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SUPPLEMENTARY INFORMATION

In format as provided by the authors

Advances in protein structure prediction and design

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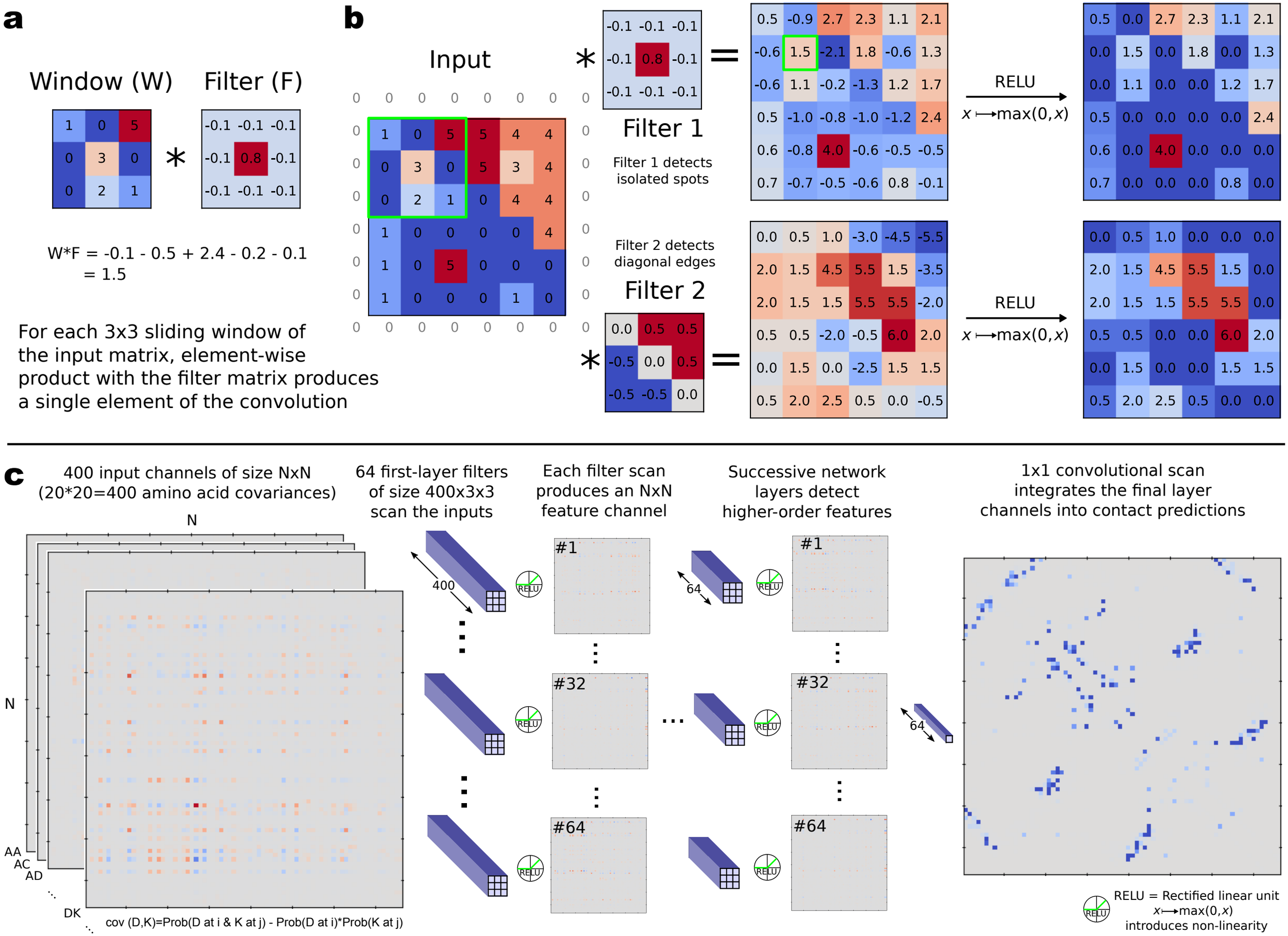

Supplementary Figure 1. Elements of convolutional neural networks. A convolutional neural network transforms arrays of input features into output predictions through the application of multiple layers of convolutional filters, mathematical operators that scan the input features (or the outputs of previous filters) to identify patterns of interest. The overall architecture of the network (the number of layers, the number of filters in each layer, and the size of the convolutional filters) as well as the real-valued filter weights are chosen to optimize network performance through an iterative training process. **(a)** A 3x3 convolutional filter (F) is applied to an input matrix by scanning the filter across the input matrix and computing for each sliding 3x3 window (W) an element-wise product and summation. **(b)** The application of two different 3x3 filters to a 6x6 input array yields two 6x6 output arrays (zeros are added on the border of the input array); the top filter, which contains a positive value surrounded by negative values, responds most strongly to isolated dots, while the arrangement of positive and negative values in the bottom filter detects diagonal edges (compare location of the red (higher) values in the two output arrays on the right). The output of the convolutional scan is then filtered through a non-linear response function such as the rectified linear unit (RELU) shown here. **(c)** A simplified and schematized convolutional neural network for prediction of residue contacts from amino acid covariances takes as input 400 NxN (where N is the length of the protein) amino acid covariance channels, one for each pair of amino acid types (of which there are 20*20=400: AA, AC, ..., YW, YY). Successive convolutional filters with non-linear response functions extract higher-order patterns from the raw covariances in order to predict the protein's contact map. The filters in the first layer have a depth of 400 (the number of input channels) and window size of 3x3, meaning that the entry (i,j) in the output channel of each filter integrates information from all 400 input channels over a 3x3 window of residue-pairs surrounding (i,j). With each successive convolutional filtering operation, information from a larger local neighborhood is incorporated into the output values, such that the final prediction for the contact probability of residues i and j uses covariation information from a neighborhood of residues around i and around j, with the size of the neighborhood depending on the number of network layers.