch in range(Epochs):
    model = model.train()
    progress_bar = notebook.tqdm_notebook(train_dataloader, leave=False)
    for batch in progress_bar:

        x_train, y_train = batch

        #calculate output
        output = model(x_train)

        #calculate loss
        loss = loss_fn(output,y_train.reshape(-1,1))

        #backprop
        loss.backward()
        optimizer.step()
        optimizer.zero_grad()


    model = model.eval()
    with torch.no_grad():

        #accuracy
        predicted = model(torch.tensor(train_dataset.padded,dtype=torch.int64))

        train_probs =  predicted.reshape(-1).detach().numpy()
        y_pred_train = predicted.reshape(-1).detach().numpy().round()

        y_true_train = train_dataset.target

        cur_accuracy = (predicted.reshape(-1).detach().numpy().round() == train_dataset.target).mean()

        #auc
        fpr, tpr, _ = roc_curve(y_true_train, train_probs)
        roc_auc = auc(fpr, tpr)




    cur_loss = loss.item()
    progress_bar.set_description(f"Loss: {loss.item():.3f}")

    if cur_accuracy >= best_accuracy and cur_loss < best_loss:
        print(f"Epoch #{epoch+1}, Saving .......{best_accuracy} ---> {cur_accuracy}......{best_loss} ---> {cur_lo
ss}")

        best_accuracy = cur_accuracy
        best_loss = cur_loss

        output = open('sequence_embedding.pkl', 'wb')
        pickle.dump(model.embedding_layer.weight.detach().numpy(), output)
        output.close()


        print()
        best_model = deepcopy(model)

    if (epoch+1)%10 == 0:

        tqdm.write(f"\nEpoch #{epoch+1}: Train Loss: {loss:.5f} Train Accuracy: \
            {best_accuracy:.5f} Train AUC: {roc_auc:.5f}")

        tqdm.write(f"The average precision score of model is \
            {round(average_precision_score(y_true_train, train_probs),3)*100} %")


    losses.append(loss.item())
    accur.append(cur_accuracy)

torch.save(best_model.state_dict(), 'model.pt')
```

```
Epoch #1, Saving .......0 ---> 0.5815047021943573......9000000.0 ---> 0.6787745952606201


Epoch #2, Saving .......0.5815047021943573 ---> 0.6912225705329154......0.6787745952606201 ---> 0.60
37831902503967


Epoch #3, Saving .......0.6912225705329154 ---> 0.822884012539185......0.6037831902503967 ---> 0.515
0768160820007


Epoch #4, Saving .......0.822884012539185 ---> 0.8996865203761756......0.5150768160820007 ---> 0.480
01551628112793



Epoch #7, Saving .......0.8996865203761756 ---> 0.9200626959247649......0.48001551628112793 ---> 0.4
4357019662857056



Epoch #10: Train Loss: 0.30001 Train Accuracy:             0.92006 Train AUC: 0.99566
The average precision score of model is             99.5 %


Epoch #12, Saving .......0.9200626959247649 ---> 0.9655172413793104......0.44357019662857056 ---> 0.
3347391188144684


Epoch #13, Saving .......0.9655172413793104 ---> 0.9655172413793104......0.3347391188144684 ---> 0.2
770647406578064


Epoch #15, Saving .......0.9655172413793104 ---> 0.9764890282131662......0.2770647406578064 ---> 0.2
0178355276584625



Epoch #20: Train Loss: 0.46023 Train Accuracy:             0.97649 Train AUC: 0.99879
The average precision score of model is             99.9 %


Epoch #23, Saving .......0.9764890282131662 ---> 0.9921630094043887......0.20178355276584625 ---> 0.
12873563170433044
```

In [24]:

```
from sklearn.manifold import TSNE
obj = load_pickle('person_embedding_train.pkl')

X_embedded = TSNE(n_components=2, verbose=True, n_iter=5000).fit_transform(obj)

df_subset = pd.DataFrame(X_embedded, columns=['tsne-2d-one', 'tsne-2d-two'])
df_subset['person_name'] = train_dataset.df['patient_name']

df_subset['target'] = train_dataset.df['target']
df_subset['target'] = df_subset['target'].map({1: 'positive', 0: 'negative'})


df_subset.head()
```

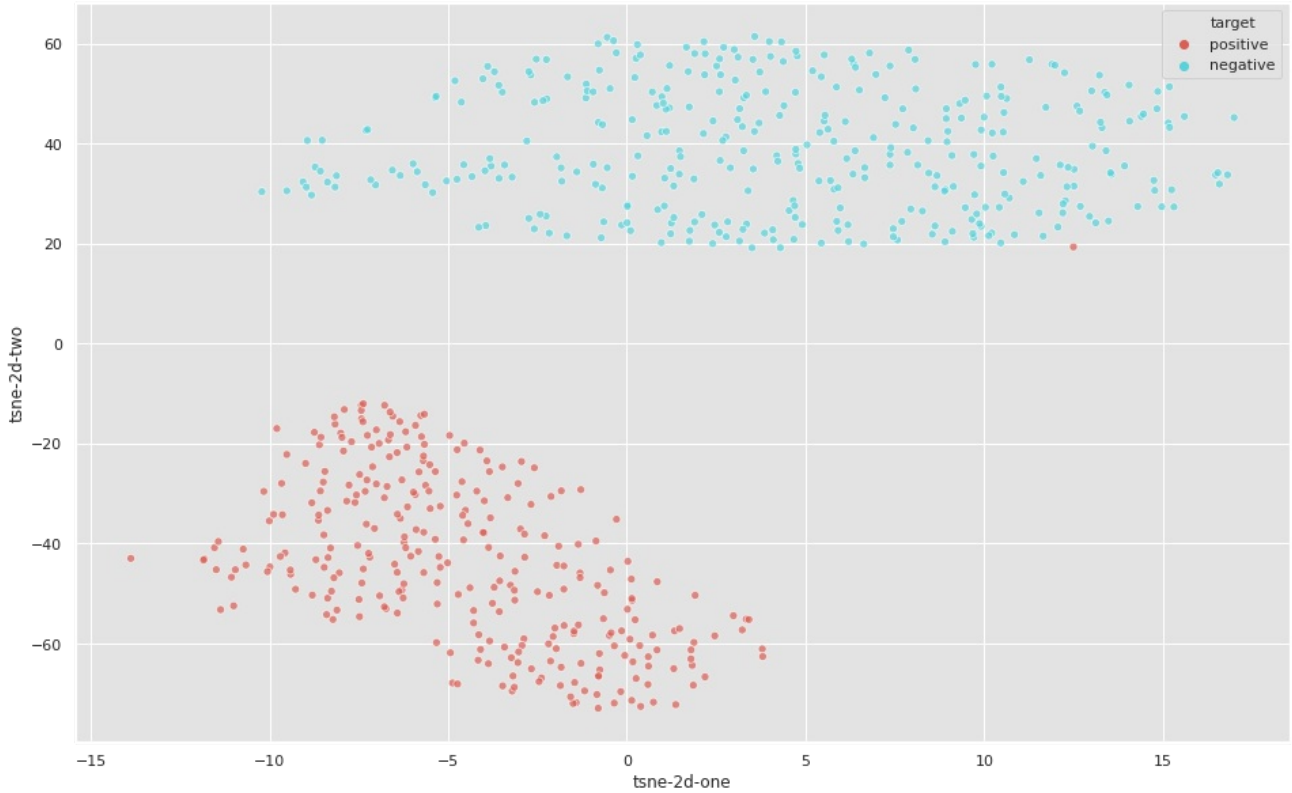
```
[t-SNE] Computing 91 nearest neighbors...
[t-SNE] Indexed 638 samples in 0.001s...
[t-SNE] Computed neighbors for 638 samples in 0.024s...
[t-SNE] Computed conditional probabilities for sample 638 / 638
[t-SNE] Mean sigma: 3.360651
[t-SNE] KL divergence after 250 iterations with early exaggeration: 61.367226
[t-SNE] KL divergence after 3950 iterations: 0.722020
```

Out[24]:

	tsne-2d-one	tsne-2d-two	person_name	target
0	-4.941134	-61.833241	HIP14361	positive
1	-4.095852	-61.167004	HIP14041	positive
2	-4.163083	-63.314800	HIP14096	positive
3	9.471843	27.191271	HIP10389	negative
4	-3.210927	-69.483009	HIP14103	positive

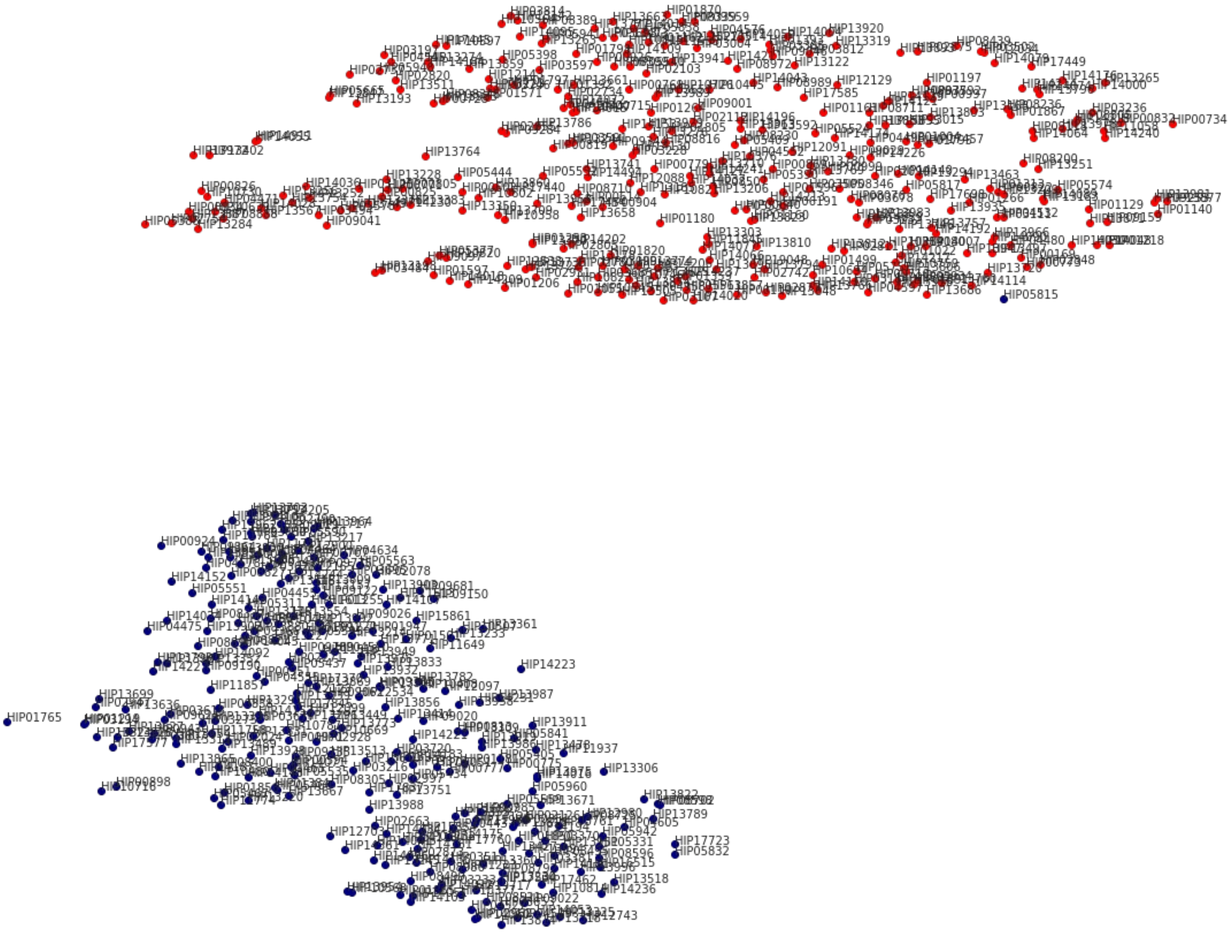
In [25]:

```
plt.figure(figsize=(16,10))
sns.scatterplot(
    x="tsne-2d-one", y="tsne-2d-two",
    palette=sns.color_palette("hls", 2),
    data=df_subset,
    hue='target',
    legend="full",
    alpha=0.7
);
```



In [26]:

```
x, y = zip(*X_embedded)
names = df_subset['person_name'].to_list()
labels = df_subset['target'].to_list()

fig, ax = plt.subplots(figsize=(20, 16))

for i, (label, target) in enumerate(zip(names,labels)):

    if target == 'positive':
        color='navy'
    elif target == 'negative':
        color='red'

    ax.scatter(x[i], y[i], c=color)
    ax.annotate(label, (x[i], y[i]))

ax.axis('off')
plt.show()
```



In [27]:

```
model = best_model.eval()
with torch.no_grad():
    #accuracy
    predicted = model(torch.tensor(train_dataset.padded,dtype=torch.int64))


    train_probs =  predicted.reshape(-1).detach().numpy()
    y_pred_train = train_probs.round()
    y_true_train = train_dataset.target


    acc = (y_pred_train == y_true_train).mean()

    fpr, tpr, _ = roc_curve(y_true_train, train_probs)
    roc_auc = auc(fpr, tpr)


    average_precision = average_precision_score(y_true_train, train_probs)

print('Average precision-recall score: {0:0.2f}'.format(
      average_precision))

print(f'Train ROC AUC Score: {roc_auc}')
print(f"The Train Accuracy of the model is {round(accuracy_score(y_true_train,y_pred_train),3)*100} %")

print(
    f"Precision & Recall Report of model is,\n\n{classification_report(y_true_train, y_pred_train)}\n"
)
```

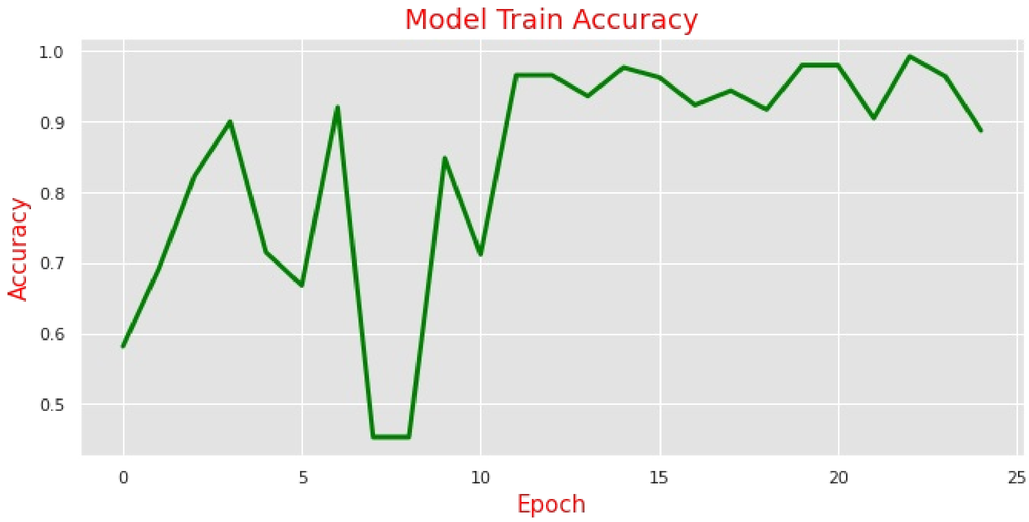
```
Average precision-recall score: 1.00
Train ROC AUC Score: 0.9992564023755465
The Train Accuracy of the model is 99.2 %
Precision & Recall Report of model is,

              precision    recall  f1-score   support

           0       0.99      0.99      0.99       349
           1       0.99      0.99      0.99       289

    accuracy                           0.99       638
   macro avg       0.99      0.99      0.99       638
weighted avg       0.99      0.99      0.99       638
```

In [28]:

```
#plotting the loss
plt.figure(figsize=(11, 5))


plt.plot(losses, c='green')

plt.title('Model Train Loss', size=18, color='red')
plt.ylabel('Loss', color='red', size=15)
plt.xlabel('Epoch', color='red', size=15)
plt.xticks(list(range(0,Epochs+1,5)))

plt.show()
```

In [29]:

```
#printing the accuracy
plt.figure(figsize=(11, 5))


plt.plot(accur, c='green')

plt.title('Model Train Accuracy', size=18, color='red')
plt.ylabel('Accuracy', color='red', size=15)
plt.xlabel('Epoch', color='red', size=15)
plt.xticks(list(range(0,Epochs + 1,5)))
plt.show()
```



In [30]:

```
model = Net(embeddings_shape=len(word2idx) , embedding_dim=7, hidden_layer=16)
model.load_state_dict(torch.load('model_best.pt'))
```

Out[30]:

```
<All keys matched successfully>
```

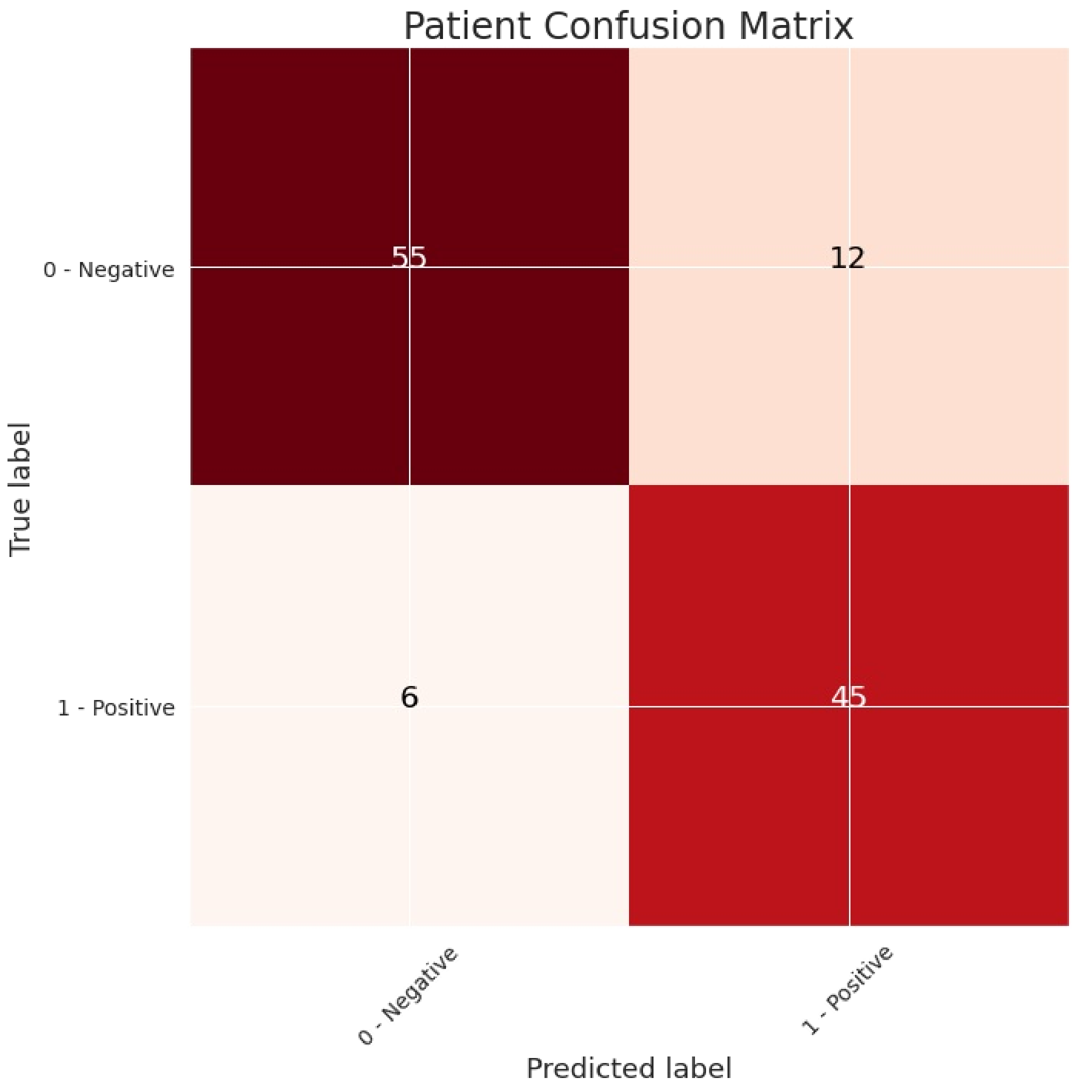
In [31]:

```
model = model.eval()
with torch.no_grad():
    #accuracy
    predicted = model(torch.tensor(test_dataset.padded,dtype=torch.int64))


    test_probs =  predicted.reshape(-1).detach().numpy()


    y_pred_test = test_probs.round()
    y_true_test = test_dataset.target

    acc = (y_pred_test == y_true_test).mean()

    fpr, tpr, _ = roc_curve(y_true_test, test_probs)
    roc_auc = auc(fpr, tpr)


    average_precision = average_precision_score(y_true_test, test_probs)

print('Average precision-recall score: {0:0.2f}'.format(
      average_precision))

print(f'Test ROC AUC Score: {roc_auc}')
print(f"The Accuracy of the model is {round(accuracy_score(y_true_test,y_pred_test),3)*100} %")

print(
    f"Precision & Recall Report of model is,\n\n{classification_report(y_true_test, y_pred_test)}\n"
)
```

```
Average precision-recall score: 0.90
Test ROC AUC Score: 0.9350307287093942
The Accuracy of the model is 84.7 %
Precision & Recall Report of model is,

              precision    recall  f1-score   support

           0       0.90      0.82      0.86        67
           1       0.79      0.88      0.83        51

    accuracy                           0.85       118
   macro avg       0.85      0.85      0.85       118
weighted avg       0.85      0.85      0.85       118
```

In [32]:

```
# Let's plot it out
cm = confusion_matrix(y_true_test, y_pred_test)
plot_confusion_matrix(cm, classes = ['0 - Negative', '1 - Positive'],
                      title = 'Patient Confusion Matrix', cmap=plt.cm.Reds)
```



In [33]:

```
evaluate_model(y_test=y_true_test,
               y_pred=y_pred_test,
               probs=test_probs,
               y_train = y_true_train,
               train_predictions=y_pred_train,
               train_probs=train_probs)
```

```
Recall Baseline: 1.0 Test: 0.88 Train: 0.99
Precision Baseline: 0.43 Test: 0.79 Train: 0.99
Roc Baseline: 0.5 Test: 0.94 Train: 1.0
```