Figure S1: Standardised residuals obtained from the NB regression model QQ plots show that negative residuals and the lower 90 percentile of the positive residuals generally follow a standard normal distribution. Deviation from the standard normal (grey line) occurs at quantiles above 2, the top 10% of positive residuals.





Figure S2: Distribution of correlation between MPCC from two parallel chains of RJMCMC run for each bait



Figure S3: Decay of CHiCAGO scores and MPPC with distance from bait. The solid line shows the median value, the dashed lines the 25th and 75th centiles, and the limits of the vertical lines the 5th and 95th centiles.



Figure S4: Comparison of CHiCAGO scores and MPPC for all potential bait-prey pairs considered for each experiment. Spearman's  $\rho$  is given in the top right of each sub figure and the black line shows a loss smooth.



Figure S5: The prevalence of expected biological characteristics at contact sites increases with CHiCAGO's and Peaky's strength of evidence for a contact in two separate datasets. Fitted values from regression models of four outcome measures in our two datasets in non-activated (left column) and activated (right column)  $CD4^+$  T cells. Row 1: promoter capture, odds that prey fragment overlaps enhancer in published T cell promoter-enhancer network [17]. Row 2: promoter capture, odds that prey fragment overlaps regions of active chromatin called by CHROMHMM of the same cells [9]. Row 3: validation, odds that prey fragment was baited in the promoter capture. Row 4: validation, average gene expression (counts,  $\log_2$  scale) of gene associated with the baited promoter in RNA-seq analysis of the same cell type [9]. Predictors are CHiCAGO score (asinh transformed) and MPPC (sqrt transformed).



Figure S6: Distribution of number of contacts called significant (score > 5) by CHiCAGO for each bait that had at least one CHiCAGO significant contact. Results from activated and non-activated cells were very similar and are combined into a single panel.



Figure S7: Comparison of number of contacts called by CHiCAGO and the posterior expected number of direct contacts derived from the joint model for each bait that had at least one CHiCAGO significant contact. The dashed line represents x = y, the coloured line the best linear fit, and *rho* gives the Spearman correlation. Results from activated and non-activated cells were very similar and are combined into a single panel.



Figure S8: Proportion of residual variance attributable to Brownian or Technical noise in the CHiCAGO analyses, as a function of distance from bait



Figure S9: Hexbin plot of predicted counts from regression models used by CHiCAGO and NB regression



Figure S10: Example autocorrelation plots for one analysis, showing (lower panel) the exploration of the model space as a function of iteration number and (upper panel) summary posterior probabilities of inclusion

Table S1: Summary of distribution of number of preys with CHiCAGO score >5 per bait, amongst those baits with at least one such prey

Experiment	Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
Promoter, non	40	202.0	256	258.5	312.0	626
Promoter, act	33	197.0	251	252.9	307.0	726
Validation, non	100	268.8	338	352.3	422.2	1112
Validation, act	95	268.2	346	355.9	429.2	1067

Table S2:  $\Delta$ BIC from the intercept only model for whether the prey fragment overlaps active chromatin states defined by [28] in non-activated and activated cells. The best fitting model (lowest  $\Delta$ BIC) is highlighted by **\***. In all cases, a robust clustered model was used to account for repeated observations at the prey fragment.

Model	Stretch length					
	2-4	5-10	11-20	21+		
non						
MPPC	-364.9	-278.6	-112.5	-98.5		
CHiCAGO	-947.0	-674.2	-356.6	-165.2		
$\mathrm{MPPC} + \mathrm{CHiCAGO}$	<b>*</b> -1111.3	<b>*</b> -747.4	<b>*</b> -359.2	<b>*</b> −175.5		
act						
MPPC	-261.7	-179.4	-105.2	-80.2		
CHiCAGO	-1054.6	-530.2	<b>*</b> -394.1	<b>*</b> -194.8		
MPPC + CHiCAGO	<b>*</b> -1150.2	<b>*</b> -568.4	-393.0	-194.1		

bin	Min Dist	Max Dist	Number of fragment pairs
Pro	moter cap	ture, non-a	nctivated
1	2502	607652	3579047
2	607653	1358092	3579041
3	1358093	2325619	3579043
4	2325620	3526852	3579046
5	3526853	5000000	3579038
Pro	moter cap	ture, activa	ated
1	2502	610510	3635118
2	610511	1371607	3635115
3	1371608	2347572	3635116
4	2347573	3543515	3635114
5	3543516	5000000	3635116
Vali	idation, no	n-activated	1
1	2506	649484	203449
2	649496	1429935	203449
3	1429942	2371494	203449
4	2371495	3546440	203449
5	3546443	4999996	203449
Vali	idation, ac	tivated	
1	2506	626939	213282
2	626940	1395426	213281
3	1395431	2331663	213282
4	2331665	3505263	213280
5	3505266	4999996	213282

Table S3: Distance bins used for NB regression

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