Mechanobiology examines the input and output of mechanical forces by cells. Contractile forces generated by the actin-myosin cytoskeleton are transmitted to the exterior environment via associated trans-membrane proteins such as integrins (1). Referred to as traction forces, these forces are detected predominantly near cell periphery or front in an orientation towards cell center (2). Active forces are located at nascent or maturing focal adhesions near the front while resistive forces are located at mature focal adhesions near the rear (3, 4).

In addition to propelling cell migration, traction forces are believed to perform important functions such as organizing the extracellular matrix (5), probing mechanical properties of the environment (6), and sensing the state of the cell itself such as shape and size (7). Adhesive cells are also keenly sensitive to mechanical forces transmitted via the surrounding matrix (8), fluid shear (9), or cell-cell contact (10). These mechanical signals elicit many profound responses to affect cell migration (11), growth (12), and differentiation (13).

Methods for mapping cellular traction forces, referred to in general as traction force microscopy (TFM; 2, 14, 15, 16), represent a fundamental tool for mechanobiology. TFM is commonly performed by culturing cells on a substrate of elastic material such as polyacrylamide embedded with particle markers for mapping force-induced strains, which are then used for calculating the distribution of stresses. However, while the calculation of strain from stress is straightforward, the inverse calculation is known mathematically as an ill-posed problem, where a unique solution may not exist and the results are prone to artifacts from measurement noise if one simply tries to optimize the fitting between predicted and measured strains (17). To mitigate these problems, most conventional approaches include in the fitting function a regularization term, which is generally a function of the magnitude of traction stress such that minimizing the fitting function balances the accuracy of fitting against noise-induced artifacts and complexity of the solution (2, 17). However, in addition to the compromise in accuracy and resolution, it is difficult to define the weight factor for regularization, represented by a parameter λ, which determines the balance between accuracy and artifacts (18).

Neural network-based deep learning has been deployed as a powerful method for solving ill-posed problems (19). It involves the optimization of a cascade of convolutional operations, with the goal of transforming the input (e.g. the distribution of strains) into the targeted solution (e.g. the distribution of stresses; 20). As an approach fundamentally different from conventional methods, it can avoid the use of regularization and associated compromises.

To deploy deep learning for TFM, we have adapted a neural network for processing images to process the vector fields of stresses and strains. We generated a large set of strain and ground truth stress fields by computer simulation for training the network. By comparing the performance of the resulting neural network and a conventional implementation of TFM, we found that deep learning based TFM are capable of mapping traction stress at a high speed, accuracy, and resolution.

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