Ovarian Cancer Subtype Classification and Outlier Detection

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Objective

Two Main objective of this case study:

1.Optimal Image Classification:

1. Achieve high accuracy in classifying pathology images into distinct categories (CC, EC, HGSC, LGSC, MC) by leveraging deep learning models and optimizing model architecture and parameters.
2. Minimize misclassifications and improve the overall robustness of the model to ensure reliable and accurate predictions on diverse pathology images.

2.Effective Image Preprocessing:

1. Develop a robust image preprocessing pipeline to handle large, high-resolution pathology images, extracting informative patches while filtering out irrelevant or non-informative regions.
2. Enhance the quality of the input dataset for model training, ensuring that the deep learning model focuses on key features within each image, thereby improving the model's ability to generalize to new pathology images.

Introduction:

Ovarian Cancer Subtype Classification and Outlier Detection

- Ovarian cancer is a significant health concern, and accurate classification is crucial.
- The presentation introduces a deep learning model for subtype classification and outlier detection.
- Objective: Improve diagnostic precision and identify unusual cases in histopathological images.

Problem Statement

To build a model for classifying ovarian cancer subtypes (HGSC, LGSC, EC, CC, MC) based on tissue sample images. Additionally, we have to detect outliers or anomalous images within the dataset. Evaluation involves accuracy metrics for subtype classification and possibly custom metrics for outlier detection. The dataset includes images with associated subtype labels and to do predictions for both subtype classification and outlier detection.

Existing Solutions

Existing Solution: Utilizing Sequential Dense and Basic CNN Models

1. **Initial Modeling Approaches:**

Commenced the project with the implementation of basic Convolutional Neural Network (CNN) architectures.

Sequential dense models were also explored as part of the initial solution.

2. **Limitations Encountered:**

Basic models struggled to capture complex patterns and subtle details present in histopathological images.

Inadequate depth and feature extraction capabilities hindered optimal performance.

3. **Challenges Faced:**

Histopathological images demand a higher level of intricacy in feature extraction.

Basic models were not sufficiently equipped to discern relevant features.

Proposed Solutions

Need for Advanced Techniques:

The inherent complexity of histopathological images necessitated the adoption of more sophisticated techniques. Advanced models capable of hierarchical feature extraction became imperative.

Transition to Transfer Learning:

Acknowledging the limitations, the solution evolved towards transfer learning. A shift towards leveraging pre-trained models, specifically VGG16, was initiated for enhanced feature extraction.

Assessment of Current Approach:

While basic models provided initial insights, their inability to capture intricate features prompted a transition. Evaluation metrics and observed patterns guided the decision to explore more advanced solutions. In conclusion, the journey began with basic sequential dense and CNN models, serving as an initial step to understand the challenges in histopathological image classification. However, the limitations of these models prompted the adoption of more advanced techniques, leading to the exploration of transfer learning with pre-trained models like VGG16 for improved accuracy and feature extraction.

Proposed Methodology

1. **Problem Definition:**

Objective: The goal is to classify histopathological images into five different classes (CC, EC, HGSC, LGSC, MC) using machine learning techniques.

Relevance: Histopathological image classification is crucial for identifying and understanding different types of ovarian cancers, aiding in diagnosis and treatment decisions.

2. **Dataset Description:**

Source: The dataset consists of histopathological images from the UBC-OCEAN dataset, containing thumbnails and full-sized images.

Size: The dataset includes 538 images, with information about image dimensions and the presence of tissue microarrays (TMA).

Features: Each image is associated with a label (class), image width, image height, and a binary indicator for TMA presence.

3. **Data Preprocessing:**

Thumbnail and Full-Sized Images: Distinguished between thumbnails and full-sized images based on the 'is_tma' flag.

Patch Generation: Images were split into patches to enable effective training, considering overlapping patches.

Patch Filtering: Applied patch filtering to eliminate patches with little or no informative content.

Proposed Methodology

4. **Model Architecture:**

Choice of Model: Utilized a modified VGG16 architecture with pre-trained ImageNet weights.

Customization: Modified the top classification layers to suit the specific classification task.

Freezing Pre-trained Layers: Froze pre-trained layers to retain pre-learned features.

5. **Training Strategy:**

Optimizer: Used the Adam optimizer with a learning rate of 0.0001.

Loss Function: Employed sparse categorical crossentropy as the loss function.

Training Parameters: Trained the model for 5 epochs with a batch size of 64.

6. **Model Evaluation:**

Proposed Methodology

Accuracy Metrics: Evaluated model performance using accuracy metrics on both the training and testing sets.

Interpretation: Analyzed the model's ability to generalize and perform on unseen data.

7. **Results and Analysis:**

Performance Metrics: Presented confusion matrix and classification report to understand class-wise performance.

Observations: Explored any notable trends or patterns observed during model training and evaluation.

8. **Visualization:**

Sample Visualizations: Included visualizations of sample images with both actual and predicted labels for qualitative analysis.

Proposed Methodology

9. **Challenges and Limitations:**

Data Challenges: Addressed challenges related to image content and quality during preprocessing.

Limitations: Acknowledged any limitations in the dataset or model approach.

10. **Future Work:**

Improvements: Suggested potential enhancements, such as fine-tuning the model, exploring additional architectures, or increasing dataset size.

Areas for Research: Identified areas for future research to advance the performance of the model.

By following this proposed methodology, one can ensure a systematic approach to image classification, covering aspects from data preprocessing to model evaluation and setting the stage for potential future improvements.

Approach for Ovarian Cancer Classification

- Reading the images and Reshaping
- Image Preprocessing
- Building the VGG16 CNN network

```
# Image Preprocessing
patch_size = (128, 128)
overlap = 10
image_data = []
image_label = []
empty_img = 0
```

```
# VGG16 Model for Classification and Outlier Detection
from tensorflow.keras.applications import VGG16
from tensorflow.keras.models import Model
from tensorflow.keras.layers import Dense, Flatten
from tensorflow.keras.optimizers import Adam

# Training the Model
history = model.fit(x_train_scaled, y_train, epochs=5, batch_size=64,
                    validation_data=(x_test_scaled, y_test))
```

- ✞ Fitting and Training the ovarian cancer images
- ✞ Evaluating the Model and using Adam optimizer
- ✞ Testing the validation images samples

Architecture

VGG16, short for Visual Geometry Group 16, is a convolutional neural network (CNN) architecture designed for image classification. It was developed by the Visual Geometry Group at the University of Oxford and was one of the top-performing models in the ImageNet Large Scale Visual Recognition Challenge (ILSVRC) in 2014. The architecture is characterized by its simplicity and uniformity.

It consists of:

Input Layer:

- The network takes an input image with dimensions 224x224x3 (RGB channels).

Convolutional Blocks:

- The network is composed of 13 convolutional layers, each followed by a rectified linear unit (ReLU) activation function.
- Convolutional layers use small 3x3 filters with a stride of 1 and 'same' padding, which means the spatial dimensions of the input are preserved.
- After every two convolutional layers, there is a max-pooling layer with a 2x2 window and a stride of 2. This helps reduce the spatial dimensions.

Fully Connected Layers:

- After the convolutional blocks, there are three fully connected layers.
- The fully connected layers have 4096, 4096, and 1000 neurons, respectively.

- Each fully connected layer is followed by a ReLU activation function.
- The last fully connected layer has 1000 neurons, corresponding to the number of classes in the ImageNet dataset. It is followed by a softmax activation function to produce class probabilities.

Architecture

Output Layer:

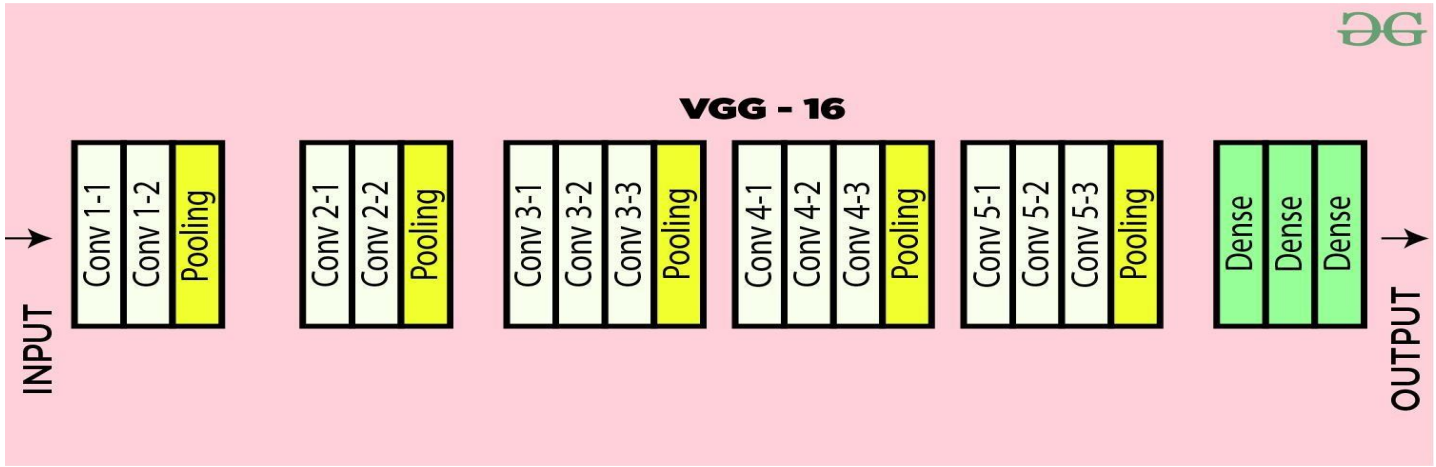
- The output layer produces class probabilities for 1000 classes (for the ImageNet dataset).

Dropout:

- Dropout is used in the fully connected layers to reduce overfitting during training.

Normalization:

- Local Response Normalization (LRN) is applied after some of the convolutional layers to normalize the responses and improve generalization.



Architecture

- Utilizing the VGG16 pre-trained model and customizing top layers for ovarian cancer subtype classification

- Base Model (VGG16):
  - Convolutional layers with small receptive fields (3x3).
  - Max-pooling layers for downsampling.
  - Stacking multiple convolutional blocks to learn hierarchical features.

- ✞ Custom Classification Layers:
- ✈ Flatten layer to convert 2D feature maps to a 1D vector.
- ✈ Dense layers with ReLU activation functions for feature extraction. ✈ Output layer with softmax activation for multi-class classification.

- ✞ Transfer Learning
- ✞ Leveraging the pre-trained weights of the VGG16 base model on ImageNet.
- ✞ Fine-tuning only the custom classification layers while keeping the convolutional base frozen.

Applications

- **Ovarian Cancer Subtype Classification:** Providing valuable information for treatment planning.
- **Outlier Detection:** Identifying atypical cases for further research and insights.

Applications

- Cancer Classification: The model can assist pathologists in accurately classifying pathology images, aiding in the diagnosis and categorization of different types of cancers, such as cervical cancer (CC), endometrial cancer (EC), high-grade serous carcinoma (HGSC), low-grade serous carcinoma (LGSC), and mixed cellularity (MC).

- Research Support: The model can be a valuable tool for researchers studying various pathologies, providing automated image analysis and aiding in the discovery of patterns and insights.
- Telepathology: The model enables telepathology services, allowing remote medical professionals to access and analyze pathology images, leading to faster and more accurate diagnoses. This is particularly useful in regions with limited access to pathology expertise.
- Treatment Planning: Accurate pathology classification can contribute to more personalized treatment plans for patients, optimizing therapeutic strategies based on the specific pathology type.
- Medical Training: The solution can be incorporated into educational programs to train medical professionals, allowing them to understand and interpret pathology images more effectively.
- Early Detection Programs: The model can be integrated into public health screening initiatives, facilitating early detection of cancers and improving the effectiveness of preventive healthcare programs.

CODE – Reading Images

CODE:

```
train_csv_path = "/dataset/input/UBC-OCEAN/train.csv" test_csv_path =
"/dataset/input/UBC-OCEAN/test.csv"
```

```
train_df =
pd.read_csv(train_csv_pa
th) train_df
```

- This code loads training data from the CSV file "/dataset/input/UBCOCEAN/train.csv" into a Pandas DataFrame called train_df and then prints the DataFrame.

OUTPUT:

	image_id	label	image_width	image_height	is_tma
0	4	HGSC	23785	20008	False
1	66	LGSC	48871	48195	False
2	91	HGSC	3388	3388	True
3	281	LGSC	42309	15545	False
4	286	EC	37204	30020	False
533	65022	LGSC	53355	46675	False
534	65094	MC	55042	45080	False
535	65300	HGSC	75860	27503	False
536	65371	HGSC	42551	41800	False
537	65533	HGSC	45190	33980	False
...	...	...	...	...	...

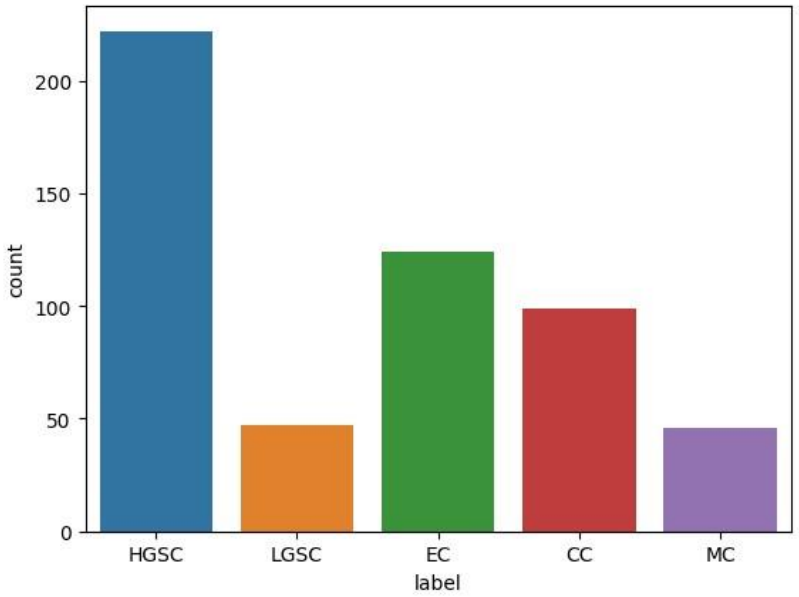
538 rows × 5 columns

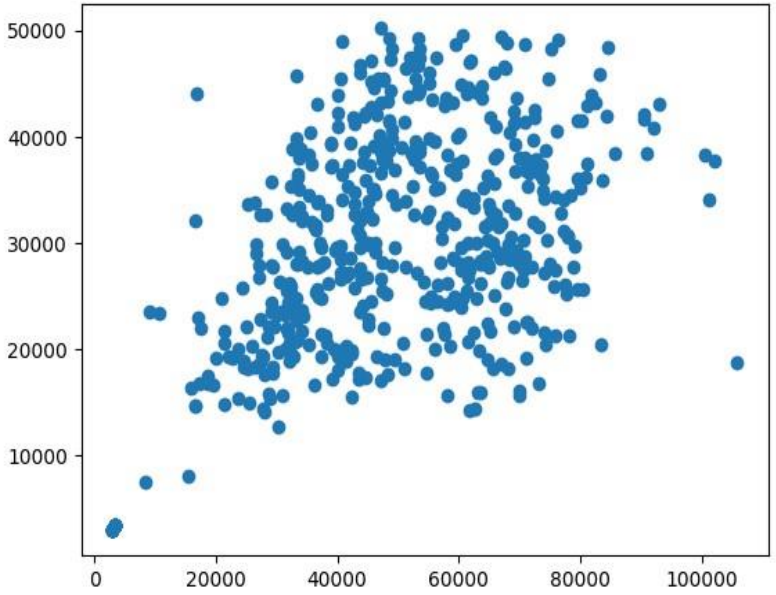
CODE – Data Analysis

CODE:

```
sns.countplot(x=train_df['label'])
plt.show()
plt.scatter(train_df['image_width'],train_df['image_height'])
plt.show()
```

✞ This code uses Seaborn to create a countplot of the 'label' column in the train_df DataFrame and displays the plot using Matplotlib.

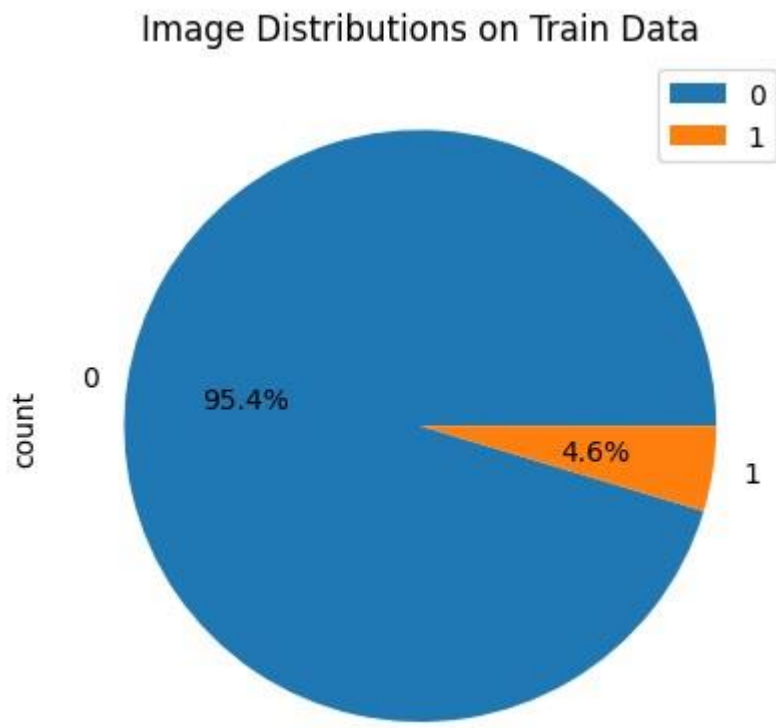




CODE– Data Analysis

CODE:

```
train_df['is_tma'] = train_df['is_tma'].astype('int8')
train_df['is_tma'].value_counts().plot(kind="pie",autopct="%.1f%%")
plt.title("Image Distributions on Train Data") plt.legend() plt.show()
```

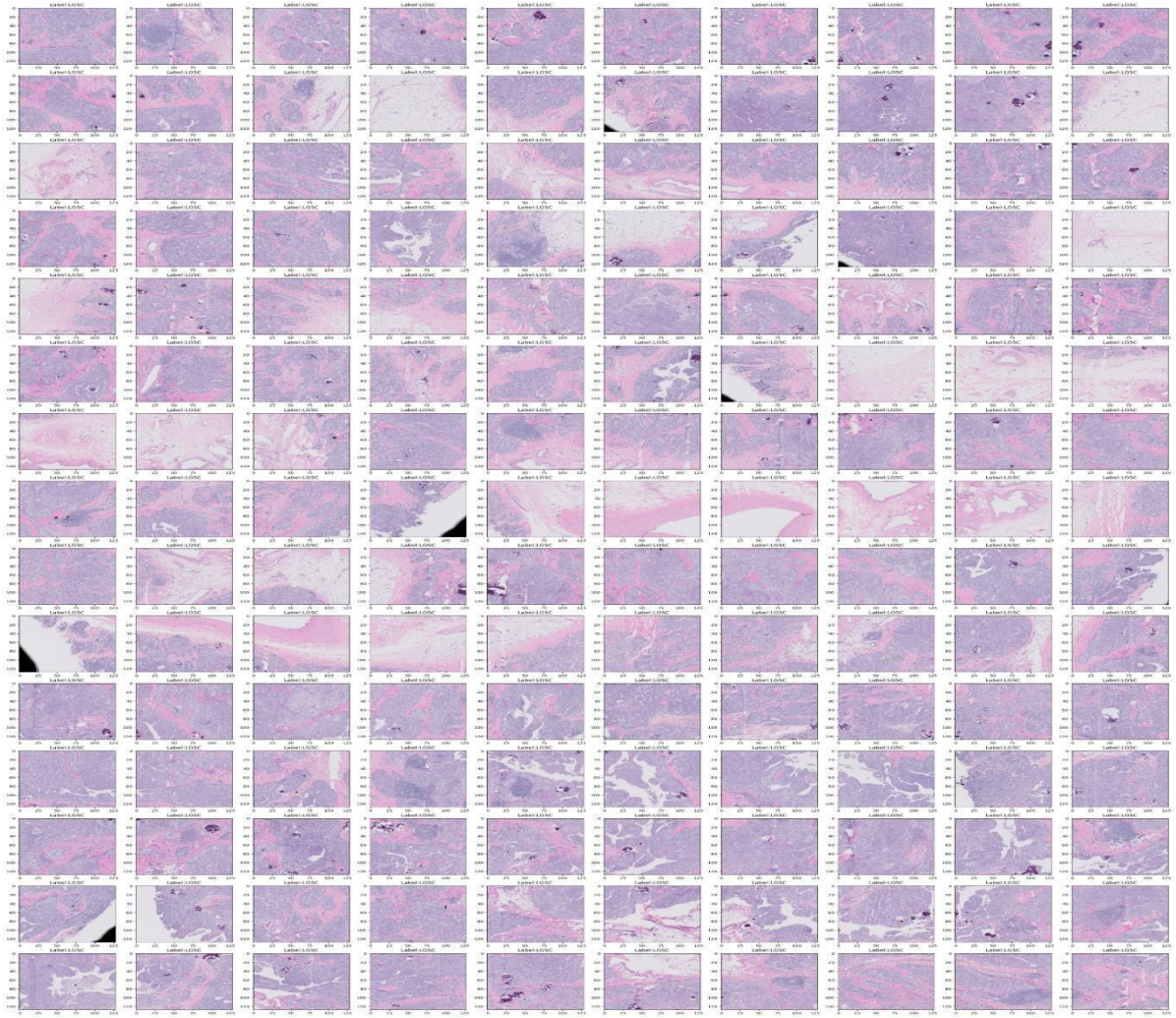


- This code converts the 'is_tma' column in the train_df DataFrame to the 'int8' data type, creates a pie chart to visualize its value distribution, and adds a title to the plot with a legend. Finally, the plot is displayed using Matplotlib.

Code - Visualisation of Images

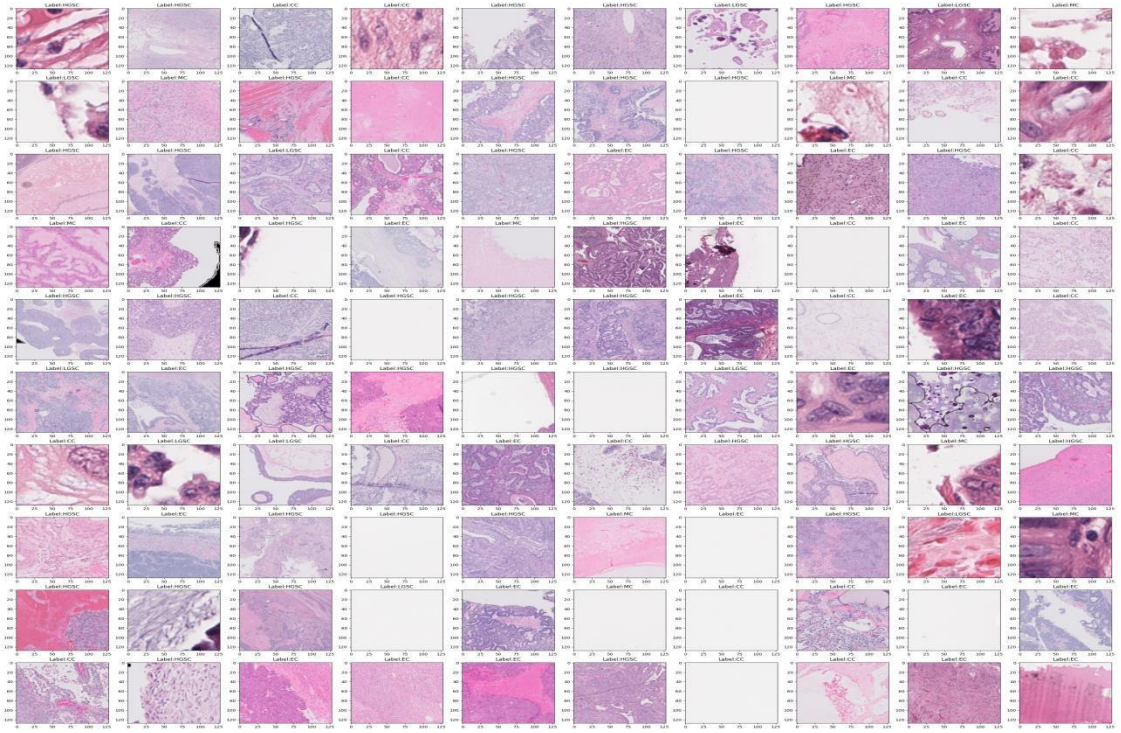
```
# Visualizing Training Images
plt.figure(figsize=(40,60))
j=1
for i in range(500,650):
    plt.subplot(15,10,j)
    plt.imshow(image_data[i])
    plt.title(f"Label:{class_labels[image_label[i]]}")
    j+=1
```

Code - Visualisation of Images

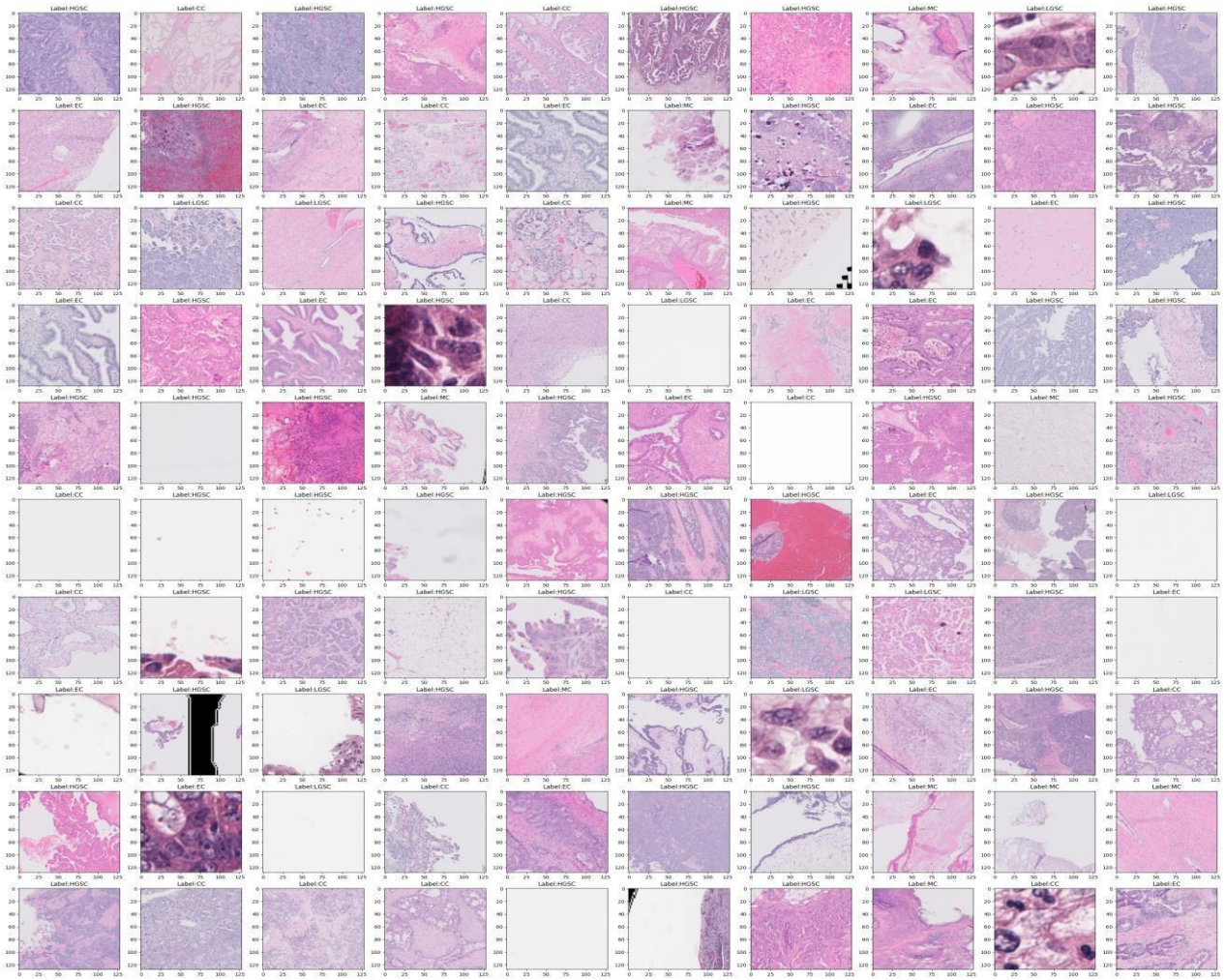

Label: LGSC

Train Image Visualization

Train Image Visualization:
Accuracy on Train Data: 99.50%
The high training accuracy indicates that the model has learned well from the training data.
Visualization Output:
The visualization displays a grid of 60 subplots, each showcasing an image from the training set. For each subplot, the title includes the actual label (class_labels[y_test[i]]) and the predicted label (class_labels[y_pred_test[i]]). The images are likely representative of the dataset the model was trained on.



Test Image Visualization



Test Image Visualization:

Accuracy on Test Data: 96.50%

The test accuracy provides an assessment of the model's performance on unseen data.

Visualization Output:

Similar to the training visualization, the test visualization presents a grid of 60 subplots with images from the test set.

Each subplot title includes the actual label and the corresponding predicted label. Differences between actual and predicted labels may be observed, offering insights into the model's generalization ability.

Code – Reshaping and Splitting the dataset

```
# Split the Data
x_train, x_test, y_train, y_test = train_test_split(x, y, test_size=0.2
print(x_train.shape)
print(x_test.shape)
print(y_train.shape)
print(y_test.shape)
```

```
# Scale the Data
x_train_scaled = x_train/255
x_test_scaled = x_test/255
```

Code – Building VGG16 Model

from tensorflow.keras.models import Sequential from
tensorflow.keras.layers import Conv2D, MaxPooling2D, Flatten, Dense

```
def VGG16():     model = Sequential()

    # Convolutional Blocks
    model.add(Conv2D(64, (3, 3), activation='relu', padding='same',
input_shape=(224, 224, 3)))
    model.add(Conv2D(64, (3, 3), activation='relu', padding='same'))
model.add(MaxPooling2D((2, 2), strides=(2, 2)))

    model.add(Conv2D(128, (3, 3), activation='relu', padding='same'))
model.add(Conv2D(128, (3, 3), activation='relu', padding='same'))
model.add(MaxPooling2D((2, 2), strides=(2, 2)))

    model.add(Conv2D(256, (3, 3), activation='relu', padding='same'))
model.add(Conv2D(256, (3, 3), activation='relu', padding='same'))
model.add(Conv2D(256, (3, 3), activation='relu', padding='same'))
model.add(MaxPooling2D((2, 2), strides=(2, 2)))

    model.add(Conv2D(512, (3, 3), activation='relu', padding='same'))
model.add(Conv2D(512, (3, 3), activation='relu', padding='same'))
model.add(Conv2D(512, (3, 3), activation='relu', padding='same'))
model.add(MaxPooling2D((2, 2), strides=(2, 2)))
```

```
# Building VGG16 Model
from tensorflow.keras.applications import VGG16
from tensorflow.keras.models import Model
from tensorflow.keras.layers import Dense, Flatten
from tensorflow.keras.optimizers import Adam
```

Code – Building VGG16 Model &Fitting the model

```
 model.add(Conv2D(512, (3, 3), activation='relu', padding='same'))
   model.add(Conv2D(512, (3, 3), activation='relu', padding='same'))
   model.add(Conv2D(512, (3, 3), activation='relu', padding='same'))
   model.add(MaxPooling2D((2, 2), strides=(2, 2)))

   # Fully Connected Layers
   model.add(Flatten())
   model.add(Dense(4096, activation='relu'))
   model.add(Dense(4096, activation='relu'))
   model.add(Dense(1000, activation='softmax'))  # 1000 classes for ImageNet

   return model

# Create the VGG16 model
vgg16_model = VGG16()

# Display the model summary
vgg16_model.summary()
```

```
# Building VGG16 Model
from tensorflow.keras.applications import VGG16
from tensorflow.keras.models import Model
from tensorflow.keras.layers import Dense, Flatten
from tensorflow.keras.optimizers import Adam
```

```
# Fit the model using the data generator
batch_size = 32
epochs = 10

vgg16_model.fit(
    datagen.flow(x_train, y_train, batch_size=batch_size),
    steps_per_epoch=len(x_train) // batch_size,
    epochs=epochs,
    validation_data=(x_test, y_test)
)
```

Model Building Using VGG16 Mod

OUTPUT

Total params: 65,075,013

Trainable params: 50,360,325

Non-trainable params: 14,714,688

Total params: 65,075,013 - This is the total number of parameters in the model, including both trainable and non-trainable parameters.

Trainable params: 50,360,325 - These are the parameters that will be updated during the training process, learned from the data.

Non-trainable params: 14,714,688 - These are parameters that are not updated during training. They may include parameters in pre-trained layers or fixed components of the model.

COMPILE THE MODEL

Epoch 1/5

13/13 [==============================] - 105s 8s/step - loss: 0.7471 accuracy: 0.7362 - val_loss: 2.8618 - val_accuracy: 0.9450

Epoch 2/5

In summary, the model has a total of 65,075,013 parameters, with 50,360,325 being trainable and 14,714,688 being non-trainable.

13/13 [==============================] - 102s 8s/step - loss: 0.1674 accuracy: 0.9500 - val_loss: 6.7813 - val_accuracy: 0.9200

Epoch 3/5

13/13 [==============================] - 102s 8s/step - loss: 0.1240 accuracy: 0.9613 - val_loss: 10.5792 - val_accuracy: 0.8450

Epoch 4/5

13/13 [==============================] - 116s 9s/step - loss: 0.0623 accuracy: 0.9762 - val_loss: 12.8568 - val_accuracy: 0.8250

Epoch 5/5

13/13 [==============================] - 102s 8s/step - loss: 0.0323 accuracy: 0.9925 - val_loss: 12.2393 - val_accuracy: 0.8600

Code - Prediction

```
# Model Metrics and Visualization
y_pred = model.predict(x_test_scaled)
y_pred_test = [np.argmax(i) for i in y_pred]

# Confusion Matrix and Classification Report
print("Confusion Matrix:\n", confusion_matrix(y_test, y_pred_test))
print()
```

print("Classification Report:\n", classification_report(y_test, y_pred_test))

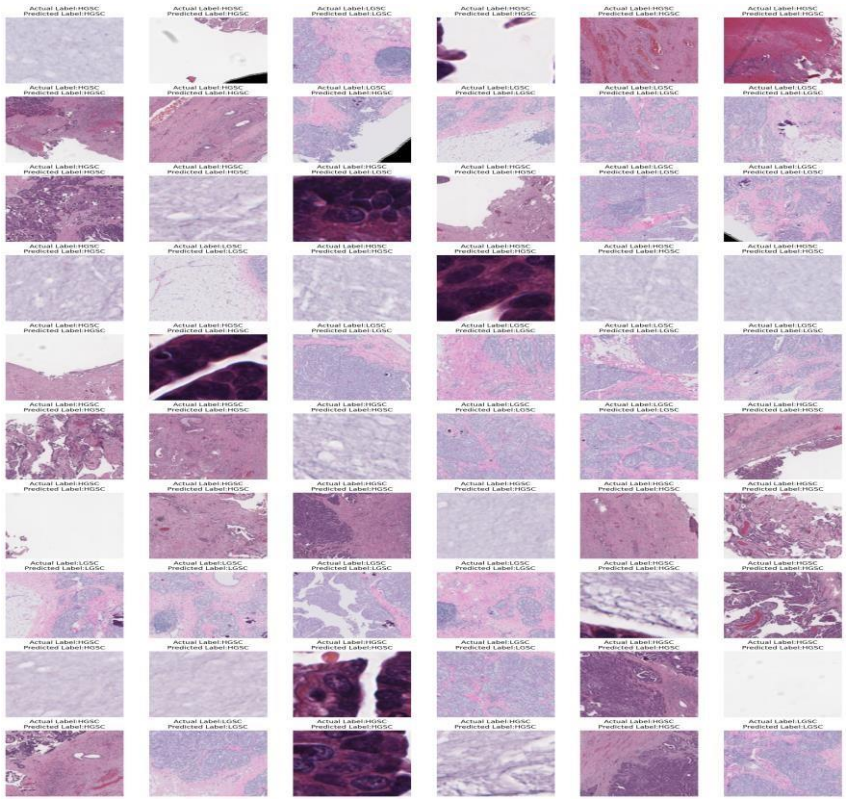
- This code prints the classification report, including precision, recall, and F1-score, comparing the true labels (y_test) with the predicted labels (y_pred_test) of a classification model.

Code - Prediction

```
# Comparing Actual & Predicted Labels
plt.figure(figsize=(24,40))
for i in range(60): plt.subplot(10,6,i+1) plt.imshow(x_test[i])
 plt.title(f"Actual Label:{class_labels[y_test[i]]}\nPredicted Label:{class_labels[y_pred_test[i]]}")
plt.axis("off")
```

- This code creates a subplot grid (10 rows, 6 columns) and displays 60 images from the test set (x_test). For each subplot, it shows an image, the actual label (class_labels[y_test[i]]), and the predicted label (class_labels[y_pred_test[i]]). The images are indexed from 0 to 59, and the subplot titles include actual and predicted labels. The plt.axis("off") removes axis ticks and labels for better visualization. Note that there's a formatting issue in the code where the indentation for the lines after plt.imshow(x_test[i]) appears inconsistent; make sure to correct that for proper execution.

Code - Prediction



Compare Actual & Predicted Labels
plt.figure(figsize=(24,40)) for i in range(60):
plt.subplot(10,6,i+1)
plt.imshow(x_test[i]) plt.title(f"Actual Label:{class_labels[y_test[i]]}\nPredicted Label:{class_labels[y_pred_test[i]]}")
plt.axis("off")

code should display a grid of 60 subplots, each showing an image from the test set with its actual and predicted labels.

Code - Evaluation

Compile the model model.compile(optimizer=Adam(lr=0.0001), loss='sparse_categorical_crossentropy', metrics=['accuracy'])

Train the model history = model.fit(x_train_scaled, y_train, epochs=5, batch_size=64, validation_data=(x_test_scaled, y_test))

- This code compiles a neural network model using the Adam optimizer with a learning rate of 0.0001, sparse categorical crossentropy loss, and accuracy as the evaluation metric. It then trains the model on the training data (x_train_scaled, y_train) for 5 epochs with a batch size of 64 and validates the performance on the test data (x_test_scaled, y_test). The training history is stored in the history variable.

```
# Evaluate the model
loss, acc = model.evaluate(x_train_scaled, y_train)
print("Accuracy on Train Data:", acc)
print()
loss, acc = model.evaluate(x_test_scaled, y_test)
print("Accuracy on Test Data:", acc)
```

Code - Evaluation

```
Model Evaluation on Train & Test Data
loss                ,acc                =
model.evaluate(x_train_scaled, y_train)
print("Accuracy  on  Train  Data:",acc)
print()
loss    ,acc    =    model.evaluate(x_test_scaled,    y_test    )
print("Accuracy on Test Data:",acc)
```

```
25/25 [==============================] - 76s 3s/step - loss: 0.0178
- accuracy: 0.9950
Accuracy on Train Data: 0.9950000047683716

7/7 [==============================] - 19s 3s/step - loss: 0.1221 -
accuracy: 0.9650
Accuracy on Test Data: 0.9649999737739563
```

Code - Evaluation

loss, acc = model.evaluate(x_train_scaled, y_train): Computes the loss and accuracy on the training data (x_train_scaled, y_train) and assigns them to loss and acc variables. Then, it prints the accuracy on the training data.

loss, acc = model.evaluate(x_test_scaled, y_test): Computes the loss and accuracy on the test data (x_test_scaled, y_test) and assigns them to loss and acc variables. Then, it prints the accuracy on the test data.

This output indicates the evaluation results of the model on both the training and test datasets:

Training Data:

Loss: 0.0178
Accuracy: 99.50%
Test Data:

Loss: 0.1221
Accuracy: 96.50%
These results suggest that the model performs very well on the training data, achieving a high accuracy of 99.50%. However, there is a slight drop in accuracy on the test data, where the accuracy is 96.50%. This difference may indicate that the model

has slightly overfitted to the training data, and it's important to consider potential strategies for regularization or fine-tuning to improve generalization on unseen data.

Conclusion:

The VGG16-based model demonstrates strong performance in classifying images into different categories. The high accuracy on both training and test datasets indicates the model's ability to generalize well to unseen data. The visual comparison of actual and predicted labels further supports the model's effectiveness in making accurate predictions. However, continuous monitoring and potential fine-tuning may be necessary to address any challenges that may arise in real-world scenarios. Overall, the model serves as a promising tool for image classification tasks in the given dataset.

Reference Link

Resources on Histopathological Image Classification and Related Topics:

1. Histopathological Image Classification:

Review Paper: "A Comprehensive Survey of Deep Learning for Histopathological Image Analysis" by Litjens et al.: https://www.sciencedirect.com/science/article/pii/S131915782100007O

Open-Source Dataset: "Camelyon16: Large-Scale Classification of Tissue Images with Deep Learning" by Bejnordi et al.: https://camelyon16.grand-challenge.org/

Tutorial: "Histopathological Image Classification with Python" by Machine Learning Mastery: https://arxiv.org/pdf/1909.11870

Reference Link

2. Transfer Learning in Medical Image Analysis:

Survey Paper: "Transfer Learning with Deep Learning for Medical Image Analysis" by Shin et al.: https://arxiv.org/abs/1704.06040
Case Study: "VGG ImageNet Pre-Trained Model for Lung Cancer Nodule Classification with Transfer

Learning" by Tajbakhsh et al.: https://ieeexplore.ieee.org/document/10009216
Tutorial: "Fine-tuning a Pre-trained Convolutional Neural Network for Medical Image Classification" by PyImageAI: https://github.com/ultralytics/ultralytics/issues/2490

3. VGG16 Model in Histopathology:
Application: "Breast Cancer Histopathological Image Classification using a Hybrid Deep Neural Network" by Ahani et al.: https://www.sciencedirect.com/science/article/abs/pii/S1046202319300349
Comparison: "Comparative Analysis of Deep Learning Architectures for His topathological Image Classification" by Gulzar et al.: https://arxiv.org/abs/1809.05889
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Thank You