# ABSTRACT

Remarkable advances in biomedical research have led to the generation of large amounts of data. Using artificial intelligence, it has become possible to extract meaningful information from large volumes of data, in a shorter frame of time, with very less human interference. In effect, convolutional neural networks (a deep learning method) have been taught to recognize pathological lesions from images. Diabetes to be screened for diabetic retinopathy (DR). Diabetic Retinopathy is a significant complication of diabetes, produced by high blood sugar level, which causes damage to the retina. Effective diabetic retinopathy screening is required because diabetic retinopathy does not show any symptoms in the initial stages, and can cause blindness if it is not diagnosed and treated promptly. Deep neural networks offer a great advantage of screening for DR from retinal images, in improved identification of DR lesions and risk factors for diseases, with high accuracy and reliability. This report presents a novel This paper presents a novel diabetic retinopathy automatic detection in retinal images by implementing efficient image processing and deep learning techniques. The paper investigates the capability of image pre-processing techniques based on data augmentation as well as deep learning for diabetic retinopathy. Computer-assisted clinical decision-making is inevitably transforming the diabetic retinopathy detection and management today, which is crucial for clinicians and patients alike. Therefore, a high degree of accuracy, with which computer algorithms can detect the diabetic retinopathy is absolutely needed.

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# 1. PROBLEM STATEMENT

The problem statement is an open challenge problem in Kaggle Competition. This problem aims to develop a system which could help ophthalmologists to detect blindness before it happened. Millions of people suffer from diabetic retinopathy, the leading cause of blindness among working aged adults. In India, Aravind Eye Hospital hopes to detect and prevent this disease among people living in rural areas where medical screening is difficult to conduct. APTOS (Asia Pacific Tele-Ophthalmology Society Symposium) has provided eye fundus images under a variety of imaging conditions with labels to detect the DR level in retinal images of person. Each image is rated on a scale of 0 to 4:

0 – No DR

1 – Mild

2 – Moderate

3 – Severe

4 – Proliferative DR

Detect the locations of DR on retinal images and scale DR levels from 0 to 4.

# 2. PROJECT DESCRIPTION

Diabetic retinopathy is the leading cause of blindness in the working-age population of the developed world. It is estimated to affect over 93 million people. The US Centre for Disease Control and Prevention estimates that 29.1 million people in the US have diabetes and the World Health Organization estimates that 347 million people have the disease worldwide. Diabetic Retinopathy (DR) is an eye disease associated with long-standing diabetes. Around 40% to 45% of Americans with diabetes have some stage of the disease. Progression to vision impairment can be slowed or averted if DR is detected in time, however this can be difficult as the disease often shows few symptoms until it is too late to provide effective treatment.

Currently, detecting DR is a time-consuming and manual process that requires a trained clinician to examine and evaluate digital color fundus photographs of the retina. By the time human readers submit their reviews, often a day or two later, the delayed results lead to lost follow up, miscommunication, and delayed treatment.

Clinicians can identify DR by the presence of lesions associated with the vascular abnormalities caused by the disease. While this approach is effective, its resource demands are high. The expertise and equipment required are often lacking in areas where the rate of diabetes in local populations is high and DR detection is most needed. As the number of individuals with diabetes continues to grow, the infrastructure needed to prevent blindness due to DR will become even more insufficient.

The need for a comprehensive and automated method of DR screening has long been recognized, and previous efforts have made good progress using image classification, pattern recognition, and machine learning. With color fundus photography as input, the goal of this competition is to push an automated detection system to the limit of what is possible – ideally resulting in models with realistic clinical potential. The winning models will be open sourced to maximize the impact such a model can have on improving DR detection.

# 3. LITERATURE

## I. Diabetic Retinopathy (DR)

Diabetic retinopathy, also known as diabetic eye disease, is a medical condition in which damage occurs to the retina due to diabetes mellitus. It is a leading cause of blindness. Diabetic retinopathy is the result of damage to the small blood vessels and neurons of the retina. The earliest changes leading to diabetic retinopathy include narrowing of the retinal arteries associated with reduced retinal blood flow; dysfunction of the neurons of the inner retina, followed in later stages by changes in the function of the outer retina, associated with subtle changes in visual function; dysfunction of the blood-retinal barrier, which protects the retina from many substances in the blood (including toxins and immune cells), leading to the leaking of blood constituents into the retinal neuropile.[1]Later, the basement membrane of the retinal blood vessels thickens, capillaries degenerate and lose cells, particularly pericytes and vascular smooth muscle cells. This leads to loss of blood flow and progressive ischemia, and microscopic aneurysms which appear as balloon-like structures jutting out from the capillary walls, which recruit inflammatory cells; and advanced dysfunction and degeneration of the neurons and glial cells of the retina.[1][2]

An experimental study suggests that pericyte death is caused by blood glucose persistently activating protein kinase C and mitogen-activated protein kinase (MAPK), which, through a series of intermediates, inhibits signalling through platelet-derived growth factor receptors — signalling that supports cellular survival, proliferation, and growth. The resulting withdrawal of this signalling leads to the programmed cell death (apoptosis) of the cells in this experimental model.[3]

Small blood vessels – such as those in the eye – are especially vulnerable to poor blood sugar (blood glucose) control. An overaccumulation of glucose damages the tiny blood vessels in the retina. During the initial stage, called non-proliferative diabetic retinopathy (NPDR), most people do not notice any change in their vision. Early changes that are reversible and do not threaten central vision are sometimes termed *simplex retinopathy* or *background retinopathy*.[4]

Some people develop a condition called macular edema. It occurs when the damaged blood vessels leak fluid and lipids onto the macula, the part of the retina that lets us see detail. The fluid makes the macula swell, which blurs vision.

**Fig 1:** Image of fundus showing scatter laser surgery for diabetic retinopathy

**Proliferative diabetic retinopathy**

As the disease progresses, severe non-proliferative diabetic retinopathy enters an advanced or proliferative (PDR) stage, where blood vessels proliferate/grow. The lack of oxygen in the retina causes fragile, new, blood vessels to grow along the retina and in the clear, gel-like vitreous humour that fills the inside of the eye. Without timely treatment, these new blood vessels can bleed, cloud vision, and destroy the retina. Fibrovascular proliferation can also cause tractional retinal detachment. The new blood vessels can also grow into the angle of the anterior chamber of the eye and cause neovascular glaucoma.

Non-proliferative diabetic retinopathy shows up as cotton wool spots, or microvascular abnormalities or as superficial retinal haemorrhages. Even so, the advanced proliferative diabetic retinopathy (PDR) can remain asymptomatic for a very long time, and so should be monitored closely with regular checkups.

## II. Statistics of blindness caused by DR

**Table 1:** Zone-wise distribution of diabetic patients screened and zone-wise prevalence**(Indian Journal of Ophthalmology)**

| Zones | Total screened patients | Percentage of screened patients from each zone | Zone-wise prevalence |
|---|---|---|---|
| North | 276 | 5.3 | 34.06 |
| East | 943 | 18.3 | 22.59 |
| West | 1646 | 31.9 | 21.75 |
| Central | 554 | 10.7 | 12.27 |
| Northeast | 106 | 2.1 | 14.15 |
| South | 1638 | 31.7 | 22.65 |

**Table 2:** Prevalence of diabetic retinopathy in relation to duration of diabetic mellitus **(Indian Journal of Ophthalmology)**

| Duration of Diabetic Mellitus | Prevalence of DR |
|---|---|
| < 6 months | 9.23 |
| 6 months - 5 years | 15.12 |
| > 5 years | 35.12 |

**Table 3:** Prevalence of diabetic retinopathy at different levels of visual acuity. The vision in the lesser seeing eye was considered for the purpose of evaluation **(Indian Journal of Ophthalmology)**

| Visual acuity in lesser seeing eye | Prevalence (%) |
|---|---|
| 6/6 | 11.17 |
| 6/9 | 19.41 |
| 6/12 | 22.80 |
| 6/18 | 25.21 |
| 6/24 | 27.32 |
| 6/36 | 31.13 |
| 6/60 | 25.68 |
| <6/60 | 35.60 |
| Hand movements or less | 28.00 |

## III. Signs and Symptoms

There may not have symptoms in the early stages of diabetic retinopathy. As the condition progresses, diabetic retinopathy symptoms may include:

- Spots or dark strings floating in your system (floaters)
- Fluctuating vision
- Impaired color vision
- Dark or empty areas in your vision
- Vision loss

## IV. Causes

Over time, too much sugar in your blood can lead to the blockage of the tiny blood vessels that nourish the retina, cutting off its blood supply. As a result, the eye attempts to grow new blood vessels. But these new blood vessels don't develop properly and can leak easily.

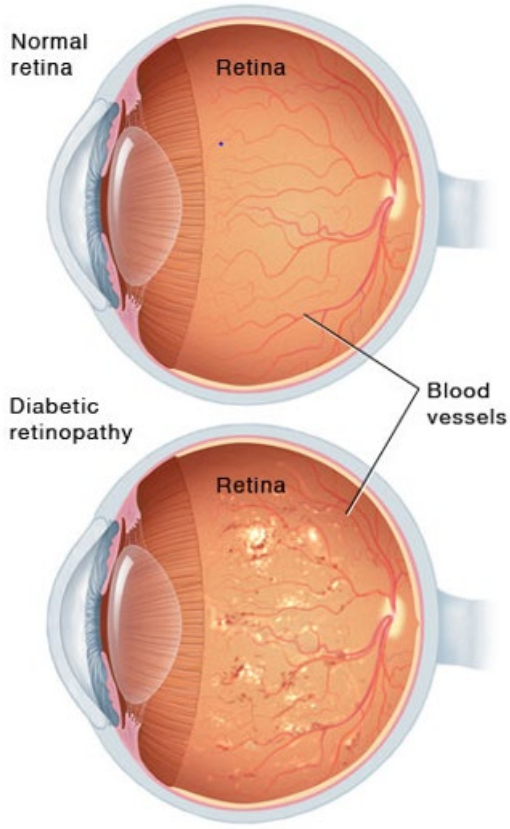


**Fig 2:** Normal Eye v/s Diabetic Retinopathy eye

There are two types of diabetic retinopathy:

- **Early diabetic retinopathy.** In this more common form — called non-proliferative diabetic retinopathy (NPDR) — new blood vessels aren't growing (proliferating).

  When you have NPDR, the walls of the blood vessels in your retina weaken. Tiny bulges (microaneurysms) protrude from the vessel walls of the smaller vessels, sometimes leaking fluid and blood into the retina. Larger retinal vessels can begin to dilate and become irregular in diameter, as well. NPDR can progress from mild to severe, as more blood vessels become blocked.

  Nerve fibres in the retina may begin to swell. Sometimes the central part of the retina (macula) begins to swell (macular edema), a condition that requires treatment.

- **Advanced diabetic retinopathy.** Diabetic retinopathy can progress to this more severe type, known as proliferative diabetic retinopathy. In this type, damaged blood vessels close off, causing the growth of new, abnormal blood vessels in the retina, and can leak into the clear, jelly-like substance that fills the center of your eye (vitreous).

  Eventually, scar tissue stimulated by the growth of new blood vessels may cause the retina to detach from the back of your eye. If the new blood vessels interfere with the normal flow of fluid out of the eye, pressure may build up in the eyeball. This can damage the nerve that carries images from your eye to your brain (optic nerve), resulting in glaucoma.

## V. Diagnosis

Diabetic retinopathy is detected during an eye examination that includes:

- **Visual acuity test:** Uses an eye chart to measure how well a person sees at various distances (i.e., visual acuity).
- **Pupil dilation:** The eye care professional places drops into the eye to dilate the pupil. This allows him or her to see more of the retina and look for signs of diabetic retinopathy. After the examination, close-up vision may remain blurred for several hours.
- **Ophthalmoscopy or fundus photography:** Ophthalmoscopy is an examination of the retina in which the eye care professional: (1) looks through a slit lamp biomicroscope with a special magnifying lens that provides a narrow view of the retina, or (2) wearing a headset (indirect ophthalmoscope) with a bright light, looks through a special

magnifying glass and gains a wide view of the retina. Hand-held ophthalmoscopy is insufficient to rule out significant and treatable diabetic retinopathy. Fundus photography generally captures considerably larger areas of the fundus, and has the advantage of photo documentation for future reference, as well as availing the image to be examined by a specialist at another location and/or time.

- **Fundus Fluorescein angiography (FFA):** This is an imaging technique which relies on the circulation of fluorescein dye to show staining, leakage, or non-perfusion of the retinal and choroidal vasculature.
- **Optical coherence tomography (OCT):** This is an optical imaging modality based upon interference, and analogous to ultrasound. It produces cross-sectional images of the retina (B-scans) which can be used to measure the thickness of the retina and to resolve its major layers, allowing the observation of swelling.

The eye care professional will look at the retina for early signs of the disease, such as:

1. leaking blood vessels,
2. retinal swelling, such as macular edema,
3. pale, fatty deposits on the retina (exudates) – signs of leaking blood vessels,
4. damaged nerve tissue (neuropathy), and
5. any changes in the blood vessels.

## VI. Risk Factors

Anyone who has diabetes can develop diabetic retinopathy. Risk of developing in the eye condition can increase as a result of:

- Duration of diabetes – the longer you have diabetes, the greater your risk of developing diabetic retinopathy
- Poor control of your blood sugar level
- High blood pressure
- High cholesterol
- Pregnancy
- Tobacco use
- Being African-American, Hispanic or Native American

## VII. Complications

Diabetic retinopathy involves the abnormal growth of blood vessels in the retina.
Complications can lead to serious vision problems:

- **Vitreous haemorrhage.** The new blood vessels may bleed into the clear, jelly-like substance that fills the center of your eye. If the amount of bleeding is small, you might see only a few dark spots (floaters). In more-severe cases, blood can fill the vitreous cavity and completely block your vision.

  Vitreous haemorrhage by itself usually doesn't cause permanent vision loss. The blood often clears from the eye within a few weeks or months. Unless your retina is damaged, your vision may return to its previous clarity.

- **Retinal detachment.** The abnormal blood vessels associated with diabetic retinopathy stimulate the growth of scar tissue, which can pull the retina away from the back of the eye. This may cause spots floating in your vision, flashes of light or severe vision loss.

- **Glaucoma.** New blood vessels may grow in the front part of your eye and interfere with the normal flow of fluid out of the eye, causing pressure in the eye to build up (glaucoma). This pressure can damage the nerve that carries images from your eye to your brain (optic nerve).

- **Blindness.** Eventually, diabetic retinopathy, glaucoma or both can lead to complete vision loss.

## VIII. Prevention

You can't always prevent diabetic retinopathy. However, regular eye exams, good control of your blood sugar and blood pressure, and early intervention for vision problems can help prevent severe vision loss.

If you have diabetes, reduce your risk of getting diabetic retinopathy by doing the following:

- **Manage your diabetes.** Make healthy eating and physical activity part of your daily routine. Try to get at least 150 minutes of moderate aerobic activity, such as walking, each week. Take oral diabetes medications or insulin as directed.

- **Monitor your blood sugar level.** You may need to check and record your blood sugar level several times a day — more-frequent measurements may be required if you're ill or under stress. Ask your doctor how often you need to test your blood sugar.
- **Ask your doctor about a glycosylated haemoglobin test.** The glycosylated haemoglobin test, or haemoglobin A1C test, reflects your average blood sugar level for the two- to three-month period before the test. For most people, the A1C goal is to be under 7 percent.
- **Keep your blood pressure and cholesterol under control**. Eating healthy foods, exercising regularly and losing excess weight can help. Sometimes medication is needed, too.
- **If you smoke or use other types of tobacco, ask your doctor to help you quit.** Smoking increases your risk of various diabetes complications, including diabetic retinopathy.
- **Pay attention to vision changes.** Contact your eye doctor right away if you experience sudden vision changes or your vision becomes blurry, spotty or hazy.

# 4. METHODOLOGY

## I. Augmentation Techniques

### Vertical And Horizontal Flip in Image Augmentation

An image flip means reversing the rows or columns of pixels in the case of a vertical or horizontal flip respectively.

The flip augmentation is specified by a boolean horizontal flip or vertical flip argument to the Image Data Generator class constructor. For photographs like the bird photograph used in this tutorial, horizontal flips may make sense, but vertical flips would not.

For other types of images, such as aerial photographs, cosmology photographs, and microscopic photographs, perhaps vertical flips make sense.

The example below demonstrates augmenting the chosen photograph with horizontal flips via the horizontal flip argument.

### Random Rotation Augmentation

A rotation augmentation randomly rotates the image clockwise by a given number of degrees from 0 to 360.

The rotation will likely rotate pixels out of the image frame and leave areas of the frame with no pixel data that must be filled in.

The example below demonstrates random rotations via the rotation range argument, with rotations to the image between 0 and 90 degrees.

Running the example generates examples of the rotated image, showing in some cases pixels rotated out of the frame and the nearest-neighbour fill.

### Random Brightness Augmentation

The brightness of the image can be augmented by either randomly darkening images, brightening images, or both.

The intent is to allow a model to generalize across images trained on different lighting levels.

This can be achieved by specifying the brightness range argument to the ImageDataGenerator() constructor that specifies min and max range as a float representing a percentage for selecting a brightening amount.

Values less than 1.0 darken the image, e.g. [0.5, 1.0], whereas values larger than 1.0 brighten the image, e.g. [1.0, 1.5], where 1.0 has no effect on brightness.

The example below demonstrates a brightness image augmentation, allowing the generator to randomly darken the image between 1.0 (no change) and 0.2 or 20%.

Running the example shows the augmented images with varying amounts of darkening applied.

## II. Visualizing first 10 test images

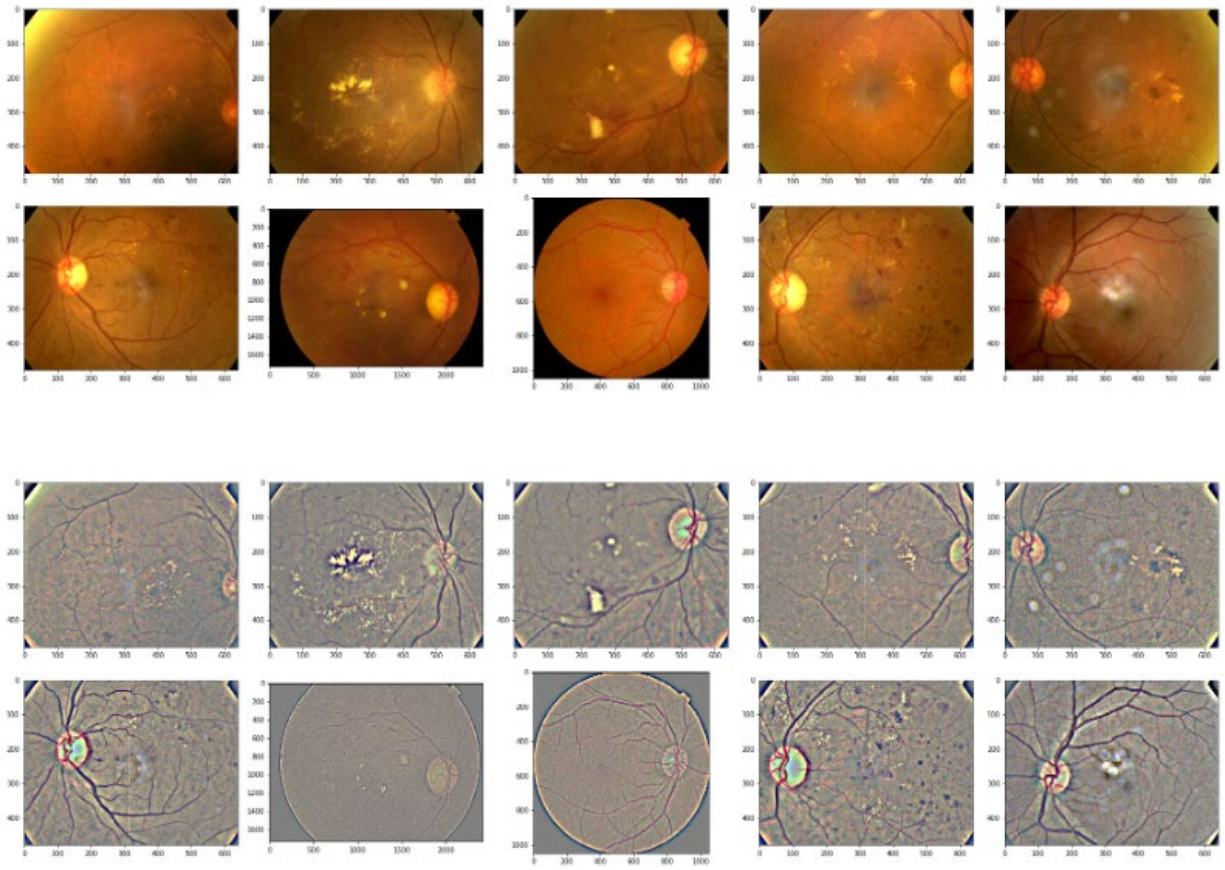

**Fig 3**

## III. Visualizing testing images by training of DenseNet121 and predicting the scale of DR for each label

```
test pic no.1
raw output from model :
1.000 0.966 0.520 0.268 0.109
```

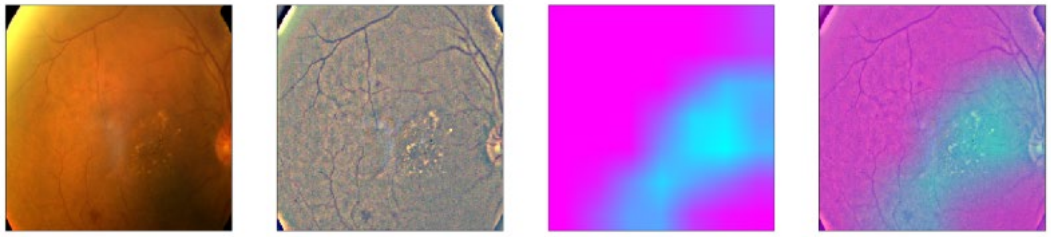

**Fig 4**

```
test pic no.2
raw output from model :
0.998 0.999 0.999 0.931 0.153
```

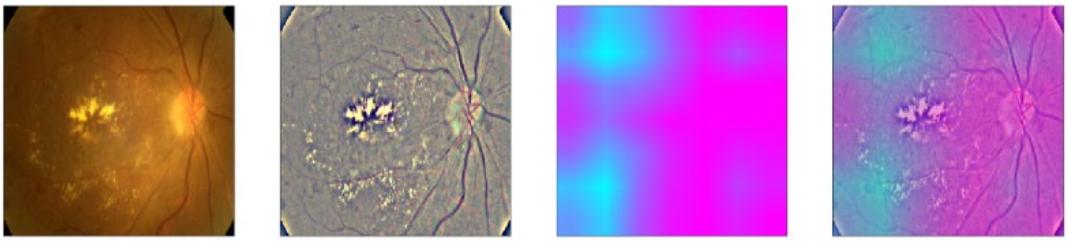

**Fig 5**

```
test pic no.9
raw output from model :
0.998 1.000 0.999 0.953 0.068
```

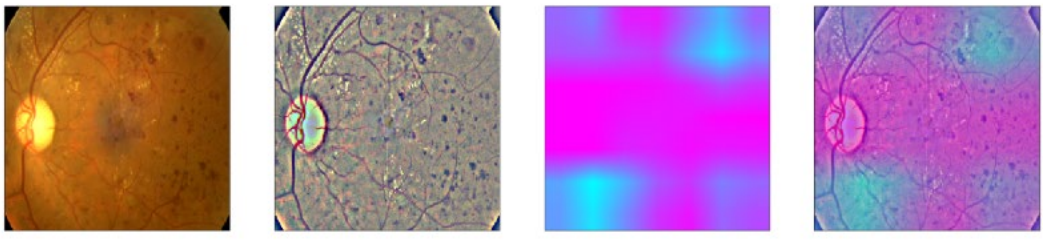

**Fig 6**

## IV. DenseNet 121 Architecture for transfer learning

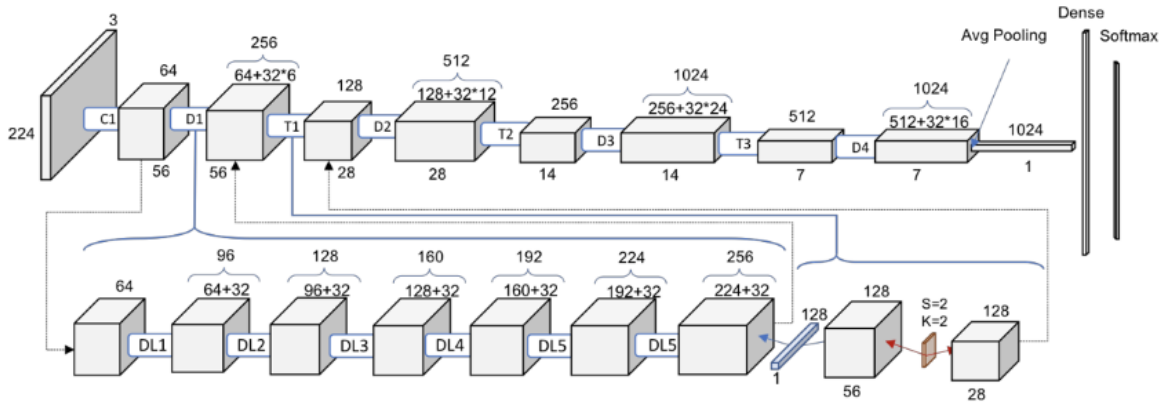


Figure 4. One level deeper look at DenseNet-121. Dense Block and Transition Block. DLx: Dense Layer x

**Fig 7**

DenseNet is composed of Dense blocks. In those blocks, the layers are densely connected together: Each layer receive in input all previous layers output feature maps.

This extreme use of residual creates a deep supervision because each layer receive more supervision from the loss function thanks to the shorter connections.

1. Dense Block

A dense block is a group of layers connected to all their previous layers. A single layer looks like this:

- Batch Normalization
- ReLU activation
- 3x3 Convolution

The authors found that the pre-activation mode (BN and ReLU before the Conv) was more efficient than the usual post-activation mode.

2. Transition layer

Instead of summing the residual like in ResNet, DenseNet concatenates all the feature maps.It would be impracticable to concatenate feature maps of different sizes (although some resizing may work). Thus in each dense block, the feature maps of each layer has the same size.

However down-sampling is essential to CNN. Transition layers between two dense blocks assure this role.

A transition layer is made of:

- Batch Normalization
- 1x1 Convolution
- Average pooling

DenseNet for Semantic Segmentation

The typical segmentation architecture is composed of-

(a) a downsampling path responsible for extracting coarse semantic features

(b) an upsampling path trained to recover the input image resolution at the output of the model

Densely Connected Convolutional Networks (DenseNets), has shown excellent results on image classification tasks. The idea of DenseNets is based on the observation that if each layer is directly connected to every other layer in a feed-forward fashion then the network will be more accurate and easier to train.

DenseNets are built from dense blocks and pooling operations, where each dense block is an iterative concatenation of previous feature maps. This architecture can be seen as an extension of ResNets, which performs iterative summation of previous feature maps. However, this small modification has some interesting implications:

a). parameter efficiency

b). implicit deep supervision

c). feature use

The characteristics of DenseNets make them a very good fit for semantic segmentation as they naturally skip connections and multi-scale supervision.

## V. UNet Architecture

U-Net is a convolutional neural network that was developed for biomedical image segmentation at the Computer Science Department of the University of Freiburg, Germany. The network is based on the fully convolutional network and its architecture was modified and extended to work with fewer training images and to yield more precise

segmentations. Segmentation of a 512*512 image takes less than a second on a modern GPU.

The main idea is to supplement a usual contracting network by successive layers, where pooling operations are replaced by upsampling operators. Hence these layers increase the resolution of the output. What's more, a successive convolutional layer can then learn to assemble a precise output based on this information.

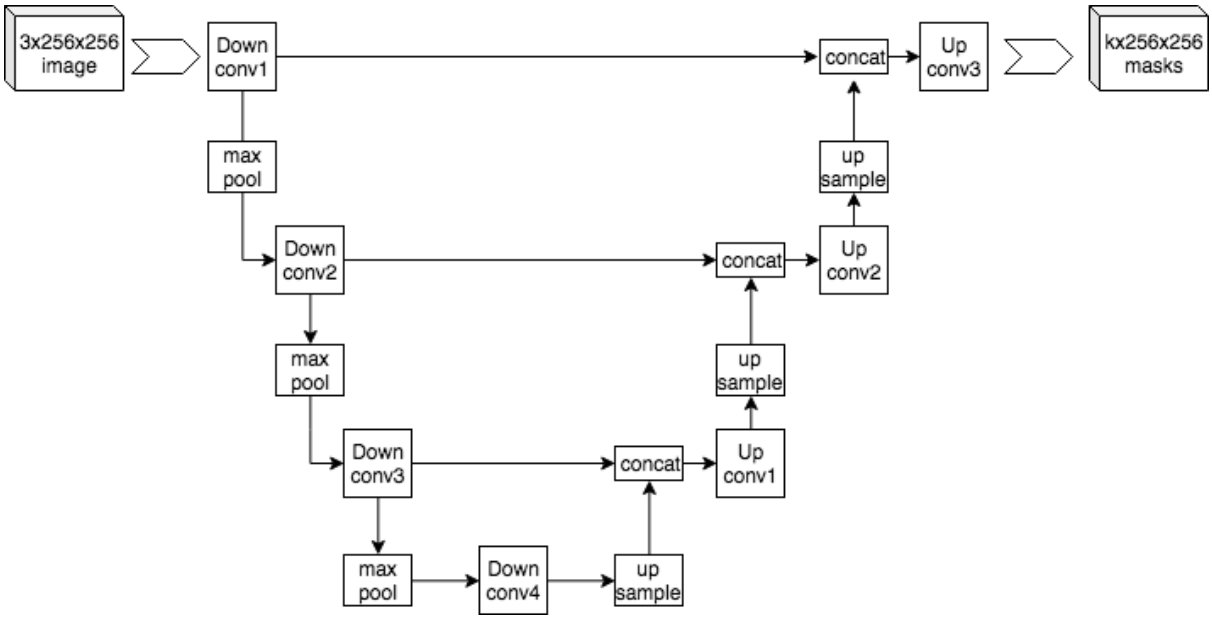


**Fig 8**

The network consists of a contracting path and an expansive path, which gives it the u-shaped architecture. The contracting path is a typical convolutional network that consists of repeated application of convolutions, each followed by a rectified linear unit (ReLU) and a max pooling operation. During the contraction, the spatial information is reduced while feature information is increased. The expansive pathway combines the feature and spatial information through a sequence of up-convolutions and concatenations with high-resolution features from the contracting path.

## VI. Capsule Network

Hinton and Sabour borrowed ideas from neuroscience that suggest the brain is organized into modules called capsules. These capsules are particularly good at handling features of objects like pose (position, size, orientation), deformation, velocity, albedo, hue, texture, etc.

The brain, they theorize, must have a mechanism for routing low-level visual information to what it believes is the best capsule for handling it. Capsule networks and dynamic routing algorithms have been proposed as solutions to problems where convolutional neural network models are inadequate.

Capsules represent the various features of a particular entity that are present in the image. One very special feature is the existence of the instantiated entity in the image. The instantiated entity is a parameter such as position, size, orientation, deformation, velocity, albedo, hue, texture, etc.

An obvious way to represent its existence is by using a separate logistic unit, whose output is the probability that the entity exists. To get better results than CNNs, we should use an iterative routing-by-agreement mechanism. These features are called instantiation parameters.

In the classic CNN model, such attributes of the object in the image are not obtained. The average / max-pooling layer reduces the size of a set of information while the size is reduced.

$$\mathbf{v}_j = \frac{||\mathbf{s}_j||^2}{1 + ||\mathbf{s}_j||^2} \frac{\mathbf{s}_j}{||\mathbf{s}_j||}$$

In deep neural networks, activation functions are simple mathematical operations applied to the output of layers. They are used to approximate non-linear relationships that exist in data. Activation layers typically act on scalar values—for example, normalizing each element in a vector so that it falls between 0 and 1.

In Capsule Networks, a special type of activation function called a squash function is used to normalize the magnitude of vectors, rather than the scalar elements themselves.

**Procedure 1** Routing algorithm.

1: **procedure** ROUTING($\hat{\boldsymbol{u}}_{j|i}, r, l$)
2: for all capsule $i$ in layer $l$ and capsule $j$ in layer $(l+1)$: $b_{ij} \leftarrow 0$.
3: **for** $r$ iterations **do**
4: for all capsule $i$ in layer $l$: $\mathbf{c}_i \leftarrow \texttt{softmax}(\mathbf{b}_i)$
5: for all capsule $j$ in layer $(l+1)$: $\mathbf{s}_j \leftarrow \sum_i c_{ij} \hat{\mathbf{u}}_{j|i}$
6: for all capsule $j$ in layer $(l+1)$: $\mathbf{v}_j \leftarrow \texttt{squash}(\mathbf{s}_j)$
7: for all capsule $i$ in layer $l$ and capsule $j$ in layer $(l+1)$: $b_{ij} \leftarrow b_{ij} + \hat{\mathbf{u}}_{j|i}.\mathbf{v}_j$
**return** $\mathbf{v}_j$

The outputs from these squash functions tell us how to route data through various capsules that are trained to learn different concepts. The properties of each object in the image are expressed in the vectors routing them. For example, the activations of a face may route different parts of an image to capsules that understand eyes, noses, mouths, and ears.

# 5. FUTURE ENHANCEMENTS

1. We would like to train and test on NVIDIA CLARA SDK.

   NVIDIA Clara™ is a collection of Healthcare specific developer tools built on NVIDIA's compute platform aimed at accelerating data acquisition, analysis, and data integration. NVIDIA Clara™ aims at providing access to technological advancements in hardware and software for developers across medical imaging and genomics to accelerate the future of medicine.

   Clara Train SDK enables data scientists and medical researchers with state of the art tools and technologies that accelerate data annotation, adaptation and development of AI models for Medical Imaging workflows.

   Key Capabilities of Clara Train SDK include:

   - APIs to add AI-assisted annotation to any medical viewer with new features like Auto-Annotation and interactive annotation modes, Annotation Server which makes pre-trained models available to the client application and client APIs hosted on Github that make integration with your Medical viewer application seamless.
     - These capabilities are already integrated into the latest MITK workbench plugin.
   - The SDK provides capabilities to use techniques like Transfer learning to adapt or train deep learning models from scratch, enabling Data Scientists to bring their own model architectures and run workflows, this is made possible through a unified foundation of Medical Model Archive (MMAR)
   - The MMAR (Medical Model Archive) provides a model development environment; defines a standard structure for storing and organizing all artifacts produced during the model development life cycle.
   - MMAR includes NVIDIA pretrained models based on AH-Net, DenseNet, ResNet, Dextr3D packaged as complete 2D/3D model applications for organ based segmentation, classification and annotation.

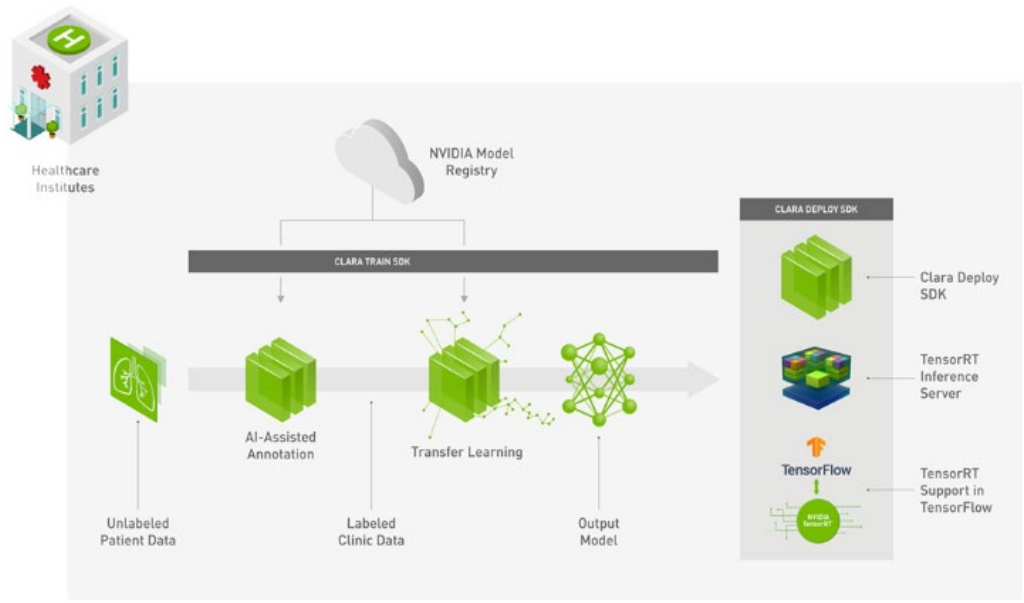


**Fig 9**

2. We will increase the accuracy of our neural network model up to 99.99% by changing hyperparameters.

# 6. RESULTS

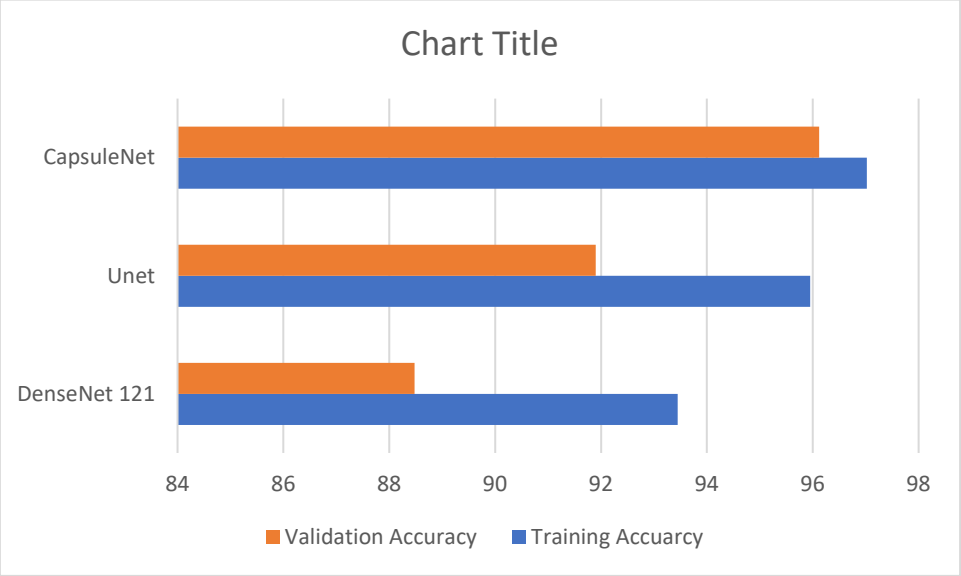


**Fig 10. Graph showing Accuracy of different neural network models**

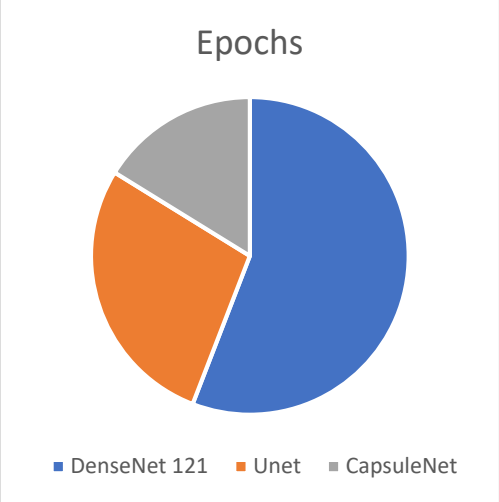


**Fig 11. Pie chart showing epochs for different models**

# 7. CONCLUSION

Image data augmentation is a technique that can be used to artificially expand the size of a training dataset by creating modified versions of images in the dataset. Image data augmentation is used to expand the training dataset in order to improve the performance and ability of the model to generalize. Image Augmentation is one of those techniques which is used for make different images from one image in any image dataset. Some methods like Vertical Flip, Horizontal Flip and Random Degree Flip etc are used for the Image Augmentation. So, Image Augmentation is used whenever training data is less for train the model we used the technique which makes replica of the dataset.

# 8. REFERENCES


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