FICM: Force Informed Cell Map Image Synthesis using Attention-gated Dual Encoder U-Net for Carcinoma Cell Line Classification

Kai-Lin Chen[1], Chun-Pei Shih[2], You-Jhu Huang[1,2], Di-Yen Chueh[2], Xiao-Fang Tang[2], Peilin Chen[2]

[1] Department of Biomedical Engineering, National Taiwan University, Taipei, Taiwan

[2] Research Center for Applied Science, Academia Sinica, Taipei 11529, Taiwan

Introduction

- ***Carcinoma Cell Line Classification Problem***: HCC827 & A549 are two types of lung adenocarcinoma cell lines that display different aggressiveness behaviors. Though they can be separated via staining, different staining methods may influence their actual behaviors. Furthermore, cellular morphology can be completely stochastic, making it very challenging and highly subjective to separate them via fluorescence signals using the naked eye.
- ***Classification via Force Map***: It is known that A549 exhibits more movement on the substrate than HCC827. Therefore, the two types are hypothesized to have different force distribution patterns which can be turned into visible signals by culturing them on force-sensing chips. Force-sensing chips are synthesized substrate with micropillars spanning across the sensor chip for cells to grid onto. When a cell exerts force onto the micropillars, displacements can be detected via reflect signals and converted into gradient force maps. However, gradient maps lack spatial information to single out individual cells.
- ***Force Informed Cell Map***: To address these issues, we propose a new modality that combines both information from a target cell's morphology and its internal force map synthesized completely based on deep learning with an attention gated dual encoder U-Net with SE-Fusion module model architecture. The proposed modality possesses a clear boundary mask along with force gradients inside the mask that represents the force patterns of a cell.

Materials & Methods

- ***Dataset Introduction:***

Our dataset comprises 300 fluorescence and force-sensing chip image pairs each for HCC827 and A549, 600 pairs in total, all 256 × 256 and z-score normalized. Ground truth boundary masks and force gradients were generated via a proposed low-resource training strategy **[1]** with minimum human-made labels for faster annotation and lower subjectivity. Consensus ground truths were created by overlaying boundary and force gradient pairs. Each image was labeled as HCC827 or A549 for downstream classification task. For both image synthesis and classification analyses, 200 images were assigned to training and 100 to testing per type. (400 training / 200 testing in total)

- ***Cell Line Classification Model Architecture:***

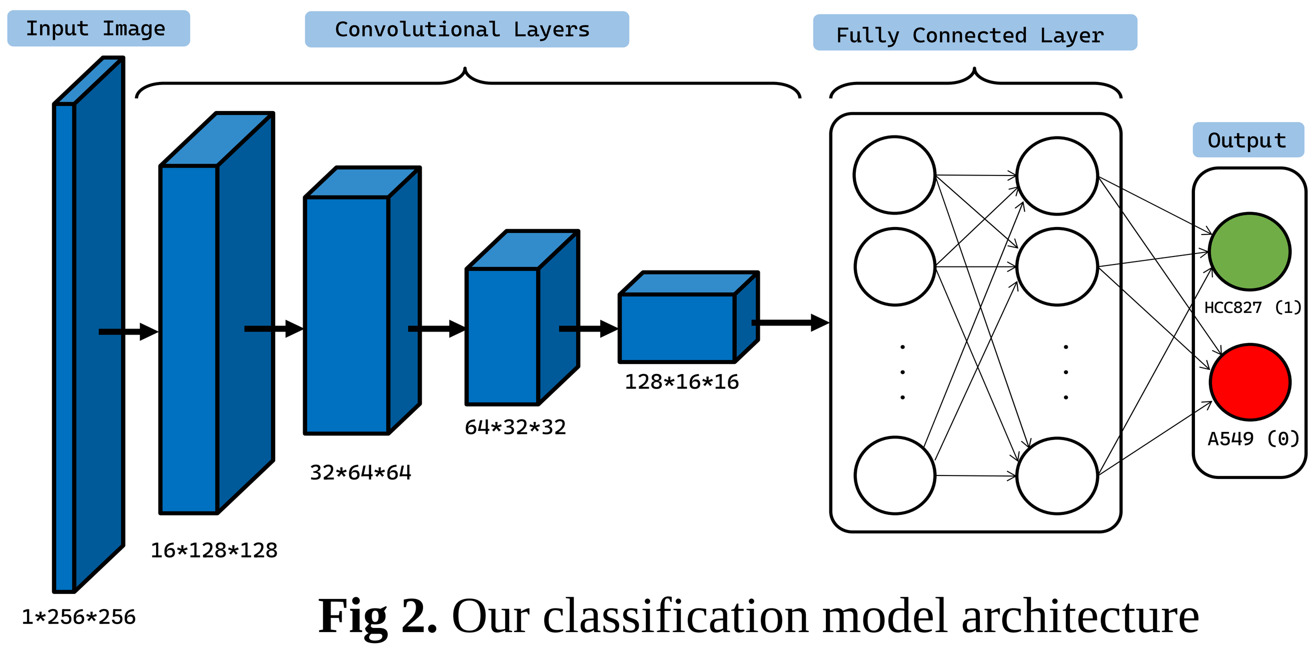
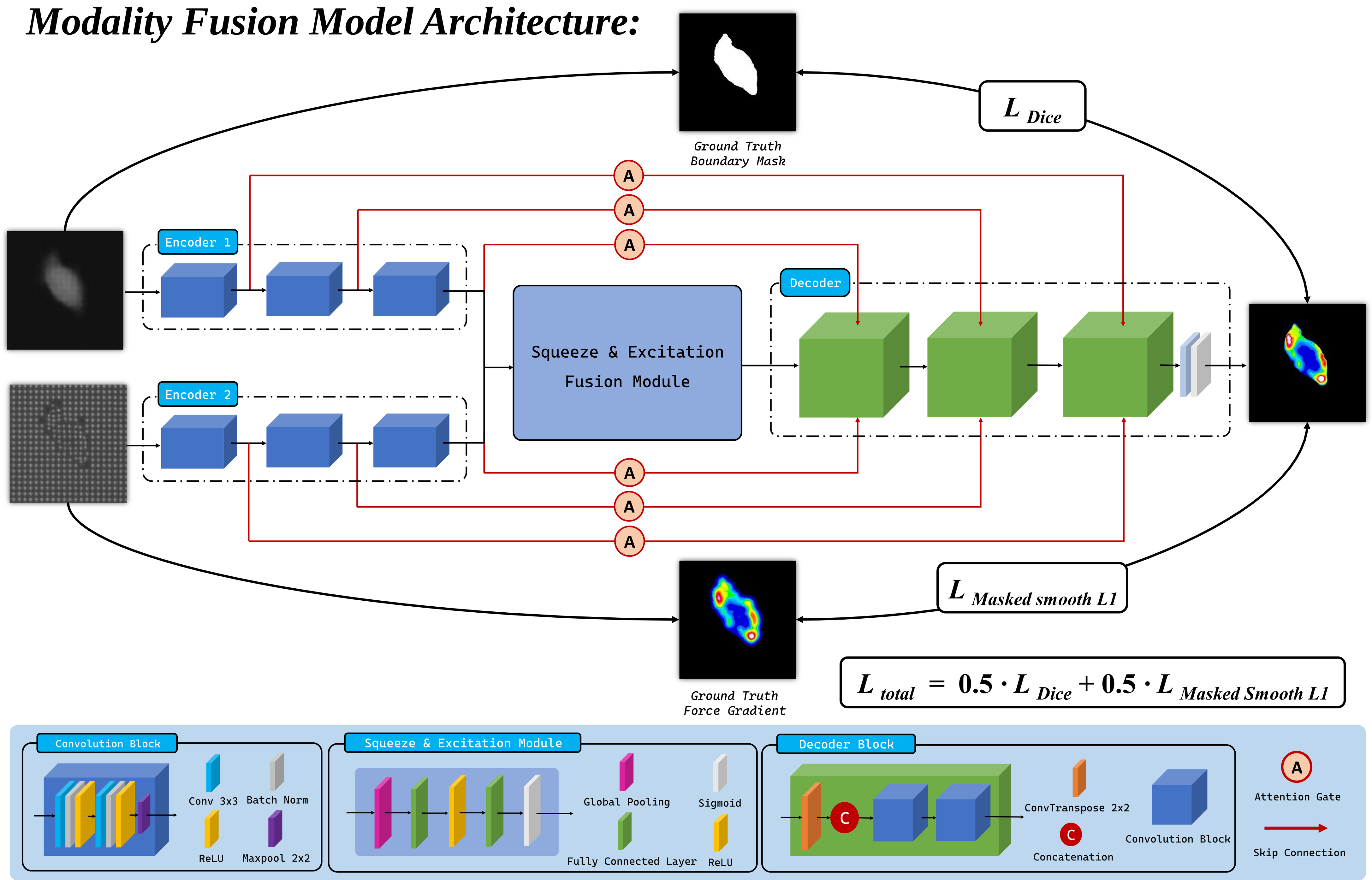


Fig 2. Our classification model architecture

- ***Modality Fusion Model Architecture:***



L_{Dice}

$L_{Masked\ smooth\ L1}$

$$L_{total} = 0.5 \cdot L_{Dice} + 0.5 \cdot L_{Masked\ Smooth\ L1}$$

Fig 1. Our proposed Attention-gated Dual Encoder U-Net with SE-Fusion Module

Results

- ***FICM Synthesis Analysis***

To justify our synthesized images' credibility, we calculated the average Dice score after thresholding the synthesized images. Average mean square error (MSE) and structural similarity (SSIM) are calculated based on the consensus ground truths of the datasets.

Dataset	Dice Score	MSE	SSIM
HCC 827	**0.9497**	0.0025	**0.9683**
A 549	**0.9533**	0.0021	**0.9702**

Table 1. Performance metrics of our synthesized images on the test set, showing a high boundary overlap and high structural similarity with the consensus ground truths.

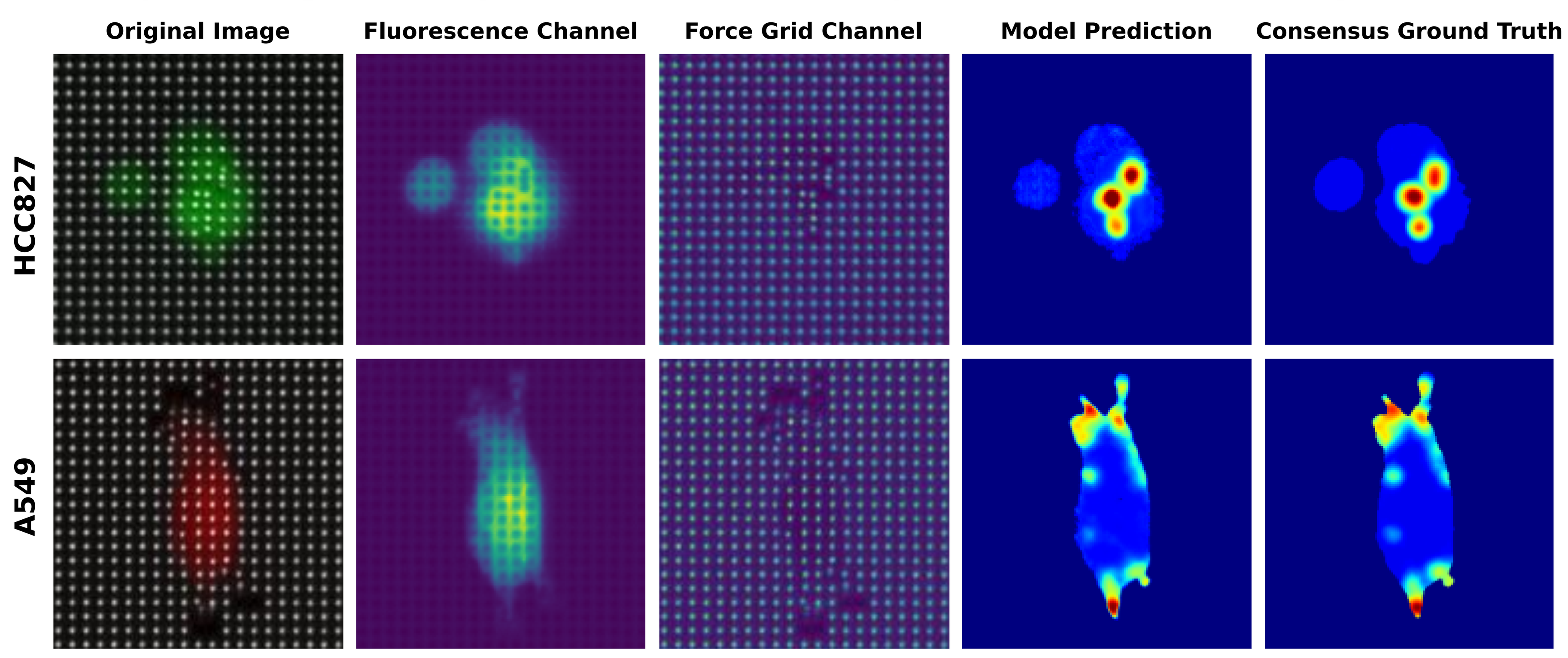


Fig 3. Montage of original images and synthesized images of HCC827 and A549.

- ***Carcinoma Cell Line Classification Analysis***

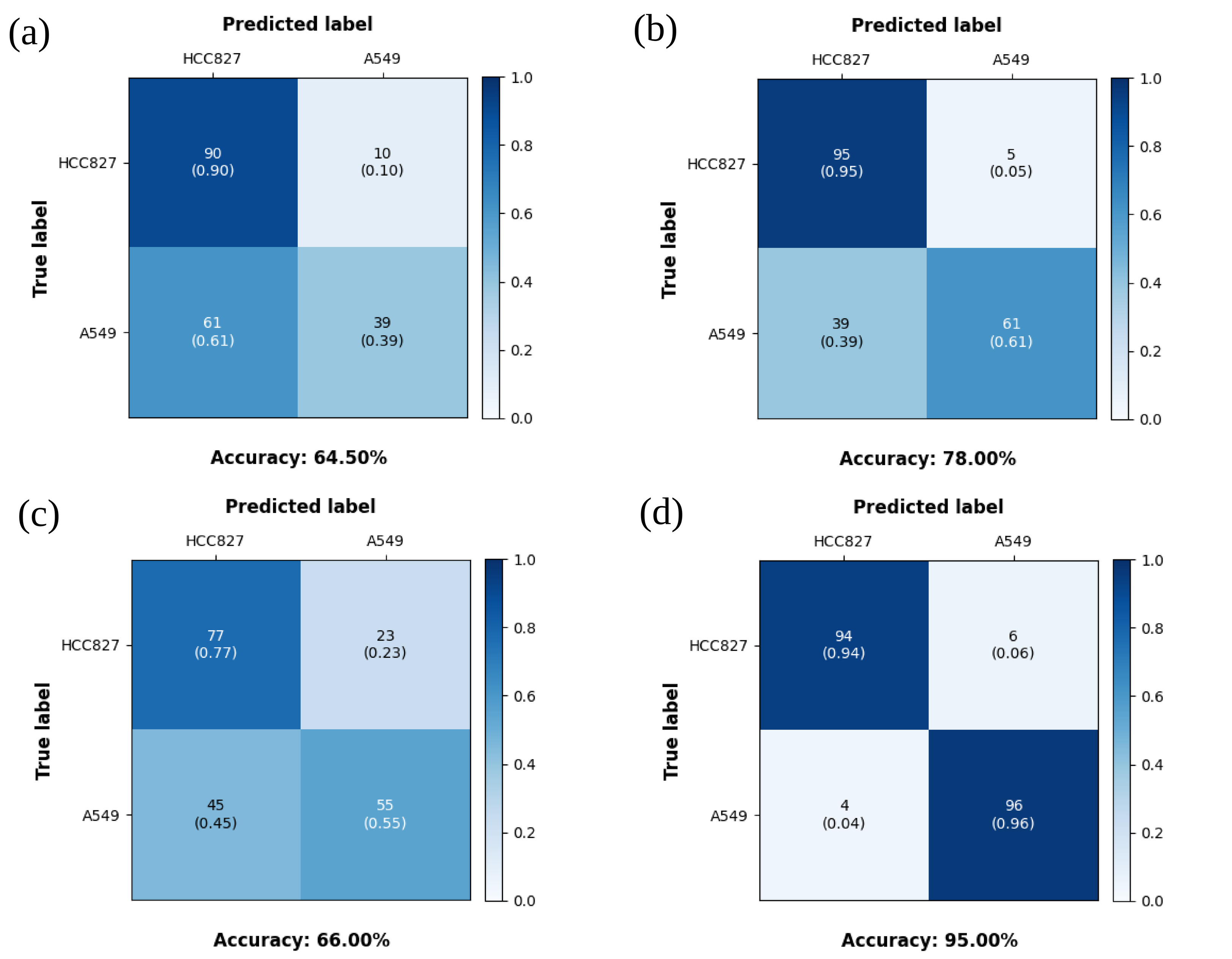


Fig 4. Confusion matrices of using (a) pure fluorescence images (b) pure force grid images (c) stacked fluorescence and force grid (d) our proposed modality.

Conclusions

- We developed a **new medical image modality for cell mechanobiology studies**.
- Our proposed dual modality fusion network generates images with **high structural similarity (average ≈ 0.9693) and high overlap** with the consensus ground truths.
- **Enhances classification accuracy by 37.67%** compared to unprocessed modalities.
- **Mechanical force pattern provide discriminative features** to classify cell lines.
- **Hypothesis validation:** Many A549 cells exerts force on endpoints for linear movement, while HCC827 cells show scattered focal adhesions for anchoring.

References

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[2] Lin, Y.-N.; Huang, S.-Y.; Chung, M.-C.; Tsai, C.-H.; Wang, H.-W.; Gong, E.; Hsiao, I.-T.; Chen, K. T. MRI-Styled PET: A dual modality fusion approach to PET partial volume correction. *IEEE TRPMS* **2025** 1-1, DOI: 10.1109/TRPMS.2025.3549617

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