Deep Learning

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Deep Learning & Robotics for Biomedical, Nuclear Applications

Ratnesh S. Sengar*, R. Sharma, S. Mishra and A. K. Upadhyay

Division of Remote Handling and Robotics (DRHR), Bhabha Atomic Research Centre, Mumbai 400085, INDIA

Spot Picker Robot

ABSTRACT

Recent advances in the computation capabilities, Artificial Intelligence (AI) has opened up new dimensions for solving real-world problems. Vision-based automation systems have been indigenously developed comprising of AI capabilities to cater to the needs of robotics, biological and nuclear science. In this article, we have discussed four such systems i.e., Biochip reader system, Spot picker robot, Protein crystallography imaging system and In-cell video microscopic system. These systems are in active use at various laboratories of BARC and thus enhancing the fields of biomedical and nuclear science research.

KEYWORDS: *Biomedical and nuclear applications, Artificial intelligence, Robots*

Deep Learning based Fluorescence Signal Detection for Biochip

A novel fluorescence-based portable biochip reader system has been developed, which has deep learning algorithms for fluorescence measurement of multianalyte. It is used for reading DNA/protein biochips in clinical diagnosis and basic research. The compact designed system having size of 13 cm x 13 cm x 16 cm is shown in Fig.1. The system consists of a monochromatic light source (LEDs), excitation and emission filters, dichroic mirror or beam-splitter and a CCD/CMOS camera. It can read the whole biochip at a time. Depending upon the excitation and emission maxima of the fluorescent label used, LEDs and filters can be easily changed. The focusing collimator also contains a beam shaper causing excitation light to carry an almost uniform distribution, instead of Gaussian. Images obtained by the camera are stored with 16-bits gray scale levels and analyzed using in-house developed software that exploits the deep learning method.

Deep learning Network for Biochip Data Quantification

To meet the challenge of detection and quantification of low contrast signals, a specific deep learning network as described in Fig.2 has been developed[1] and deployed. Each block in the contracting path of the network consists of two successive 3 x 3 convolutions followed by batch normalization, a Rectified Linear Unit (ReLU) activation function and a max-pooling layer. This arrangement is repeated several times. The expansive path of the network replaces the max-pooling layer with the up-sampling layer and also concatenates the high-resolution information coming from the contracting path. The network has several advantages over other similar available networks. It is asymmetrical, i.e., the decoder side of the network has fewer feature maps than encoder to reduce the number of parameters and computation time. The original skip connection which transfers high-resolution features to deeper layers has been modified by introducing "processing blocks" on it without making any changes to feature maps. Each processing block is a residual block consisting of a sigmoid layer sandwiched between the two Convolution layers. This arrangement is intended to help in denoising and contrast enhancement features and resulted in better detection of low-intensity spots. The depth wise separable convolution filters are also used instead of standard convolution filters, which

Fig.1: Biochip Reader.

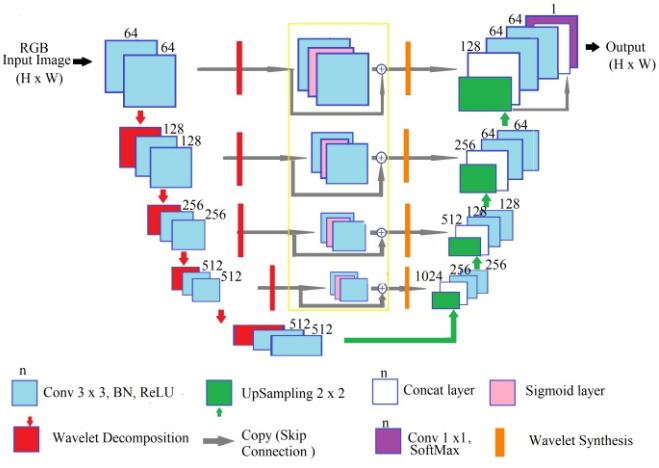


Fig.2: Deep learning Network-Bio-UNet.

*Author for Correspondence: Ratnesh S. Sengar
E-mail: rssengar@barc.gov.in

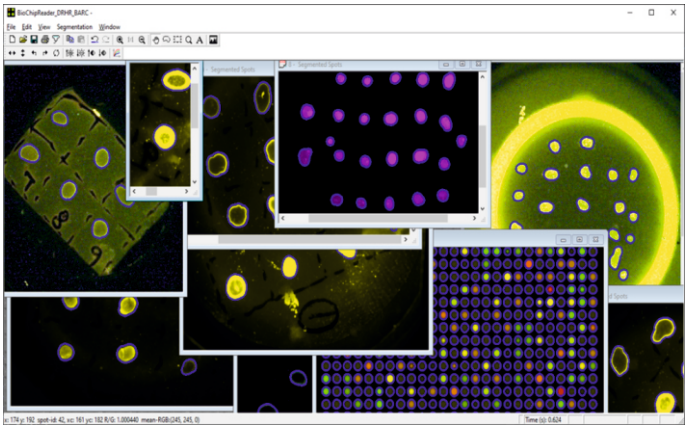


Fig.3: Results & User interface software.

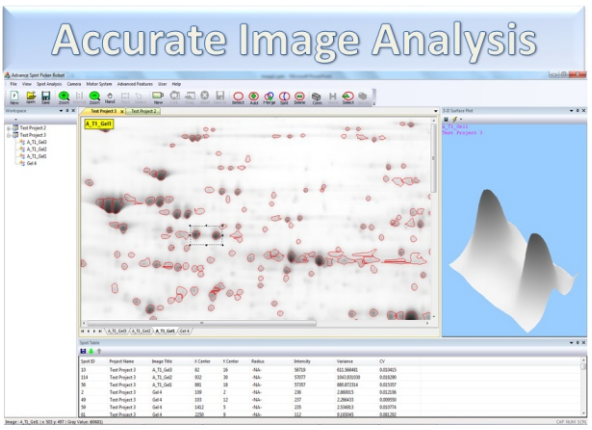


Fig.5: 2DGE Image Analysis Software.

Fig.4: Spot Picker Robot.

reduces the number of parameters in the network by a large factor (from 13M to 2 M) without any significant adverse effect on the segmentation results of biochip images. To enhance the accuracy of detection, a hybrid loss function having a combination of binary cross entropy and a dice loss has been adopted for training. Our deep learning method has been compared with the other available deep learning networks and traditional methods and it is found to be superior by a large margin. It has been demonstrated to provide hierarchal feature segmentation with an accuracy of 98.4%. The results and user interface have been illustrated in Fig.3. The developed bio-chip reader has been clinically tested with DNA as well as antibody biochips and is under clinical use at RMC, Mumbai.

Spot Picker Robot for Proteomics Applications

This robotic system has been indigenously developed and it demonstrates the state-of-the-art technology in precise positioning and powerful imaging algorithm in the field of proteomics as shown in Fig.4 & Fig.5 respectively. It accurately locates and identifies the protein spots from 2D gel electrophoresis (2DGE) and picks and transfers the proteins for further analysis, thus enhancing data quality and reliability in the field of proteomics. The application of this robot has helped in discovering new proteins to develop biomarkers for new diagnostic tests.

The nature of 2-D Gel Electrophoresis (2DGE) images poses difficulties, such as a very noisy and inhomogeneous background with several irregular protein spots. These irregular protein spots are of varying size, shape and intensity. A novel non separable wavelet based image processing algorithm as described in Fig.6 has been developed to detect complex and faint protein spots in non linear background[2], where the available commercial imaging software is not suitable for such detection.

This algorithm is implemented in the Spot Picker Robotic system to provide automation for screening of large number of proteins. Presently the system is in experimental use at RMC.

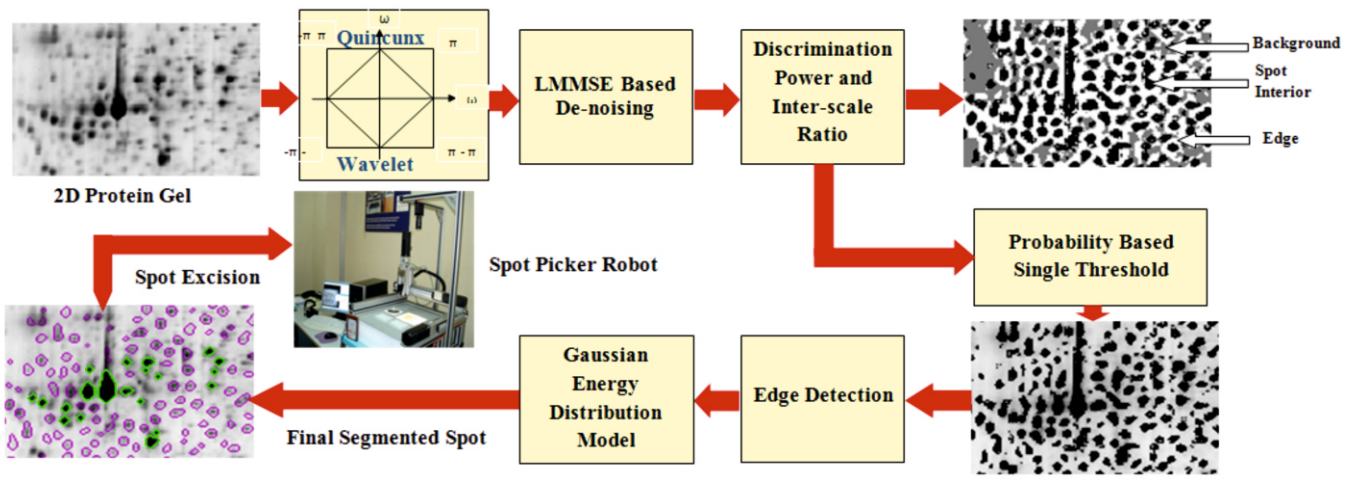


Fig.6: Analysis of 2D-Gel Images for Detection of Protein Spots Using Non-Separable Wavelet.

Real Time Crystal Classification using Deep Convolutional Neural Network for Protein Crystallography Imaging System

X-ray crystallographic technique provides the atomic positions of biological macromolecules for the development of new drugs and vaccines. Correct combination of numerous factors like protein purity, pH, temperature, protein concentration, the type of precipitant and the crystallization methods is essential for the formation of crystals. However, it is difficult to predict these exact conditions for protein crystallization. Therefore, thousands of trials are often required for successful crystallization experiment. Because of the high throughput crystallization approach, manual inspection becomes tedious and prone to errors. Therefore, automated image classification system has been developed to acquire and classify the crystallization images.

Bench-top imaging system[3] has been indigenously developed to monitor the real time protein crystal growth and classification of different state of crystals for X-ray crystallography (Fig.7). Robotics and custom designed microscopic imaging system are used for capturing multi focal images of protein crystals of few microns in size. Advanced computation methods based image processing algorithms have been developed to generate 3D slices of the crystal images. The crystal images acquired by the system are shown in Fig.8.

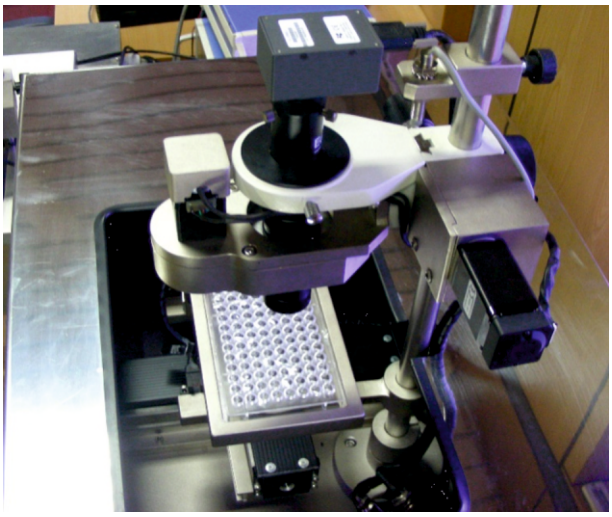
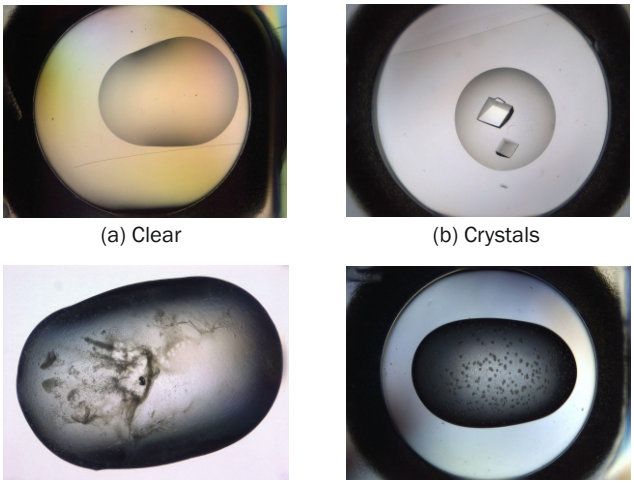


Fig.7: Protein Crystallography Imaging System.



(a) Clear (b) Crystals

(c) Precipitate (d) Other

Fig.8: Different state of the crystals captured by Imaging System.

Image classification during crystallization process

Automated image classification system has been built to classify the images into four classes (Crystals, Precipitate, Clear and Other) to reduce the time in labeling the crystals. The CoAtNet architecture[4] was conceptualized by combining convolution and self-attention to develop fast and accurate neural networks for large-scale image recognition.

Dataset has been randomly partitioned into 75000 training, 7000 tests and 5000 validation images. Each image was resized to 1200x1200 and was centrally cropped. Then, they are randomly flipped in horizontal and vertical directions. The saturation, hue and brightness are randomly adjusted in the ranges of [0.3, 1.5], [0, 0.5], and [0.1, 0.5], respectively. CoAtNet model was modified and tuned for our classification task and the network is shown in Fig.9. For training purposes four Nvidia 3080 RTX 10 GB GPUs are used. The optimizer was Adam with a batch size of 8, a decaying learning rate with an initial setting of 0.045 and maximum epochs of 30. The total time taken for training was 7 hours. Overall test accuracy achieved was 94.1% and validation accuracy of 92.11%. Two systems with software containing real time crystal classification are in used at RBHSD, BARC. The CNN network was found working efficiently for accurate classification thus minimizing the manual efforts and time for predicting the correct crystal category.

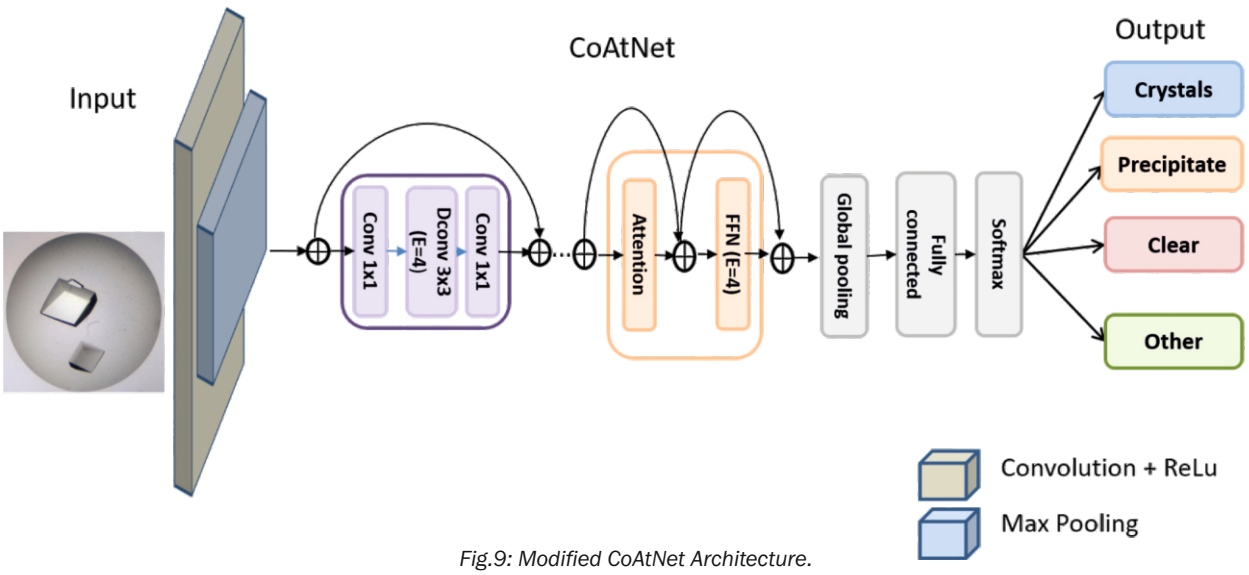


Fig.9: Modified CoAtNet Architecture.

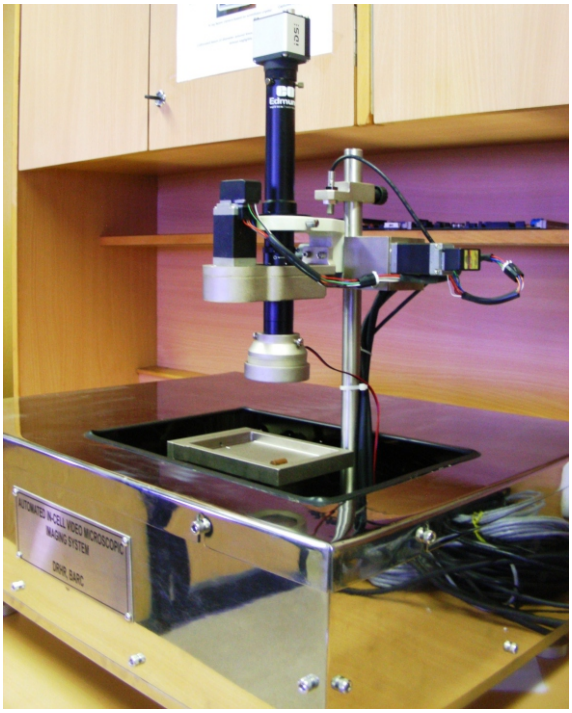


Fig.10: In-cell Video Microscopic Imaging System.

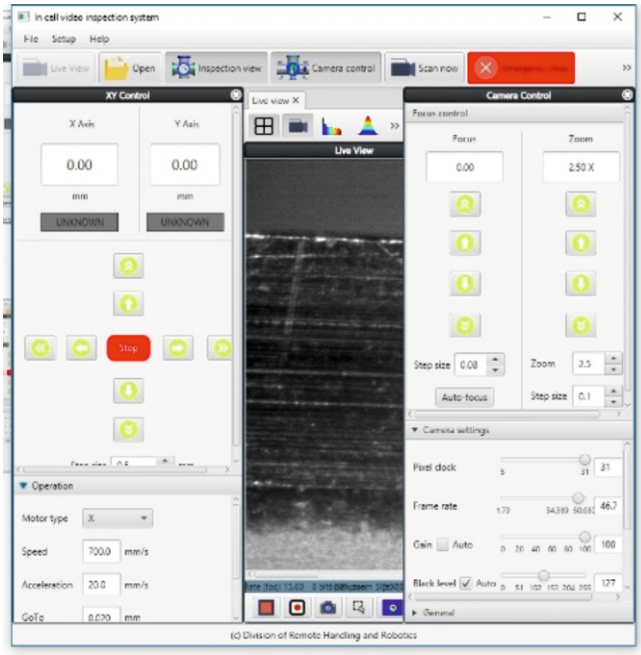


Fig.11: Control Software GUI.

In-cell Video Microscopic Imaging System

The in-cell video microscopic imaging system (Fig.10) has been indigenously developed for automated analysis and dimensional measurements of various reactor core components inside the hot cell. It provides visual inspection and automated analysis of reactor core components at different zoom levels (up to 100x). The system is useful for observing the nodule on Inner Diameter (ID) and flaw characterization in the pressure tubes and defects in the low burn-up fuels of PHWR type nuclear reactors.

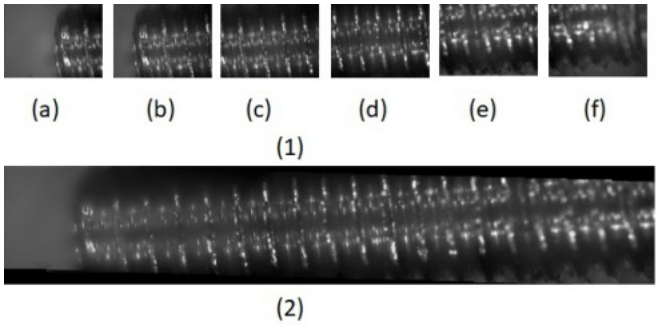


Fig.12: Images captured at different scan positions (1) and stitched image mosaicing (2).

The system consists of a precise robotic system with custom design radiation resistance motorized microscopic imaging system and illumination source. It provides motion travel of 100x100x50mm with positional accuracy of 5µm and the system automatically captures images of reactor core components at different heights and zoom levels. A control system has been developed for stable operation. The multi axis robotic motion is controlled remotely by Ethernet-IP based PLC through PC. This assembly provides a fully automated and optimized multidimensional imaging of the nuclear reactor core components. The proper shielding is provided to the lens and illumination source for working in a radiation environment.

Control GUI software as shown in Fig.11 has been developed for the movement of different axes in various positions, mapping of image magnification to robotics coordinates, automatic scan of inspection material by selecting the region of interest (ROI) and live view of scanning process. Scanning results images are stored in the database in various formats. The system hardware has been integrated with control software and tested with 2D and 3D objects for automated analysis and visualization as demonstrated in Fig.12.

Conclusion

The article presents that the robotics and AI techniques have been implemented in biomedical and nuclear applications for high throughput systems. It is aimed to build more technologies by a combination of both robotics and AI for better perspectives of intelligent automation.

References

[1] Ratnesh S Sengar, A. K. Upadhyay and B. Jain, “Deep Learning Aided Small-Sized Portable Fluorescence Biochip Reader,” IEEE Transactions on Instrumentation and Measurement, 2022, Art no.2507709, vol. 71, pp. 1-9.

[2] Ratnesh S Sengar, A. K. Upadhyay, M. Singh, V. M. Gadre, “Analysis of 2D-Gel Images for Detection of Protein Spots Using a Novel Non-Separable Wavelet Based Method”, Biomedical Signal Processing and Control (Elsevier),2016, Vol.25, pp62-75.

[3] Ratnesh S Sengar, R. Sharma, K. Madhusoodanan and A. Das, “Real Time Protein Crystal Monitoring System”, 2022 IEEE 7th International conference for Convergence in Technology (I2CT), 2022, pp. 1-6, doi: 10.1109/I2CT54291.2022.9825287.

[4] Zihang Dai, Hanxiao Liu, Quoc V. Le, Mingxing Tan. (2021). “CoAtNet: Marrying Convolution and Attention for All Data Sizes”. Computer Vision and Pattern Recognition, 2021. doi: 10.48550/arXiv.2106.04803.