

Table S3: Cross Validation Results of Nucleotide-ligand ipHMMs

Domain	SMART Abr.	Sens ¹	Spec ²	Acc ³
Zinc finger	ZnFC2H2	0.67	0.48	0.50
RNA recognition motif	RRM	0.89	0.62	0.64
Actin	ACTIN	0.56	0.61	0.61
Cyclic nucleotide-monophosphate binding domain	cNMP	0.67	0.75	0.75
DNA polymerase X family	POLXc	1.00	0.85	0.85
3'-5' exonuclease	35EXOc	1.00	0.55	0.55
Histidine kinase-like ATPases	HATPasec	0.56	0.64	0.63
Pancreatic ribonuclease	RNAsePc	0.67	0.51	0.52
Pumilio-like repeats	Pumilio	1.00	0.85	0.87
Serine/Threonine protein kinases, catalytic domain	STKc	0.55	0.82	0.81
DNA polymerase A domain	POLAc	1.00	0.63	0.64
ATPases associated with a variety of cellular activities	AAA	0.50	0.98	0.98
Homeodomain	HOX	0.71	0.58	0.61
Helix-hairpin-helix DNA-binding motif class 1	HhH1	1.00	0.82	0.84
Basic region leucine zipper	BRLZ	0.88	0.71	0.73
C4 zinc finger in nuclear hormone receptors	ZnFC4	1.00	0.58	0.65
Rab subfamily of small GTPases	RAB	1.00	0.63	0.65
Helix-turn-helix lactose operon repressor	HTHLACI	1.00	0.41	0.41
Summary		0.81	0.67	0.68

¹Sensitivity

²Specificity

³Accuracy = $\frac{TP+TN}{P+N}$