S1 Fig. (a) Leave-one-out and (b) leave-drug-out cross-validation results. The prediction accuracy was assessed with root mean squared error (RMSE) between binding affinities (pK₇) from the study by Metz et al. and those predicted using KronRLS model with different pairs of drug (rows) and protein (columns) molecular descriptors encoded as kernel matrices (c). The lower the RMSE value, the more accurate the model prediction. Of note, Gaussian interaction profile drug kernel (KD-GIP) which resulted in the highest predictive performance under the Bioactivity Imputation scenario (a) has not been evaluated under the New Drug setup (b) because it is constructed based on the bioactivity profile of a drug, information that in practice is unavailable when predicting target interactions for a new investigational drug compound.