

## Supplementary Table 2

### Network inference sub-challenge (SC1) results, metadata, and inclusion of teams in Consortium and post-challenge analysis

#### Column heading color:

	metadata
	metric for SC1A (experimental data task)
	metric for SC1B ( <i>in silico</i> data task)
	Consortium and post-challenge analyses inclusion

**Explanations for metrics can be found in main text or Online Methods. For convenience, a few definitions are provided below.**

SC1A mean rank: Teams were ranked within each context based on AUROC, resulting in 30 context-specific ranks for each team.

SC1A/B combined score: Average of SC1A final rank and SC1B final rank.

SC1A(SC1B) AUROC & AUPR combined score: Average of SC1A(SC1B) final rank (based on AUROC) and an alternative SC1A(SC1B) final rank (based on AUPR).

**Top-performing teams are indicated by a \* in the final rank columns for SC1A, SC1B and SC1A/B combined.**

**Note that SC1A final rank is based on "mean rank" and not "mean AUROC". However, these two metrics are highly correlated.**

**For SC1A, several teams used the prior network submitted by Team2; these teams are indicated in the "Used prior?" column.**

**Team names are anonymized. Team's with an "X" in their anonymized name did not provide any details of their approach.**

**Synapse project IDs link to individual team Synapse project pages, where team submission files, code and prior network are available.**

**Further metrics can be found on the final challenge leaderboards on Synapse ([https://www.synapse.org/HPN\\_DREAM\\_I](https://www.synapse.org/HPN_DREAM_I)).**

Anonymized Name	Summary of approach	Method Classification (Where different classifications apply to each task, classifications are given as SC1A / SC1B)
Team1	"PropheticGranger with heat diffusion prior": an extension of L1-penalized Granger causality constructed specifically to consider "future data", combined with a prior derived from known biological pathways.	Linear regression
Team2	For experimental data, a biological prior is created by applying a simulated heat diffusion process to the constituent pathways from Pathway Commons. For <i>in silico</i> data, the network inference method ARACNE is used.	Prior only / Pairwise score
Team3	Edges are removed from a literature-based network by considering time-lagged correlation between phosphoprotein pairs, fold-changes in abundance through time and results from the time-course prediction challenge	Pairwise score
Team4	An ensemble approach combining prior knowledge with results from L1-penalized Granger causality and the GENIE3 algorithm.	Ensemble
Team5	A random forest classifier, with a literature-derived network used as a "gold standard", predicts existence of edges from several measures of pair-wise association, calculated using multiple sources of data	Nonlinear regression (tree-based approach)

Team6	Network topology and parameters are optimized by minimizing an objective function based on a linear Ordinary Differential Equation (ODE) model, using a greedy search starting from a knowledge-based network topology.	ODEs
Team7	"FunChisq": a functional chi-square test to infer causal network topology based on nonparametric functional dependency from data discretized by optimal k-means clustering for each variable.	Pairwise score
Team8	Gradient tree boosting regression and a Markov assumption are used to model the time series data, with network connectivity derived using a combination of the most frequently selected features over the boosting rounds and information from a prior knowledge network	Nonlinear regression (tree-based approach)
Team9	Network structure is predicted by integrating a prior knowledge network with results of time-lagged correlation analysis on pair-wise phosphoprotein abundances.	Pairwise score
Team10	A regression approach using a stationary Markov assumption and truncated singular value decomposition to predict network structure.	Linear regression
Team11	Boruta, a wrapper feature selection method, utilizing random ferns classifier as an importance source, is used to perform feature selection for each node in the network.	Nonlinear regression (tree-based approach)
Team12	Network inference based on (static and time-lagged) mutual information and Bayesian model averaging for linear regression (the latter was applied to <i>in silico</i> data only).	Pairwise score / Ensemble
Team13	A generalized outranking approach to aggregate data-driven predictions from multiple network inference methods with prior biological interaction data.	Ensemble
Team14	Inferelator, an ODE-based method with model selection, is combined with prior information to infer network structure.	ODEs
Team15	For experimental data, information from interaction databases is combined with pair-wise correlation scores and relational logic. For <i>in silico</i> data, a network is obtained by studying stimulus- and inhibitor-mediated effects together with a novel data visualization.	Pairwise score / Other
Team16	An adaptive lasso regression model was used to infer connections between proteins.	Linear regression
Team17	The GENIE3 algorithm was used to infer weights and directions for regulatory edges between phosphoproteins, with incorporation of a prior knowledge network.	Nonlinear regression (tree-based approach)
Team18	Network inference is formulated as a linear programming problem designed specifically for perturbation time series data and models signaling as information flow.	Other
Team19	Edges contained in prior knowledge networks are selected and ranked using Pearson correlation scores between protein pairs and feature weights from a gradient boosting regression approach.	Ensemble
Team20	A constraint-based Bayesian network learning methods that infers dependencies between proteins using correlation tests or mutual information tests of various orders.	Bayesian networks

Team21	Random forests were combined with mutual information to yield protein networks that were integrated with prior literature and logic-based domain knowledge.	Ensemble
Team22	Networks are inferred by combining prior information with the output of a lasso regression model, adopted to capture the time-varying effect of protein phosphorylation between adjacent time points.	Linear regression
Team23	Protein signaling networks are learned using formal methods (formal methods are used in engineering to specify and verify concurrent software and hardware systems).	Other
Team24	Bayesian network structure learning with Hill Climbing (experimental data) or Max-Min Hill Climbing (in silico data), combined with model averaging to identify weighted networks.	Bayesian networks
Team25	Ensemble network inference approach that incorporated a prior knowledge network with results from L1-penalized Granger causality, GENIE3, and ARACNE.	Ensemble
Team26	A protein signaling network is inferred by comparing phosphoprotein abundance levels between intervention and no-intervention treatments.	Other
Team27	Cross-correlation is applied to interpolated time series data (resulting in a data point for each minute) to determine dependencies through time between pairs of phosphoproteins.	Pairwise score
Team28	A network inference method using Partial Least Squares Regression (PLSR) with the Variable Influence on Projection (VIP) score as a measure of edge confidence	Linear regression
Team29	An MCMC-based EM algorithm is used to infer network structure and parameters for a logistic regression model with latent variables representing protein phosphorylation and functional states.	Bayesian networks
Team30	Time-lagged correlation scores are calculated between the abundance of a target protein and abundances of proteins in a set of potential regulators	Other
Team31	An ensemble approach that combines prior information with the results from three existing methods: ordinary differential equations, dynamic Bayesian networks, and Bayesian Regression.	Ensemble
Team32	A consensus network learning method that integrates results from several representative network-inference algorithms, applied separately to data from each inhibitor condition	Ensemble
Team33	Dynamic Bayesian networks are combined with mutual information and an analysis of intervention-mediated effects to infer network structure.	Ensemble
Team34	An integrated approach was used to construct consensus signaling networks with high confidence interactions from three different network inference algorithms, weighted according to their agreement with a prior knowledge network.	Ensemble

Team35	A dynamic Bayesian network approach that uses exact model averaging to determine the weight of each possible network edge (see Team38 for a related static Bayesian network approach)	Bayesian networks
Team36	A network inference method based on algorithmic information theory using the Normalized Information Distance and its computable version, Normalized Compression Distance.	Pairwise score
Team37	The DDEPN (Dynamic Deterministic Effects Propagation Networks) algorithm is used to capture signaling dynamics with a Boolean model and determine optimal network structure from the time series interventional data in conjunction with a prior network.	Other
Team38	A (static) Bayesian network approach that uses exact model averaging to determine the weight of each possible network edge (see Team35 for a related dynamic Bayesian network approach)	Bayesian networks
Team39	Targets of each inhibitor are identified using the training proteomics data and external information, followed by Bayesian network inference using the GIES algorithm (Greedy Interventional Equivalence Search) with undirected edges oriented using Granger causality.	Bayesian networks
Team40	Direct cause-effect relationships, inferred from a large-scale literature-based phosphorylation network, are used to construct shortest-path trees that explain the experimental data.	Other
Team41	Lasso-based regression with iterative random feature selection to identify regulators that best predict the expression level of target proteins.	Linear regression
TeamX45		
TeamX46		
TeamX47		
TeamX48		
TeamX49		
TeamX50		
TeamX51		
TeamX52		
TeamX53		
TeamX54		
TeamX55		
TeamX56		
TeamX57		
TeamX58		
TeamX59		
TeamX60		
TeamX61		
TeamX62		
TeamX63		
TeamX64		

TeamX65		
TeamX66		
TeamX67		
TeamX68		
TeamX69		
TeamX70		
TeamX71		
TeamX72		
TeamX73		
TeamX74		
TeamX75		
TeamX76		
TeamX77		
TeamX78		
TeamX79		
TeamX80		
TeamX81		
TeamX82		
TeamX83		

yses. This extends the information provided in Table 1 in main text.

elow:  
eam (2 contexts were excluded from scoring). These were averaged to produce a mean rank score for each team.

SC1B) ranking based on AUPR.

lated (Supplementary Figure 3c).  
umn by the text "(Team2)".  
h and are therefore not members of the HPN-DREAM Consortium (see Supplementary Note 7).

s can be found. Links to all team pages can also be found under the "HPN-DREAM Community Resource" section  
Network\_Challenge).

Final team rankings and associated metrics (see also Fig. 3 & Supplementary Fig. 3)							AUROC & AUPR c (see also Supple	
SC1A mean AUROC	SC1A mean rank	SC1A final rank (based on mean rank)	SC1B AUROC	SC1B final rank (based on AUROC)	SC1A/B combined score	SC1A/B combined final rank (based on SC1A/B combined score)	SC1A AUROC & AUPR combined score	SC1A rank (based on AUROC & AUPR combined score)
0.782	6.40	1*	0.557	28	14.5	11	1.5	1
0.771	7.73	2	0.458	65	33.5	24	1.5	1
0.755	8.20	3	0.564	23	13	9	5.0	5
0.746	10.40	4	0.620	11	7.5	3	3.5	3
0.732	11.50	5	0.601	13	9	6	4.5	4

0.715	12.27	6	0.658	7	6.5	2	6.0	6
0.715	14.10	7	0.764	1*	4	1*	8.0	8
0.699	15.33	8	0.577	17	12.5	8	8.0	8
0.696	15.77	9	0.495	58	33.5	24	7.0	7
0.677	18.17	10	0.662	5	7.5	3	11.5	11
0.641	21.40	13	0.735	2	7.5	3	13.5	12
0.650	21.80	14	0.640	10	12	7	16.5	15
0.630	22.63	17	0.646	9	13	9	16.5	15
0.662	22.80	18	0.619	12	15	12	17.5	18
0.630	24.87	22	0.565	22	22	16	21.0	21
0.627	26.07	23	0.517	47	35	30	22.0	22
0.608	30.23	26	0.674	4	15	12	18.5	19
0.569	34.17	29	0.683	3	16	14	30.5	29
0.566	35.27	30	0.518	46	38	33	32.0	33
0.555	36.73	32	0.549	35	33.5	24	29.5	28

0.541	37.47	33	0.578	16	24.5	18	31.0	31
0.544	40.20	37	0.579	15	26	20	42.0	41
0.521	42.43	40	0.472	61	50.5	45	42.0	41
0.525	43.90	41	0.548	37	39	35	39.0	38
0.523	44.20	43	0.464	64	53.5	50	44.5	44
0.500	44.77	44	0.548	36	40	36	46.5	46
0.504	45.33	45	0.501	55	33	43	45.0	45
0.510	45.63	48	0.659	6	27	21	48.0	48
0.511	45.90	51	0.508	51	51	47	52.5	51
0.497	46.60	52	0.511	48	50	43	55.5	56
0.496	46.73	53	0.467	62	57.5	53	56.5	57
0.508	46.97	56	0.560	25	40.5	37	59.0	60
0.503	47.70	57	0.652	8	32.5	24	57.0	59
0.499	49.13	61	0.509	50	55.5	51	62.0	63



0.495	50.97	64	0.538	41	52.5	48	64.5	64
0.489	51.20	65	0.532	44	54.5	51	67.0	67
0.486	52.17	70	0.504	53	61.5	56	68.0	69
0.492	52.33	71	0.559	26	48.5	41	69.5	71
0.541	39.60	36					36.0	36
0.499	45.73	49					50.5	50
			0.552	33				
0.653	19.67	11	0.498	56	33.5	24	14.5	14
0.655	20.47	12					11.0	10
0.658	21.97	15	0.574	19	17	15	20.0	20
0.645	22.37	16					14.0	13
0.642	23.30	19	0.504	54	36.5	32	17.0	17
0.642	23.70	20					22.0	22
0.625	24.27	21	0.554	29	25	19	22.0	22
0.612	27.10	24					25.0	26
0.609	28.07	25	0.544	38	31.5	23	26.5	27
0.603	30.57	27	0.511	49	38	33	24.5	25
0.584	33.07	28	0.576	18	23	17	31.5	32
0.549	36.30	31					30.5	29
0.538	37.77	34					36.0	36
0.564	38.70	35					33.0	34
0.520	41.57	38	0.572	20	29	22	35.0	35
0.518	41.93	39					39.0	38
0.525	43.97	42					41.0	40
0.517	45.33	45	0.571	21	50	24	43.5	43
0.498	45.47	47	0.561	24	35.5	31	49.0	49
0.510	45.87	50	0.539	40	45	39	46.5	46

0.509	46.77	54	0.473	60	57	52	55.0	53
0.497	46.87	55					55.0	53
0.496	47.80	58					54.0	52
0.506	48.13	59					60.0	61
0.510	48.57	60	0.467	63	61.5	56	56.5	57
0.490	50.30	62	0.497	57	59.5	55	65.5	65
0.481	50.37	63	0.553	32	47.5	40	60.0	61
0.481	51.3	66	0.542	39	52.5	48	68.5	70
0.488	51.533	67	0.554	30	48.5	41	65.5	65
0.497	51.83	68					67.5	68
0.485	52.03	69	0.592	14	41.5	37	55.0	53
0.448	58.37	72	0.475	59	65.5	56	72.0	72
0.441	60.00	73	0.526	45	59	54	73.0	73
0.394	64.90	74	0.558	27	50.5	45	74.0	74
			0.553	31				
			0.549	34				
			0.538	42				
			0.534	43				
			0.508	52				

of the challenge webpage at [https://www.synapse.org/HPN\\_DREAM\\_Network\\_Challenge](https://www.synapse.org/HPN_DREAM_Network_Challenge).

Combined metrics (Supplementary Fig. 6)		Statistical significance (see also Supplementary Fig. 3 & 7)			
SC1B AUROC & AUPR combined score	SC1B rank (based on AUROC & AUPR combined score)	SC1A number of statistically significant AUROC scores (across 32 contexts, FDR<0.05)	SC1B AUROC statistical significance (FDR)	Used prior?	SC1A vs. SC1B method
33.0	33	23	0.131	Yes (Team2)	Same, except for use of prior network in SC1A
65.0	65	24	0.857	Yes	Different
24.0	21	23	0.108	Yes	Same, except for use of prior network in SC1A
7.5	8	20	3.00E-03	Yes (Team2)	Same
15.0	14	20	0.015	Yes	Same, except for use of prior network in SC1A

8.5	10	19	8.60E-05	Yes	Different
1.0	1	18	3.11E-11	No	Same
26.0	25	17	0.063	Yes	Same, except for use of prior network in SC1A
60.0	61	12	0.585	Yes	Same, except for use of prior network in SC1A
5.5	3	13	6.75E-05	No	Same
7.5	8	9	3.45E-09	No	Same
6.0	4	7	4.46E-04	No	Different
7.0	7	7	2.63E-04	Yes	Same, except for use of prior network in SC1A
10.0	11	13	3.00E-03	Yes	Same, except for use of prior network in SC1A
21.0	18	9	0.106	Yes	Different
37.5	39	9	0.416	No	Same
3.5	2	8	2.01E-05	Yes (Team2)	Same, except for use of prior network in SC1A
6.0	4	4	7.74E-06	No	Same
47.0	48	4	0.413	Yes	Same, except for use of prior network in SC1A
39.5	42	0	0.154	Yes	Same, except for use of prior network in SC1A

16.0	15	0	0.063	Yes	Same, except for use of prior network in SC1A
16.5	16	0	0.063	Yes	Same, except for use of prior network in SC1A
60.5	62	0	0.804	No	Same
29.0	29	2	0.158	No	Different
63.5	64	0	0.827	Yes (Team2)	Same, except for use of prior network in SC1A
27.5	27	0	0.158	No	Same
53.0	53	2	0.546	No	Same
6.5	6	6	8.60E-05	No	Same
52.5	52	0	0.486	No	Same
50.5	51	0	0.476	No	Same
63.0	63	0	0.821	Yes	Same
19.5	17	3	0.126	No	Different
10.0	11	0	1.51E-04	No	Same
53.0	53	0	0.486	Yes	Same

35.0	36	0	0.215	No	Same
46.5	47	0	0.263	No	Same
55.5	56	0	0.521	Yes	Same, except for use of prior network in SC1A
24.0	21	0	0.126	No	Same
		0		Yes	n/a
		0		Yes	n/a
33.5	34		0.141	n/a	n/a
57.5	57	11	0.569		
		13			
35.5	37	8	0.070		
		12			
50.0	50	9	0.521		
		9			
22.0	19	7	0.140		
		7			
38.5	41	8	0.179		
46.0	46	5	0.476		
14.5	13	2	0.065		
		2			
		0			
		5			
25.0	23	0	0.073		
		1			
		4			
22.5	20	0	0.075		
27.5	27	0	0.118		
41.0	43	0	0.214		

55.0	55	1	0.802		
		0			
		0			
		1			
59.0	59	0	0.821		
59.0	59	0	0.571		
34.5	35	2	0.141		
32.5	32	0	0.195		
26.5	26	0	0.140		
		0			
25.0	23	0	0.027		
58.0	58	0	0.802		
45.0	45	0	0.319		
29.5	31	0	0.127		
29.0	29		0.141		
37.0	38		0.154		
41.5	44		0.215		
38.0	40		0.248		
49.5	49		0.486		

				See Supplementary Note 7	See Suppleme
Synapse project ID	Prior network available on Synapse?	Code available on Synapse?	Methodological Innovation? (Novel method or standard method with some novel adaptations/additions; self-reported by team)	Member of HPN- DREAM Consortium?	Included in aggregate submission network formation for SC1A & SC1B
<a href="#">syn2347433</a>	Yes	Yes (R, Python)	Yes	Yes	Yes
<a href="#">syn2211033</a>	Yes	Yes (R, Python)	SC1A: Yes SC1B: No	Yes	Yes
<a href="#">syn2356612</a>	Yes	Yes (R)	No	Yes	Yes
n/a	No	No	No	No	Yes
<a href="#">syn2341926</a>	Yes	Yes (Python and software: WEKA, BIANA, iGPS)	Yes	Yes	Yes



<a href="#">syn2343026</a>	Yes	Yes (Matlab, R)	Yes	Yes	Yes
<a href="#">syn2331245</a>	n/a	Yes (R)	Yes	Yes	Yes
<a href="#">syn2337247</a>	Yes	Yes (Python)	No	Yes	Yes
<a href="#">syn2341955</a>	Yes (see notes)	Yes (Perl)	No	Yes	Yes
<a href="#">syn2341963</a>	n/a	Yes (Matlab, Perl)	Yes	Yes	Yes
<a href="#">syn2344753</a>	n/a	Yes (R)	Yes	Yes	Yes
<a href="#">syn2343782</a>	n/a	Yes (Matlab)	Yes	Yes	Yes
<a href="#">syn2337266</a>	Yes	No	Yes	Yes	Yes
<a href="#">syn2377038</a>	Yes	Yes (R)	Yes	Yes	Yes
n/a	No	No	Yes	No	Yes
<a href="#">syn2331255</a>	n/a	Yes (R)	Yes	Yes	Yes
<a href="#">syn2345443</a>	Yes	Yes (R, Python)	No	Yes	Yes
<a href="#">syn2341842</a>	n/a	Yes (R)	Yes	Yes	Yes
<a href="#">syn2343035</a>	Yes	Yes (R)	Yes	Yes	Yes
n/a	No	No	Yes	No	Yes

n/a	No	No	Yes	Yes	Yes
n/a	No	No	No	Yes	Yes
n/a	n/a	No	Yes	No	Yes
<a href="#">syn2342945</a>	n/a	Yes (R)	No	Yes	Yes
n/a	No	No	No	Yes	Yes
<a href="#">syn2371315</a>	n/a	Yes (R)	No	Yes	Yes
n/a	n/a	No	Yes	No	Yes
n/a	n/a	No	Yes	Yes	Yes
<a href="#">syn2344929</a>	n/a	Yes (Python)	Yes	Yes	Yes
<a href="#">syn2342961</a>	n/a	Yes (C++)	Yes	Yes	Yes
<a href="#">syn2375076</a>	No	Yes (Matlab)	No	Yes	Yes
n/a	n/a	No	Yes	Yes	Yes
n/a	n/a	No	Yes	No	Yes
<a href="#">syn2343054</a>	No	No	Yes	Yes	Yes

n/a	n/a	No	Yes	Yes	Yes
<a href="#">syn2343030</a>	n/a	Yes (Mathematica)	Yes	Yes	Yes
n/a	No	No	Yes	No	Yes
n/a	n/a	No	Yes	Yes	Yes
n/a	No	No	Yes	No	Yes
n/a	No	No	Yes	Yes	Yes
n/a	n/a	No	Yes	Yes	Yes
				No	Yes
				No	Yes
				No	Yes
				No	Yes
				No	Yes
				No	Yes
				No	No (see note)
				No	Yes
				No	No (see note)
				No	Yes
				No	Yes
				No	Yes
				No	No (see note)
				No	Yes
				No	Yes
				No	Yes
				No	Yes
				No	No (see note)
				No	No (see note)
				No	Yes

[illegible]

ntary Note 10	See Online Methods	
Included in SC1A vs. SC1B score comparison (Fig. 2d)	Included in aggregate prior network formation?	Notes
Yes	No (see notes)	SC1A top-performer Used same prior network as Team2 - only included in aggregate prior formation once
Yes	Yes	
Yes	Yes	
Yes	No (see notes)	Used same prior network as Team2 - only included in aggregate prior formation once
Yes	Yes	

Yes	Yes	
Yes	n/a	SC1B top-performer and most consistent performer across SC1A & SC1B
Yes	Yes	
Yes	No (see notes)	Bug discovered in formation of prior network
Yes	n/a	
Yes	n/a	
Yes	n/a	
Yes	Yes	
Yes	Yes	
Yes	No	
Yes	n/a	
Yes	No (see notes)	Used same prior network as Team2 - only included in aggregate prior formation once
Yes	n/a	
Yes	Yes	
Yes	No	

Yes	Yes	
Yes	No (see notes)	Bug discovered in formation of prior network
Yes	n/a	
Yes	n/a	
Yes	No (see notes)	Used same prior network as Team2 - only included in aggregate prior formation once
Yes	n/a	
Yes	n/a	
Yes	n/a	
Yes	n/a	
Yes	n/a	
Yes	n/a	
Yes	No	
Yes	n/a	
Yes	n/a	
Yes	No	

Yes	n/a	
Yes	n/a	
Yes	No	
Yes	n/a	
n/a	No	
n/a	Yes	
n/a	n/a	
Yes		
n/a		
Yes		
n/a		
Yes		
n/a		
No (see note)		SC1A submission correlated with TeamX49 (r=0.77)
n/a		
No (see note)		SC1A submission correlated with TeamX49 (r=0.89)
Yes		
Yes		
n/a		
n/a		SC1A submission correlated with TeamX56 (r=0.89)
n/a		
Yes		
n/a		
n/a		
No (see note)		SC1B submission correlated with TeamX59 (r=0.89)
No (see note)		SC1A submission correlated with TeamX49 (r=0.84)
Yes		



Yes		
n/a		
n/a		
n/a		
Yes		
Yes		
No (see note)		SC1B submission correlated with TeamX59 (r=0.87)
No (see note)		SC1B submission correlated with Team35 (r=1)
No (see note)		SC1B submission correlated with Team38 (r=1)
n/a		
Yes		
Yes		
Yes		
Yes		
n/a		
n/a		
n/a		
n/a		
n/a		