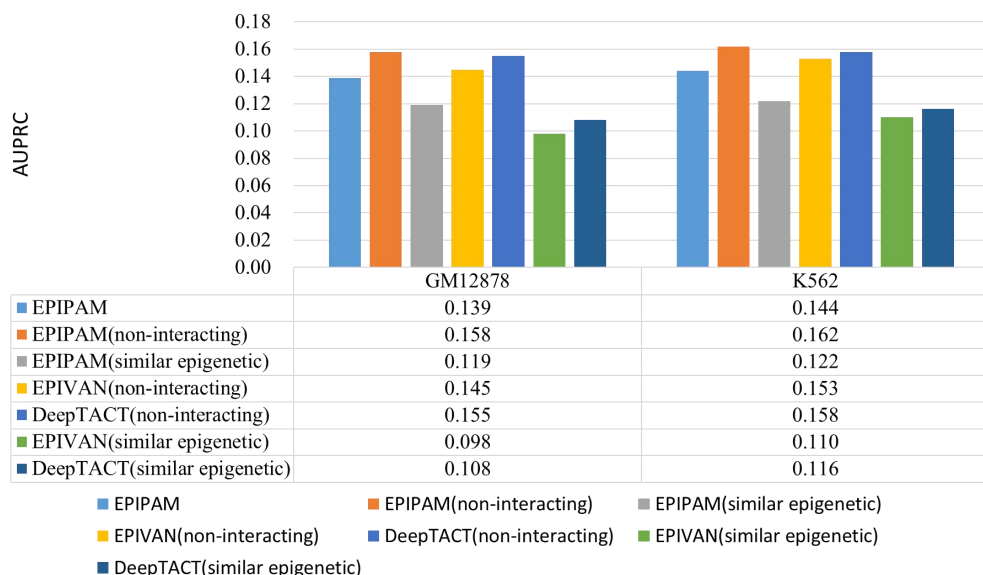


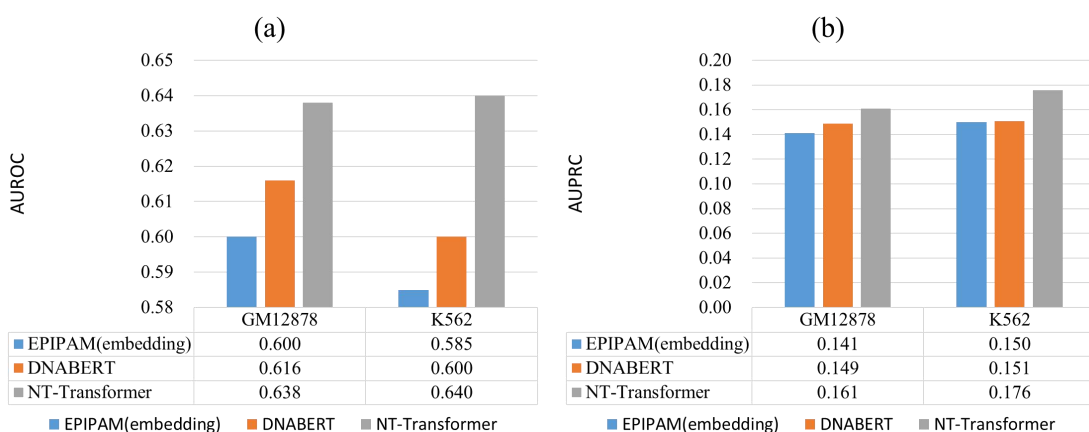
## Supplementary information

# A deep learning framework with positional attention for modeling enhancer-promoter interactions

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**Figure S1.** The performance of all methods using different negative-sample selective strategies. To investigate the performance of EPIPAM using different negative-sample selective strategies, we selected non-interacting enhancers under the same promoter, and non-paired fragments with similar epigenetic signals by disturbing the positive set. As shown in this Figure, we observe that the performance of EPIPAM with different negative-sample selective strategies is diverse but generally better than that of competing methods, demonstrating the model’s robustness.



**Figure S2.** The performance of EPIPAM using different embedding technologies. To investigate the performance of EPIPAM using different embedding technologies, we have conducted comparative experiments to explore other types of pretrained representations such as DNABERT or NT-Transformer, in which DNABERT adopts the k-mer embeddings while NT-Transformer adopts the nucleotide embeddings. As shown in this Figure, we find that the performance of DNABERT and NT-Transformer is better than that of embedding-based EPIPAM, demonstrating the embeddings from DNABERT and NT-Transformer provide much more prior regulatory information.

Table S1. Architecture settings of EPIPAM.

Enhancer branch	Settings	Output shape	Promoter branch	Settings	Output shape
Input layer	one-hot/embedding	(100,4,3000)/(100,100,3000)	Input layer	one-hot/embedding	(100,4,2000)/(100,100,2000)
Conv1D	kernels = 64, size=25, stride = 1, padding=0	(100,64,2976)	Conv1D	kernels = 64, size = 25, stride = 1, padding = 0	(100,64,1976)
ReLU	#	(100,64,2976)	ReLU	#	(100,64,1976)
Max-pooling1D	size = 10, stride = 10	(100,64,297)	Max-pooling1D	size = 10, stride = 10	(100,64,197)
Dropout	ratio = 0.2	(100,64,297)	Dropout	ratio = 0.2	(100,64,197)
PAM	ratio = 0.01	(100,64,297),(100,64,197),(100,585)			
Conv1D	kernels = 64, size = 13, stride = 1, padding = 0	(100,64,285)	Conv1D	kernels = 64, size = 13, stride = 1, padding = 0	(100,64,185)
ReLU	#	(100,64,285)	ReLU	#	(100,64,185)
Max-pooling1D	size = 10, stride = 10	(100,64,28)	Max-pooling1D	size = 10, stride = 10	(100,64,18)
Dropout	ratio = 0.2	(100,64,28)	Dropout	ratio = 0.2	(100,64,18)
PAM	ratio = 0.1	(100,64,28),(100,64,18),(100,50)			
Conv1D	kernels = 64, size = 7, stride = 1, padding = 0	(100,64,22)	Conv1D	kernels = 64, size = 7, stride = 1, padding = 0	(100,64,12)
ReLU	#	(100,64,22)	ReLU	#	(100,64,12)
Max-pooling1D	size = 5, stride = 5	(100,64,4)	Max-pooling1D	size = 5, stride = 5	(100,64,2)
Dropout	ratio = 0.2	(100,64,4)	Dropout	ratio = 0.2	(100,64,2)
PAM	ratio = 1	(100,64,4),(100,64,2),(100,8)			
<b>Prediction branch1</b>	<b>Settings</b>	<b>Output shape</b>	<b>Prediction branch2</b>	<b>Settings</b>	<b>Output shape</b>
Concatenate layer	#	(100,384)	Concatenate layer	#	(100,643)
BN	#	(100,384)	BN	#	(100,643)
Linear	units = 64	(100,64)	Linear	units = 64	(100,64)
ReLU	#	(100,64)	ReLU	#	(100,64)
Dropout	ratio = 0.5	(100,64)	Dropout	ratio = 0.5	(100,64)
Linear	units = 1	(100,)	Linear	units = 1	(100,)
Sigmoid	#	(100,)	Sigmoid	#	(100,)

**Table S2.** The mean and standard variance of the 8 folds cross-validation on all methods across EPI datasets and ChIA-PET datasets.

EPIs/AUC	EPIPAM		EPIVAN		DeepTACT	
	mean	std	mean	std	mean	std
GM12878	0.628	0.033	0.611	0.037	0.619	0.033
HeLa-s3	0.658	0.077	0.630	0.026	0.648	0.062
HUVEC	0.653	0.042	0.633	0.039	0.644	0.037
IMR90	0.645	0.051	0.637	0.032	0.625	0.030
K562	0.631	0.038	0.611	0.021	0.626	0.041
NHEK	0.619	0.052	0.608	0.045	0.596	0.050
EPIs/AUPRC	EPIPAM		EPIVAN		DeepTACT	
	mean	std	mean	std	mean	std
GM12878	0.630	0.038	0.601	0.040	0.617	0.025
HeLa-s3	0.648	0.084	0.625	0.032	0.637	0.058
HUVEC	0.659	0.047	0.646	0.046	0.648	0.049
IMR90	0.649	0.043	0.652	0.055	0.637	0.056
K562	0.627	0.037	0.607	0.031	0.614	0.037
NHEK	0.620	0.032	0.610	0.055	0.606	0.043
ChIA-PET/AUC	EPIPAM		EPIVAN		DeepTACT	
	mean	std	mean	std	mean	std
HeLa3Pol2	0.939	0.016	0.935	0.016	0.934	0.017
K562Ctcf	0.988	0.001	0.987	0.002	0.980	0.003
K562Pol2	0.939	0.011	0.936	0.011	0.935	0.010
Mcf7Ctcf	0.992	0.001	0.991	0.001	0.986	0.002
ChIA-PET/AUPRC	EPIPAM		EPIVAN		DeepTACT	
	mean	std	mean	std	mean	std
HeLa3Pol2	0.816	0.044	0.805	0.042	0.794	0.048
K562Ctcf	0.951	0.007	0.949	0.009	0.932	0.009
K562Pol2	0.837	0.024	0.828	0.027	0.822	0.020
Mcf7Ctcf	0.963	0.004	0.960	0.006	0.940	0.008