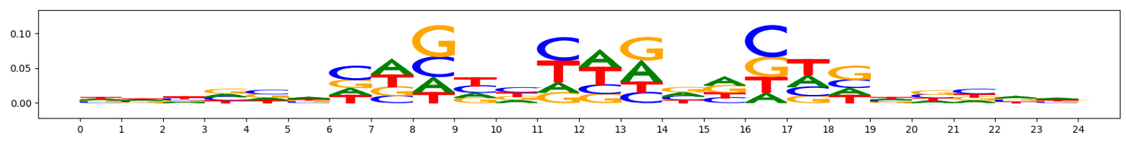
Bias model training and quality check report

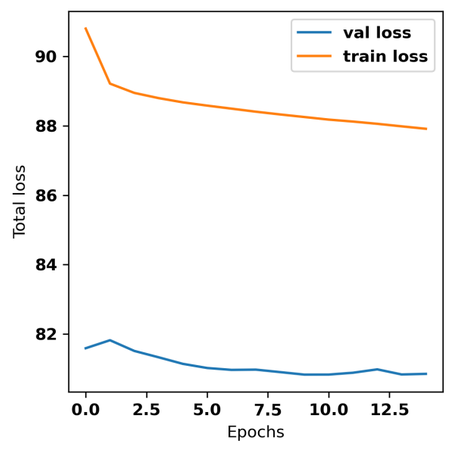
Preprocessing report

The image below should look closely like a Tn5 or DNase bias enzyme motif.



Training report

The val loss (validation loss) will decrease and saturate after a few epochs.



Bias model performance in peaks and non-peaks

Counts Metrics: The pearsonr in non-peaks should be greater than 0 (higher the better). The pearsonr in peaks should be greater than -0.3 (otherwise the bias model could potentially be capturing AT bias). MSE (Mean Squared Error) will be high in peaks.

Profile Metrics: Median JSD (Jensen Shannon Divergence between observed and predicted) lower the better. Median norm JSD is median of the min-max normalized JSD where min JSD is the worst case JSD i.e JSD of observed with uniform profile and max JSD is the best case JSD i.e 0. Median norm JSD is higher the better. Both JSD and median norm JSD are sensitive to read-depth. Higher read-depth results in better metrics.

What to do if your pearsonr in peaks is less than -0.3? In the range of -0.3 to -0.5 please be wary of your chrombpnet_wo_bias.h5 (that wil potentially be trained with this bias model) TFModisco showing lots of GC rich motifs (> 3 in the top-10). If this is not the case you can continue using the chrombpnet_wo_bias.h5. If you end up seeing a lot of GC rich motifs it is likely that bias model has learnt a different GC distribution than your GC-content in peaks. You might benefit from increasing the bias_threshold_factor argument input to the *chrombpnet bias pipeline* or *chrombpnet bias train* command used in training the bias model and retrain a new bias model. For more intuition about this argument refer to the FAQ section in wiki. If the value is less than -0.5 the chrombpnet training will automatically throw an error.

	nonpeaks.pearsonr	nonpeaks.rmse	peaks.pearsonr	peaks.rmse
counts metrics	-0.2	2.66	-0.45	12.12

	nonpeaks.median_jsd	nonpeaks.median_norm_jsd	peaks.median_jsd	peaks.median_norm_jsd
profile metrics	0.64	0.15	0.5	0.25

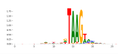
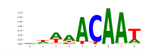
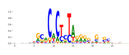
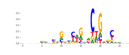
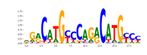
TFModisco motifs learnt from bias model (bias.h5) model

TFModisco motifs generated from profile contribution scores of the bias model. cwm_fwd, cwm_rev are the forward and reverse complemented consolidated motifs from contribution scores in subset of random peaks. These CWM motifs should be free from any Transcription Factor (TF) motifs and should contain either only bias motifs or random repeats. For each of these motifs, we use TOMTOM to find the top-3 closest matches (match_0, match_1, match_2) from a database consisting of both MEME TF motifs and heterogenous enzyme bias motifs that we have repeatedly seen in our datasets. The qvals (qval0,qval1,qval2) should be high (> 0.0001) if the closest hit is a TF motif (i.e indicating that the closest match is not the correct match) - this is also generally verifiable by eye as the closest match will look nothing like the CWMs. The qvals should be low if the closest hit is enzyme bias motif and generally verifiable that the top match looks like the CWM. The first 3-5 motifs in the list below should look like enzyme bias motif.

What to do if you find an obvious TF motif in the list?
Do not use this bias model as it will regress the contribution of the TF motifs (along with bias motifs) from the chrombpnet_nobias.h5. Reduce the bias_threshold_factor argument input to the *chrombpnet bias pipeline* or *chrombpnet bias train* command used in training the bias model and retrain a new bias model. For more intuition about this argument refer to the FAQ section in wiki.

What to do if you are unsure if a given CWM motif is resembling the match_0 logo for example?
Get marginal footprint on the match_0 motif logo (using the command *chrombpnet footprints* and make sure that the bias models footprint is closer to that of controls with no motif inserted - for examples look at FAQ)

pattern	NumSeqs	cwm_fwd	cwm_rev	match0	qval0	match0_logo	match1	qval1	match1_logo	match2	qval2	match2_logo
pos_0	9333			TN5_2	1.708290e-06		TN5_1	0.000020		TN5_7	0.000469	
pos_1	6211			TN5_4	2.383960e-02		TN5_5	0.023840		TN5_8	0.041770	
pos_2	3883			TN5_3	1.530650e-01		KLF4_MA0039.3	0.153065		TN5_4	0.153065	
pos_3	3813			TN5_1	2.403700e-05		TN5_2	0.000025		TN5_3	0.000350	
pos_4	2820			TN5_3	1.033020e-03		TN5_7	0.002835		TN5_1	0.048250	
pos_5	1938			TN5_3	1.059630e-10		TN5_4	0.000120		TN5_5	0.000120	
pos_6	1108			TN5_3	2.597330e-07		TN5_2	0.239220		TN5_4	0.487050	
pos_7	923			TN5_3	1.840000e-06		TN5_1	0.004382		TEX21_TEX_3	0.035461	
pos_8	743			TN5_3	8.579450e-13		TN5_4	0.001044		TN5_5	0.001044	
pos_9	398			ZNF384_MA1125.1	5.112750e-02		PRDM6_HUMAN.H11MO.0.C	0.051127		ANDR_HUMAN.H11MO.0.A	0.204980	
pos_10	304			NFATC1_NFAT_1	1.000000e+00		None	NaN		None	NaN	
pos_11	213			ZNF384_MA1125.1	5.872460e-03		CPEB1_RRM_1	1.000000		SRY_HUMAN.H11MO.0.B	1.000000	
pos_12	197			_NS4_MA0019.1	1.000000e+00		ZNF384_MA1125.1	1.000000		ONECUT3_CUT_1	1.000000	
pos_13	141			MEF2A_MOUSE.H11MO.0.A	2.159200e-01		ZNF384_MA1125.1	0.215920		ONECUT3_CUT_1	0.215920	
pos_14	117			TN5_7	4.013820e-05		SOX8_HMG_3	0.751547		SOX4_HMG_1	1.000000	

pattern	NumSeqs	cwm fwd	cwm rev	match0	qval0	match0 logo	match1	qval1	match1 logo	match2	qval2	match2 logo
pos 15	92			FOXJ3_HUMAN.H11MO.0.A	5.215270e-02		FOXJ3_MOUSE.H11MO.0.A	0.052153		ONECUT3_CUT_1	0.052153	
pos 16	76			DNASE_2	2.335010e-01		ZNF384_MA1125.1	1.000000		SRY_MA0084.1	1.000000	
pos 17	27			TN5_3	5.018390e-01		TN5_1	0.005895		P53_HUMAN.H11MO.0.A	0.022577	
pos 18	25			SRF_MADS_1	9.087150e-02		SRF_MA0083.3	0.090871		SRF_MADS_2	0.090871	

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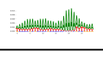
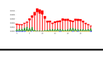
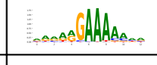
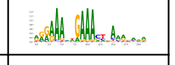
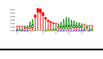
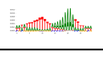
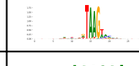
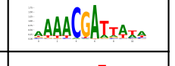
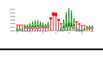
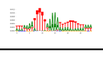
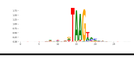
pattern	NumSeqs	cwm fwd	cwm rev	match0	qval0	match0 logo	match1	qval1	match1 logo	match2	qval2	match2 logo
pos 0	14297			DNASE_2	2.038460e-01		ZNF384_MA1125.1	2.319410e-01		_HX3_HUMAN.H11MO.0.C	2.319410e-01	
pos 1	4373			ZNF384_MA1125.1	2.912580e-02		PRDM6_HUMAN.H11MO.0.C	2.912580e-02		STAT1_MOUSE.H11MO.0.A	1.744390e-01	
pos 2	3792			ZNF384_MA1125.1	2.822410e-03		DNASE_2	2.583300e-02		HOMEZ_HOMEZ_1	3.881010e-01	
pos 3	1870			DNASE_2	3.285700e-02		ZNF384_MA1125.1	1.000000e+00		FOXD2_forhead_1	1.000000e+00	
pos 4	1127			DNASE_2	1.704790e-01		CPEB1_RRM_1	1.704790e-01		RF1_MA0050.2	1.704790e-01	
pos 5	45			FOXD2_forhead_1	4.332070e-02		FOXD3_forhead_1	1.387830e-01		PIT1_HUMAN.H11MO.0.C	1.387830e-01	
pos 6	22			HSF1_MOUSE.H11MO.0.A	1.725320e-02		HSF1_HUMAN.H11MO.0.A	2.822410e-01		HSF2_HUMAN.H11MO.0.A	2.822410e-01	