# The information theory of higher-order interactions

From surprisal to Ising interactions, and beyond

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# Outline

- Goal: quantify higher-order structure.
  - Information theory: Multivariate entropy & mutual information
  - Partial information decomposition: Unique, redundant & synergistic information
  - Statistical physics: Interactions in energy-based models
  - Are these related?
- Today:
  - Relating interactions in energy-based models to information theory.
  - Some ways in which synergy is better captured by these interactions than by entropy-based measures.



Article

Higher-Order Interactions and Their Duals Reveal Synergy and Logical Dependence beyond Shannon-Information

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# Higher-order structure

• Graph:



• Hypergraph:



- Pairwise edges
- *e.g.* correlations, mutual information, regression, etc.
- Higher-order edges
- Higher-order dependence?

# Part 1: Higher-order information theory

- What is higher-order information?
- Why is it problematic?

# Information and entropy

- Discrete random variable X, distributed as p(X = x)
- Question: how to quantify information/surprise *S* upon realisation X = x?
  - $S(X = x) = 0 \iff p(X = x) = 1$  (no surprise)
  - *S* decreases monotonically with p(x)
  - $X \perp Y \implies S(X = x, Y = y) = S(X = x) + S(Y = y)$
- $\implies$   $S(X = x) = -\log p(x)$
- Surprisal/Shannon information
- Expected surprise of X under p(X):  $H(X) = \mathbb{E}_p[S(x)] = -\sum_x p(x) \log p(x)$
- Entropy of *X*.

#### How to quantify dependence?

- Random variables X and Y
- Independence:  $X \perp Y \implies p(x, y) = p(x)p(y)$
- Question: *How far is the joint from the product of marginals?*
- Relative entropy/KL divergence:  $D_{KL}(p(z)||q(z)) = \sum_{z} p(z) \log \frac{p(z)}{q(z)}$
- Mutual information:

$$MI(X; Y) = D_{KL}(p(x, y)||p(x)p(y)) = \sum_{x,y} p(x, y) \log \frac{p(x, y)}{p(x)p(y)}$$
$$= \sum_{x,y} p(x, y) \log p(x, y) - \sum_{x} p(x) \log p(x) - \sum_{y} p(y) \log p(y)$$
$$= -H(X, Y) + H(X) + H(Y)$$

• Conditional mutual information: MI(X; Y|Z) = H(X|Z) + H(Y|Z) - H(X, Y|Z)

### Higher-order dependence

• Difference between joint and product of marginals

$$D_{KL}\left(p(x_1, x_2, \dots, x_n) \mid\mid \prod_{i=1}^n p(x_i)\right) = \sum_{i=1}^n H(X_i) - H(X_1, X_2, \dots, X_n)$$
  
= TC(X<sub>1</sub>, X<sub>2</sub>, ..., X<sub>n</sub>)

- Problem: TC only considers terms of order 1 and *n*.
- Alternative: How does knowledge of  $X_3$  affect  $MI(X_1, X_2)$ ?

$$MI(X_1, X_2, X_3) = MI(X_1, X_2) - MI(X_1, X_2 \mid X_3)$$

 $= H(X_1) + H(X_2) + H(X_3) - H(X_1, X_2) - H(X_1, X_3) - H(X_2, X_3) + H(X_1, X_2, X_3)$ 

- (note: this is symmetric)
- Then continue inductively (up to minus sign):

$$MI(X_1, X_2, \dots, X_n) = MI(X_1, X_2, \dots, X_{n-1}) - MI(X_1, X_2, \dots, X_{n-1} \mid X_n)$$

# Information and set theory

- Mutual information as a Venn diagram:
- Question: How many elements in the intersection of finite sets *A* and *B*?

$$|A \cup B| = |A| + |B| - |A \cap B|$$
$$\implies |A \cap B| = |A| + |B| - |A \cup B|$$
$$\implies MI(X, Y) = H(X) + H(Y) - H(X, Y)$$



- Coincides with previous definition.
- Is information like a set measure?

# Information and set theory

- Question: How many elements in the union of three finite sets *A*, *B*, and *C*?
- $|A \cup B \cup C| = |A| + |B| + |C| |A \cap B| |A \cap C|$ -  $|B \cap C| + |A \cap B \cap C|$
- Recall:  $MI(X_1, X_2, X_3) = H(X_1) + H(X_2) + H(X_3) H(X_1, X_2) H(X_1, X_3) H(X_2, X_3) + H(X_1, X_2, X_3)$
- Union instead of intersection?!
- Venn diagrams are misleading—entropy is not a measure!
- Intersection of two entropies is not an entropy.
- Mutual information can be negative.



# **Negative information**

• XOR gate:  $X_3 = X_1 \oplus X_2$ 

$$MI(X_1, X_2, X_3) = MI(X_1, X_2) - MI(X_1, X_2 \mid X_3)$$
$$= 0 - 1 = -1$$

$X_1$	$X_2$	$X_3$
0	0	0
0	1	1
1	0	1
1	1	0

#### • Problems:

- How to interpret negative information? (*Partial information decomposition*)
- *MI*(*X*<sub>1</sub>, *X*<sub>2</sub>, *X*<sub>3</sub>) is bounded by pairwise quantities—can we separate the dependencies at different orders?
- Why does the cardinality of a *union* of sets show up?
- To answer these questions, let's first look at a *different* approach to higher-order dependence.

# Part 2: Higher-order interactions

- Two different perspectives on the Ising model
- A model-free solution to the inverse Ising problem

# The Ising model: a physical perspective

- A model of interacting spins  $\sigma$  on a lattice, in a magnetic field h.

• 
$$\sigma = \{\sigma_1, \ldots, \sigma_N\}, \ \sigma_i \in \{0, 1\}.$$

• The energy of a configuration—at equilibrium—is given by:

$$E(\sigma) = -\sum_{i,j} \tilde{J}_{ij}\sigma_i\sigma_j - \sum_i h_i\sigma_i$$

- High energy:  $\uparrow \ \downarrow \ \uparrow \ \downarrow$
- Low energy:  $\uparrow \uparrow \uparrow \uparrow$
- The probability of a configuration is given by:

$$p(\sigma) = \frac{1}{Z} \exp(-\beta E(\sigma))$$

- $\mathcal{J}_{ij}$  is called the *coupling*, or interaction, between spins *i* and *j*.
- · Description of magnets, neurons, bird flocks, social dynamics, etc.

# The Ising model: a statistical perspective (Jaynes '57)

- Observe binary variables  $\sigma = \{\sigma_1, \ldots, \sigma_N\}$ .
- Write down a probability distribution  $p(\sigma)$ .
- Fewest assumptions: maximum entropy distribution

$$H(p) = -\sum_{\sigma} p(\sigma) \log p(\sigma)$$

- Subject to constraints  $\sum_{\sigma} p(\sigma) = 1 \implies p(\sigma) = 2^{-N}$
- Add more constraints:

$$\sum_{\sigma} p(\sigma)\sigma_i = \mu_i, \quad \sum_{\sigma} p(\sigma)\sigma_i\sigma_j = \mu_{ij}$$

- $\implies p(\sigma) = \frac{1}{Z} \exp(-\sum_{i,j} \mathcal{J}_{ij}\sigma_i\sigma_j \sum_i h_i\sigma_i)$
- Ising model!
- Interactions and field fixed by observed moments.

# Higher-order interactions & the inverse problem

- What if you constrain the higher-order moments?
- MaxEnt solution:

$$E(\sigma) = -\sum_{i} h_{i}\sigma_{i} - \sum_{i,j} \mathcal{J}_{ij}\sigma_{i}\sigma_{j} - \sum_{i,j,k} \mathcal{J}_{ijk}\sigma_{i}\sigma_{j}\sigma_{k} - \dots$$

- An Ising model with **higher-order** interactions.
- Predicting properties of  $p(\sigma)$  is the *forward* Ising problem.
- Fitting to data is the *inverse* Ising problem.
- Distentangles all orders of interactions.
- The inverse problem is hard.
  - MLE inference (exponential, pairwise only?)
  - Pseudolikelihood (polynomial, approximate but consistent, pairwise only?)
  - Restricted Boltzmann machines (approximate, unstable)

#### Interactions from the ground up

- What do we really mean when we say interaction? (Beentjes & Khamseh, 2020)
- A difference which makes a difference. (Bateson, 1972)
- A change in effect on an outcome, determined by the value of another variable, in the absence of other variables.

*1-point interaction* with respect to outcome *Y*:

$$I_i = \frac{\partial Y}{\partial X_i} \Big|_{\underline{X}=0} \qquad \qquad \underline{X} = X \setminus \{X_i\}$$

2-point interaction:

$$I_{ij} = \frac{\partial I_i}{\partial X_j}\Big|_{\underline{X}=0} = \frac{\partial^2 Y}{\partial X_j \partial X_i}\Big|_{\underline{X}=0} \qquad \qquad \underline{X} = X \setminus \{X_i, X_j\}$$

#### Interactions from the ground up

• A change in 2-point interaction is a *3-point interaction*:

$$I_{ijk} = \frac{\partial I_{ij}}{\partial X_k}\Big|_{\underline{X}=0} = \frac{\partial^3 Y}{\partial X_k \partial X_j \partial X_i}\Big|_{\underline{X}=0}$$

$$\underline{X} = X \setminus \{X_i, X_j, X_k\}$$

- And so on.
- Interactions are defined with respect to an outcome.
- Now: let  $Y = \log p(X)$ , and  $X \in \{0, 1\}^N$ . Then:

$$I_{i} = \frac{\partial \log p(X)}{\partial X_{i}} \Big|_{\underline{X}=0}$$
  
= log  $p(X_{i} = 1 \mid \underline{X} = 0) - \log p(X_{i} = 0 \mid \underline{X} = 0)$   
= log  $\frac{p(X_{i} = 1 \mid \underline{X} = 0)}{p(X_{i} = 0 \mid \underline{X} = 0)}$ 

#### Interactions from the ground up

- Notation  $p_{abc} = p(X_i = a, X_j = b, X_k = c \mid \underline{X} = 0)$
- 1-point interactions:

$$I_{i} = \frac{\partial \log p(X)}{\partial X_{i}}\Big|_{\underline{X}=0} = \log \frac{p_{1}}{p_{0}}$$

2-point:

$$I_{ij} = \frac{\partial^2 \log p(X)}{\partial X_j \partial X_i} \Big|_{\underline{X}=0} = \log \frac{p_{11}p_{00}}{p_{01}p_{10}}$$

3-point:

$$I_{ijk} = \frac{\partial^3 \log p(X)}{\partial X_k \partial X_j \partial X_i} \Big|_{\underline{X}=0} = \log \frac{p_{111} p_{100} p_{010} p_{001}}{p_{000} p_{011} p_{101} p_{110}}$$

- Symmetric in terms of the variables:  $I_S = I_{\pi(S)}$
- Conditionally independent variables do not interact:  $X_i \perp\!\!\!\perp X_j \mid \underline{X} \implies I_{ij} = 0$

#### Model-free interactions solve the inverse Ising problem!

$$E(X) = -\sum_{i} h_{i}X_{i} - \sum_{i,j} \mathcal{J}_{ij}X_{i}X_{j} - \sum_{i,j,k} \mathcal{J}_{ijk}X_{i}X_{j}X_{k} - \dots$$

$$I_{ijk} = \frac{\partial^{3}\log p(X)}{\partial X_{k}\partial X_{j}\partial X_{i}}\Big|_{\underline{X}=0}$$

$$= -\frac{\partial^{3}E(X)}{\partial X_{k}\partial X_{j}\partial X_{i}}\Big|_{\underline{X}=0}$$

$$= \mathcal{J}_{ijk}$$

$$= \log \frac{p_{111}p_{100}p_{010}p_{001}}{p_{000}p_{011}p_{101}p_{110}} \approx \log \frac{\hat{n}_{111}\hat{n}_{100}\hat{n}_{010}\hat{n}_{001}}{\hat{n}_{000}\hat{n}_{011}\hat{n}_{101}\hat{n}_{110}}$$

- $\hat{n}_{abc}$  is the number of samples that look like  $(0, \ldots, 0, a, b, c, 0, \ldots, 0)$
- NB: This solves the *untruncated* problem.

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### **Model-free interactions**

- Surprisal of a state  $X = x : -\log p(x)$
- Interactions are sums of surprisals:

$$I_{i} = \log \frac{p_{1}}{p_{0}} = \log p_{1} - \log p_{0}$$

$$I_{ij} = \log \frac{p_{11}p_{00}}{p_{01}p_{10}} = \log p_{11} + \log p_{11} - \log p_{01} - \log p_{10}$$

$$I_{ijk} = \log \frac{p_{111}p_{100}p_{010}p_{001}}{p_{000}p_{011}p_{110}} = \dots$$

- What determines the alternating signs? (Even/odd)
- Similar to **mutual information**

• Higher-order mutual information:

MI(X, Y) = H(X) + H(Y) - H(X, Y)MI(X, Y, Z) = H(X) + H(Y) + H(Z) - H(X, Y) - H(X, Z) - H(Y, Z) + H(X, Y, Z)

- Sign determined by even/odd number of variables
- Inclusion/Exclusion principle
- Higher-order structure is captured by Möbius inversion

# Part 3: Higher-order structure as Möbius inversions

- The Möbius inversion formula
- Interactions and information as inversions
- Dualities

# **Möbius function**

- Subsets form a lattice under inclusion:
- $\bullet \ S \leq T \iff S \subseteq T$
- Capture relationships in poset P: Möbius function μ<sub>P</sub> : P × P → ℝ

$$\mu_P(x, y) = \begin{cases} 1 & \text{if } x = y \\ -\sum_{z: x \le z < y} \mu_P(x, z) & \text{if } x < y \\ 0 & \text{otherwise} \end{cases}$$



#### Definition: Möbius inversion over a poset, Rota (1964)

Let P be a poset  $(S, \leq)$ , let  $\mu_P : P \times P \to \mathbb{R}$  be the Möbius function, and let  $g : P \to \mathbb{R}$  be a function on *P*. Then, the function

$$f(y) = \sum_{x \leq y} \mu_P(x, y) g(x)$$

is called the Möbius inversion of g on P. Furthermore, this can be inverted:

$$f(y) = \sum_{x \le y} \mu_P(x, y) g(x) \iff g(y) = \sum_{x \le y} f(x)$$

### Möbius function: Examples

• Let 
$$P = (\mathbb{N}, \leq), \quad f : P \to \mathbb{R}, \quad F(x) = \sum_{y \leq x} f(y).$$
  
 $\mu(a, a) = 1$   
 $\mu(a, a + 1) = -1$   
 $\mu(a, a + k) = 0, \text{ for } k > 1$ 

- Then the Möbius inversion of *F* is  $f(x) = \sum_{y \le x} \mu(y, x) F(y) = F(x) F(x-1)$
- A discrete version of the fundamental theorem of calculus!
- If *P* is  $\mathbb{N}$  ordered by divisibility, then  $\mu$  is the inverse of the Riemann zeta function.
- Given an interval [a, b] on a poset *P*,  $\mu(a, b)$  is the *reduced Euler characteristic* of the associated simplicial complex.

# Möbius functions on Boolean algebras

A powerset ordered by inclusion is a Boolean algebra.

$$\begin{split} \mu(\emptyset, \{Y, Z\}) &= -\sum_{\eta: \ \emptyset \le \eta < \{Y, Z\}} \mu(\emptyset, \eta) \\ &= -(\mu(\emptyset, \emptyset) + \mu(\emptyset, \{Y\}) + \mu(\emptyset, \{Z\})) \\ &= -(1 + \mu(\emptyset, \{Y\}) + \mu(\emptyset, \{Z\})) \\ &= -(1 - \mu(\emptyset, \emptyset) - \mu(\emptyset, \emptyset)) \\ &= -(1 - 1 - 1) = 1 \end{split}$$



- On a Boolean algebra  $\mu(x, y) = (-1)^{|y| |x|}$
- The Möbius inversion of the intersection cardinality function  $|*|: S \mapsto |\bigcap_i S_i|$  is the union cardinality.
- e.g.  $|X \cup Y \cup Z| = |X| + |Y| + |Z| |X \cap Y| |X \cap Z| |Y \cap Z| + |X \cap Y \cap Z|$
- Exactly the sign-alternating sums we saw before!

On a Boolean algebra *P* of variables *T*:

• Mutual information is the Möbius inversion of **marginal entropy**:

$$MI(\tau) = (-1)^{|\tau|-1} \sum_{\eta \le \tau} \mu_P(\eta, \tau) H(\eta)$$

• Pointwise mutual information is the Möbius inversion of marginal surprisal:

$$\mathrm{pmi}( au) = (-1)^{| au|-1} \sum_{\eta \leq au} \mu_P(\eta, au) \log p(\eta)$$

• Model-free interactions are the Möbius inversion of **surprisal**:

$$I(\tau; T) = \sum_{\eta \leq \tau} \mu(\eta, \tau) \log p(\eta = 1, T \setminus \eta = 0)$$

# **Dual quantities**

- If  $P = (S, \leq)$  is a lattice, then  $P^{\text{op}} = (S, \preceq)$  (where  $a \preceq b \iff a \geq b$ ) is a lattice.
- What is dual mutual information  $M\!I^*(\tau) = \sum_{\eta \preceq \tau} (-1)^{|\eta|+1} H(\eta)?$
- Dual MI of a single variable *X*:

$$MI^*(X) = MI(X, Y, Z) - MI(Y, Z)$$
$$= MI(Y, Z \mid X) = \Delta_X$$

- Conditional/differential mutual information.
- $MI^*(X, Y) = H(X, Y, Z) H(X, Y) = H(X | Y, Z)$
- In general context  $\mathit{T} \colon \mathit{MI}^*(\tau) = \mathit{MI}(\mathit{T} \setminus \tau \mid \tau)$



# **Dual quantities**

- Dual interactions  $I^*(\tau; T) = \sum_{\eta \preceq \tau} (-1)^{|\eta| |\tau|} \log p(\eta = 1, T \setminus \eta = 0)$
- Dual interaction of a single variable *X* in a system with 3 variables:

$$I^{*}(X; \{X, Y, Z\}) = I(X, Y, Z) + I(Y, Z)$$
$$= \log \frac{p_{111}p_{100}}{p_{110}p_{101}}$$

- This is  $I(Y, Z) \mid_{X=1}$ .
- Dual interactions are interactions in a context of 1s:
- $I^*(\tau; T) = I(T \setminus \tau) \mid_{\tau=1}$
- Outeractions

- Mutual information is the Möbius inversion of marginal entropy.
- Pointwise mutual information is the Möbius inversion of marginal surprisal.
- Model-free interactions are the Möbius inversion of surprisal.
- Dual mutual information is conditional mutual information.
- Dual interactions are interactions in a context of 1s.
- **NB:** These all imply an intuitive inverse relation:

$$f(y) = \sum_{x \le y} \mu_P(x, y) g(x) \iff g(y) = \sum_{x \le y} f(x)$$

#### Summary

- Define:  $eval_T$ :  $\log p(R = r) \mapsto \log p(R = 1, T \setminus R = 0)$
- Then:





# Part 4: Results

- What do nonzero interactions correspond to?
- Logic gates, causal dynamics, and di/triadic distributions.
- How do interactions differ from information?

# **Results: Synergy in logic gates**

• What does a 3-pt interaction correspond to?

$$I_{ABC} = \log \frac{p_{111}p_{100}p_{010}p_{000}}{p_{000}p_{011}p_{101}p_{110}}$$

• Maximally positive  $\implies$  only terms in numerator are > 0.

A	В	С
0	0	1
0	1	0
1	0	0
1	1	1

- XNOR gate!
- (XOR is maximally negative)

# **Results: Synergy in logic gates**

- XOR is *synergistic*: Knowing all but one of the input bits gives zero information on output.
- It is symmetric!
- Can be generalised to n-point XOR:

$$X_{n+1} = \sum_{i=1}^n X_i \mod 2$$

- Still maximally synergistic
- Still symmetric (consider  $X_i \leftrightarrow X_{n+1}$ )
- Still maximal 3-point interaction (parity determines sign)

# **Results: Synergy in logic gates**

- Let p(allowed state) = p and  $p(\text{forbidden state}) = \epsilon$ .
- Let  $I = 4 \log \frac{p}{\epsilon}$
- Interactions have higher resolution than MI.
- AND~NOR and OR~NAND.
- Def.  $J_A = I_{ABC} I_{BC}$
- $J_A$  has perfect resolution.
- $J_A^{\text{XNOR}} > J_A^{\text{NOR}} > J_A^{\text{AND}}$ .
- Ordered by synergistic content.

${\cal G}$	<b>I</b> <sub>ABC</sub>	MI <sub>ABC</sub>	$J_A$
XNOR	Ι	-1	$\frac{3}{2}I$
XOR	-I	-1	$-\frac{3}{2}I$
AND	$\frac{1}{2}I$	-0.189	$\frac{1}{2}I$
OR	$-\frac{1}{2}I$	-0.189	-I
NAND	$-\frac{1}{2}I$	-0.189	$-\frac{1}{2}I$
NOR	$\frac{1}{2}I$	-0.189	Ī

#### **Results: Causal dynamics**



# **Results: Dy- and Triadic distribution**

- 6 variables:  $(X_0, X_1, Y_0, Y_1, Z_0, Z_1)$
- Dyadic:  $X_0 = Y_1, Y_0 = Z_1, Z_0 = X_1$
- Triadic:  $X_0 + Y_0 + Z_0 = 0 \mod 2$ and  $X_1 = Y_1 = Z_1$
- Variables combined to form categorical variables
   X, Y, Z.
- $(X_0, X_1) = (1, 1) \implies \mathbf{X} = 3$
- Indistinguishable by almost all information measures. (James & Crutchfield, 2017)
- PID: has to identify in- and output variables.
- Symmetrised categorical interactions: I
  - Dyadic:  $I_{XYZ} = \log 1 = 0$
  - Triadic:  $\mathbf{I}_{XYZ} = 64 \log \frac{\epsilon}{p}$

	Dyadic			Triadic				
2	x	Y	Z	P(s)	x	Y	Z	P(s)
(	0	0	0	p	0	0	0	p
(	0	2	1	p	1	1	1	p
	1	0	2	p	0	2	2	p
	1	2	3	p	1	3	3	Þ
:	2	1	0	p	2	0	2	p
:	2	3	1	p	3	1	3	p
:	3	1	2	p	2	2	0	p
:	3	3	3	p	3	3	1	p
		else		$\epsilon$	else $\epsilon$			

# Part 5: Conclusion

- Teaser: model-free interactions on real data
- Conclusion

# Teaser: model-free interactions on real data

- To estimate  $p(X_i = \alpha, X_j = \beta \mid \underline{X} = 0)$ , count samples:  $X = (0, 0, ..., \alpha, ..., \beta, ..., 0)$
- Trick: find a set  $MB_{X_i} \subset \underline{X}$  s.t.  $p(X_i \mid \underline{X}) = p(X_i \mid MB_{X_i})$



- MB: Markov Blanket
- $X_i \perp X \setminus MB_{X_i} \mid MB_{X_i}$
- d-separates  $X_i$  from 'the rest'
- Finding minimal MB is 'Causal Rung 2-hard'

- Estimation on real data becomes tractable using Markov blankets.
- Error from MB estimate is bounded by pointwise mutual information (a good thing)
- MFIs in gene expression data: 1000 genes, 20k cells.
- Interactions at up to seventh order.
- +  $I_{G_1,G_2,G_3,\ldots} \neq 0 \implies$  non-random gene expression pattern.
- These revealed types of neurons and pathways not found in embryonic mice before.

- Entropy-based information measures cannot distinguish all causal dynamics.
- Ising-like interactions can offer higher resolution.
- Uniquely identify causal dynamics & logic gates.
- Möbius inversions capture higher-order structure:
  - (Pointwise) mutual information, Ising interactions are inversions on Boolean algebra
  - All have meaningful duals.
  - Other lattices:
  - categorical Ising-like interactions.
  - PID: Möbius inversion on redundancy lattice.
- Higher-order interactions are important, and estimable.

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