

Structure-based prediction of
protein–protein interactions
on a genome-wide scale

基于结构的大规模
蛋白互作预测

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PrePPI (predicting protein–protein interactions), which combines structural and non-structural interaction clues using Bayesian statistics, is comparable in accuracy to high-throughput experiments and have the ability to identify unexpected PPIs (protein–protein interactions) of considerable biological interest.

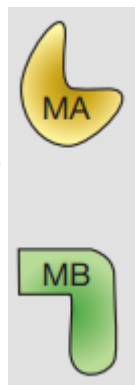
Based on structures or
homology models in
PDB/Modbase/Skybase



A pair of query
proteins

Structural
representatives

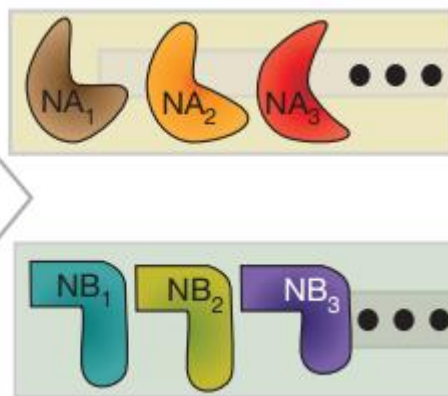
Sequence
similarity



Structural
similarity

structural
alignment tool
Ska

Structural
neighbours



Template complexes
from PDB/PQS



Interaction
models

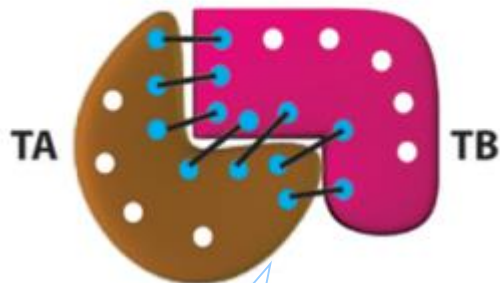
Structural
superposition



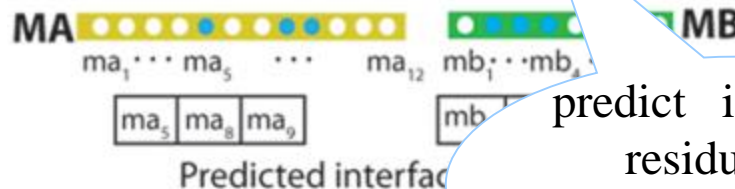
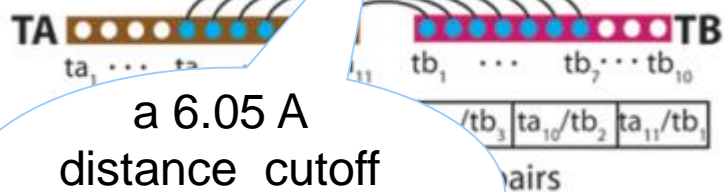
Model
evaluation

SM

Template Complex



Interaction Model

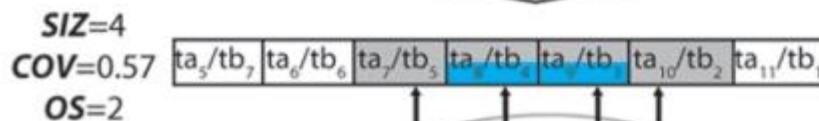


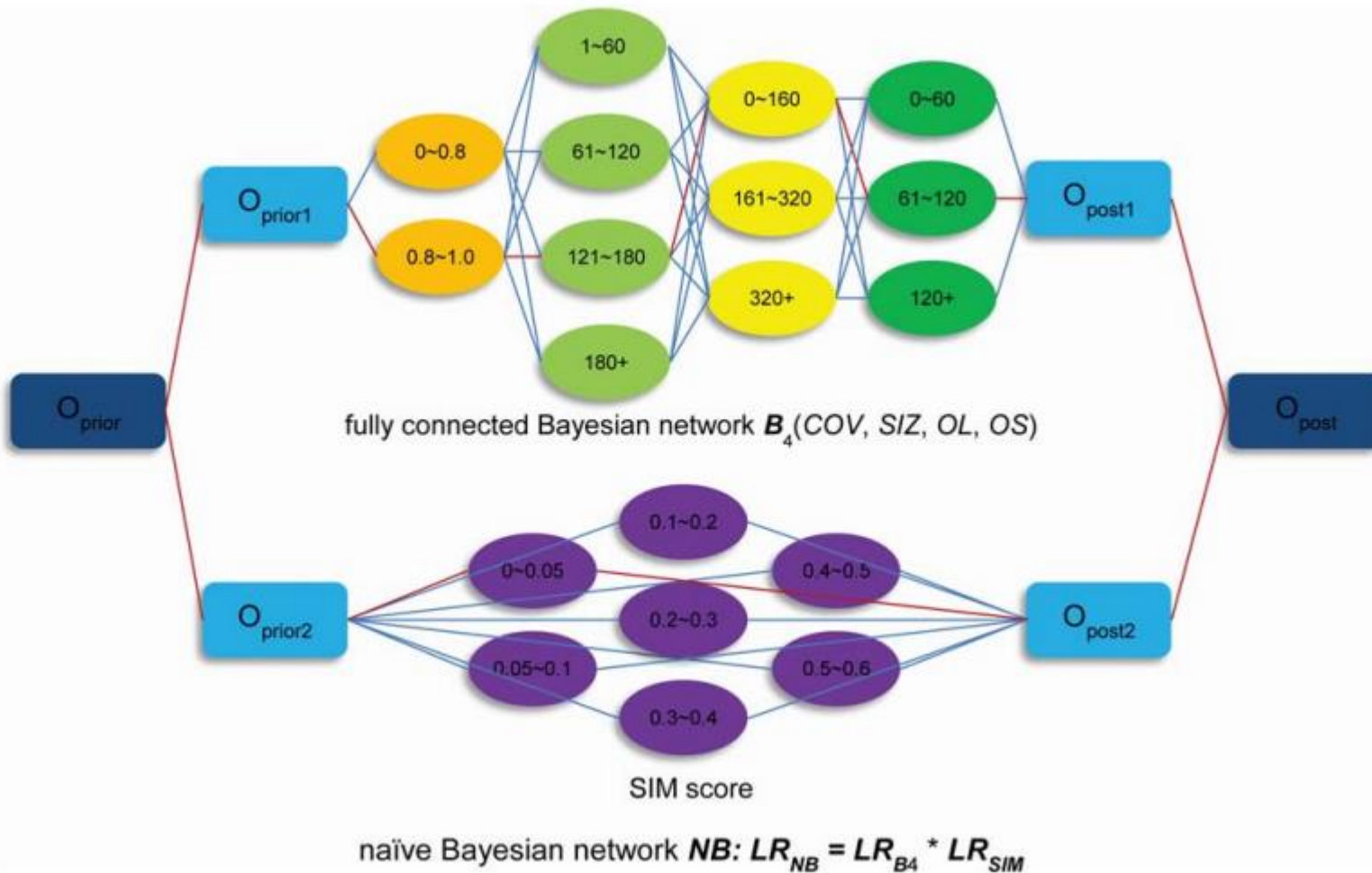
a 6.05 Å distance cutoff between heavy atoms

predict interfacial residues in PreUds PINUP and cons-PPISP

Structure-based sequence alignment

$$SIM = \frac{PSD(TA,MA) + PSD(TB,MB)}{2}$$





$$LR(bin) = \frac{O_{post}}{O_{prior}}$$

non-structural evidences

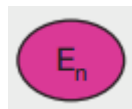
structural model



Co-expression



Functional similarity

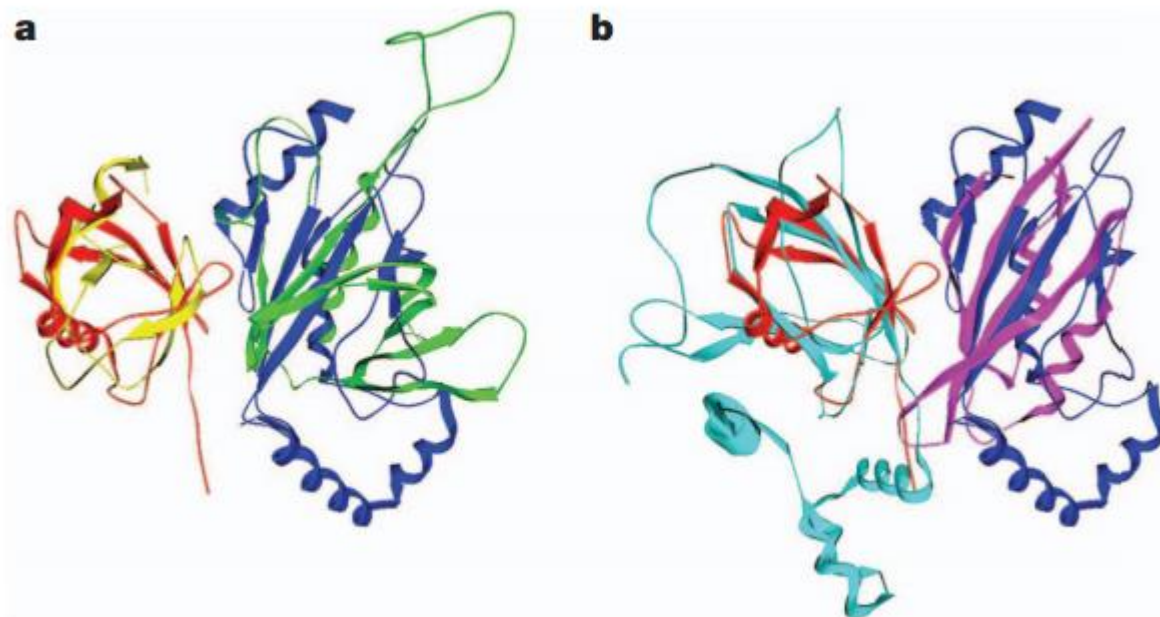


Evolutionary similarity

a single naive Bayes PPI classifier

$$LR(c_1, c_2, \dots, c_n) = \prod_{i=1}^n LR(c_i)$$

PrePPI score



**Figure 3 | Models for the PPI formed between PRKD1 and PRKCE, and
EEF1D and VHL using homology models and remote structural**



| Predicted Interaction ^a | Need homology model? | Domain1-Domain2: (model) ^b | Domain1-Domain2: (template) ^b | PrePPI_LR (probability) | Result ^c |
|--|-------------------------------|---------------------------------------|--|-------------------------|---|
| PPAR- γ \leftrightarrow LXR β | No | LBD-LBD | LBD-LBD | 3.6E6 (>0.99) | Confirmed (Fig.S10) |
| PPAR- γ \leftrightarrow PAX7 | Yes | LBD-Homeo | LBD-LBD | 4010 (0.87) | Confirmed (Fig.S10) |
| PPAR- γ \leftrightarrow PDX1 | Yes | LBD-Homeo | LBD-LBD | 3114 (0.84) | Confirmed (Fig.S10) ^d |
| PPAR- γ \leftrightarrow NKX2-2 | Yes | LBD-Homeo | LBD-LBD | 2764 (0.82) | Confirmed (Fig.S10) ^d |
| PPAR- γ \leftrightarrow HHEX | Yes | LBD-Homeo | LBD-LBD | 3602 (0.86) | Not Confirmed (Fig.S10) ^d |
| PPAR- γ \leftrightarrow CREB | No structural model was built | | | 63 (0.10) | Not Confirmed (Fig.S10) ^{d, e} |
| VHL \leftrightarrow EEF1D | Yes | VHL-EF1_GNE | Ubiquitin-UBC | 53 (0.08) | Confirmed (Fig.S14) ^f |
| SOCS3 \leftrightarrow RAF1 | Yes | SH2-RBD | Pcc1-Pcc1 | 104 (0.15) | Confirmed (Fig.S11) |
| SOCS3 \leftrightarrow GRB2 | Yes | SH2-SH2 | SH2-SH2 | 7.6E4 (0.99) | Confirmed (Fig.S11) |
| SOCS3 \leftrightarrow BTK | Yes | SH2-SH3 | SH2-SH3 | 4242 (0.88) | Confirmed (Fig.S11) |
| SOCS3 \leftrightarrow NCK1 | Yes | SH2-SH2 | SH2-SH2 | 2064 (0.77) | Not Confirmed (Fig.S10) |



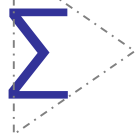
| Predicted Interaction ^a | Need homology model? | Domain1-Domain2: (model) ^b | Domain1-Domain2: (template) ^b | PrePPI_LR (probability) | Result ^c |
|--|----------------------|---------------------------------------|--|-------------------------|---|
| PCDH- α 4 \leftrightarrow RET | Yes | CA-CA | CA-CA | 3296 (0.85) | Confirmed (Fig.S12) ^g |
| PCDH- α 4 \leftrightarrow ROR2 | Yes | CA-Ig | CA-CA | 350 (0.58) | Confirmed (Fig.S12) ^{d, h} |
| PCDH-α4\leftrightarrowROR2 | Yes | CA-Ig | CA-CA | 350 (0.58) | Confirmed (Fig.S12)^{d, h} |
| PRPF19 \leftrightarrow CUL4A | Yes | Ubox-Nedd8 | Ubox-Nedd8 | 7246 (0.92) | Not Confirmed (Fig.S13) ⁱ |
| PRPF19 \leftrightarrow BMI1 | Yes | Ubox-RING | RING-RING | 1249 (0.68) | Confirmed (Fig.S13) ^j |
| SATB2 \leftrightarrow SMARCC2 | Yes | Homeo-SWIRM | Homeo-Homeo | 2486 (0.81) | Confirmed (Fig.S13) ^j |
| SATB2 \leftrightarrow RCOR1 | Yes | Homeo-SANT | Homeo-Homeo | 821 (0.58) | Confirmed (Fig.S13) ^j |



Three key elements are responsible for the success of structural modelling and PrePPI.

1. the marked expansion in the number of interactions;
2. the efficiency of our scoring scheme for interaction models;
3. the Bayesian evidence integration method.

<http://bhapp.c2b2.columbia.edu/PrePPI/>



Thank you for your
attention!