Solvable immune network models on finitely connected graphs with many short loops

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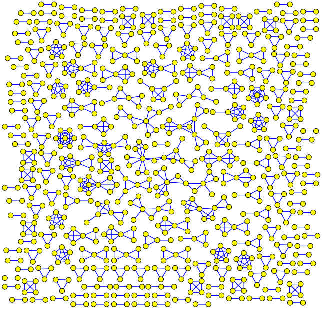
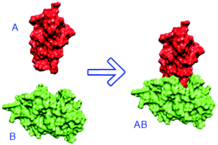


Outline

Stochastic processes on networks

Protein interaction networks

proteins: hetero-polymers that interact
via temporary *complexes*



reaction eqns:

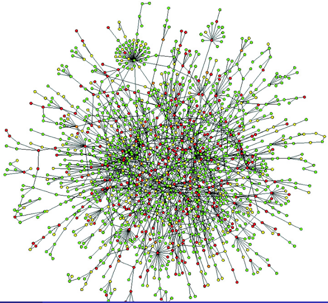
$$\frac{\mathrm{d}}{\mathrm{d}t}x_i^\alpha = \sum_j c_{ij} \sum_\beta [k_{ij}^{\alpha\beta -} x_{ij} - k_{ij}^{\alpha\beta +} x_i^\alpha x_j^\beta] + \theta_i^\alpha - \gamma_i^\alpha x_i^\alpha + \textit{noise}$$

$$\frac{\mathrm{d}}{\mathrm{d}t}x_{ij} = c_{ij} \sum_{\alpha\beta} [k_{ij}^{\alpha\beta +} x_i^\alpha x_j^\beta - k_{ij}^{\alpha\beta -} x_{ij}] + \textit{noise}$$

nodes: proteins $i, j = 1 \ldots N$

links: $c_{ij} = c_{ji} = 1$ if i binds to j
$c_{ij} = c_{ji} = 0$ otherwise

$N \sim 10^4$, ~ 7 links/node



Gene regulation networks

gene *expression level* σ_i:
degree to which gene i is 'switched on'

Boolean models:
$\sigma_i \in \{-1, 1\}$,
discrete time

$$\sigma_i(t+1) = F_i(\sigma_1(t), \ldots, \sigma_N(t))$$

$$F_i(\sigma_1, \ldots, \sigma_N) = \mathrm{sgn}[h_i(\sigma_1, \ldots, \sigma_N) + \textit{noise}]$$

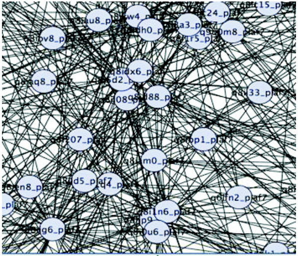
$$h_i(\sigma_1, \ldots, \sigma_N) = \sum_j J_{ij}\sigma_j + \sum_{jk} J_{ijk}\sigma_j\sigma_k + \ldots$$

nodes: genes $i, j = 1 \ldots N$

links: $c_{ij} = 1$ if σ_j appears in $F_i(\sigma_1, \ldots, \sigma_N)$
$c_{ij} = 0$ otherwise

directed network!

$N \sim 10^4$, $\sim$5 links/node



Tailoring random graphs

statistical mechanics of processes on network $\mathbf{c}^\star$,
using *random* graph c as proxy

- tailored random graph ensemble Ω_L:

  maximum entropy ensemble constrained by
  values of L observables $\boldsymbol{\omega}(\mathbf{c})=\{\omega_1(\mathbf{c}),\ldots,\omega_L(\mathbf{c})\}$

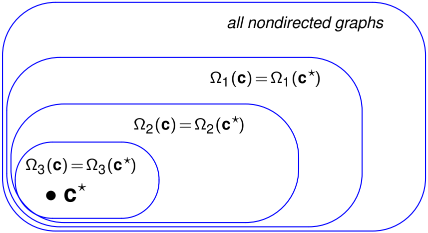
$$\Omega_L^{\rm hard}: \qquad p_{L,h}(\mathbf{c})=Z_{L,h}^{-1}\prod_{\ell\leq L}\delta_{\omega_\ell(\mathbf{c}),\omega_\ell(\mathbf{c}^\star)}$$

$$\Omega_L^{\rm soft}: \qquad p_{L,s}(\mathbf{c})=Z_{L,s}^{-1}\,{\rm e}^{\sum_{\ell=1}^L\hat{\omega}_\ell\omega_\ell(\mathbf{c})}, \qquad \sum_{\mathbf{c}}p_{L,s}(\mathbf{c})\omega_\ell(\mathbf{c})=\omega_\ell(\mathbf{c}^\star)\ \forall\ell$$

- approximate model solution:

  average generating functions
  of process over $\mathbf{c}$ in Ω_L

  larger $L\to$ better approximation



How to choose observables $\omega(\mathbf{c}) = \{\omega_1(\mathbf{c}), \ldots, \omega_L(\mathbf{c})\}$
to carry over from $\mathbf{c}^\star$ to the ensemble?

e.g. spin models $H(\boldsymbol{\sigma}) = -\sum_{i<j} c_{ij} J_{ij} \sigma_i \sigma_j$

- statics: replica method

$$\overline{\mathrm{e}^{-\beta \sum_{\alpha=1}^{n} H(\boldsymbol{\sigma}^\alpha)}} = \frac{\sum_{\mathbf{c}} \delta_{\boldsymbol{\omega},\boldsymbol{\omega}(\mathbf{c})} \mathrm{e}^{\sum_{i<j} c_{ij} A_{ij}}}{\sum_{\mathbf{c}} \delta_{\boldsymbol{\omega},\boldsymbol{\omega}(\mathbf{c})}}, \qquad A_{ij} = \beta J_{ij} \sum_{\alpha=1}^{n} \sigma_i^\alpha \sigma_j^\alpha$$

- dynamics: generating functional analysis

$$\overline{\mathrm{e}^{-\mathrm{i} \sum_{it} \hat{h}_i(t) \sum_j c_{ij} J_{ij} \sigma_j(t)}} = \frac{\sum_{\mathbf{c}} \delta_{\boldsymbol{\omega},\boldsymbol{\omega}(\mathbf{c})} \mathrm{e}^{\sum_{i<j} c_{ij} A_{ij}}}{\sum_{\mathbf{c}} \delta_{\boldsymbol{\omega},\boldsymbol{\omega}(\mathbf{c})}}, \qquad A_{ij} = -\mathrm{i} J_{ij} \sum_t [\hat{h}_i(t)\sigma_j(t) + \hat{h}_j(t)\sigma_i(t)]$$

in both cases
to be done *analytically*:

$$\sum_{\mathbf{c}} \delta_{\boldsymbol{\omega},\boldsymbol{\omega}(\mathbf{c})} \mathrm{e}^{\sum_{i<j} c_{ij} A_{ij}}$$

calculations feasible for:

$$p(k|\mathbf{c}) = \frac{1}{N}\sum_i \delta_{k,\sum_j c_{ij}}, \qquad W(k,k'|\mathbf{c}) = \frac{1}{\bar{k}N}\sum_{ij} c_{ij}\ \delta_{k,\sum_r c_{ir}}\delta_{k',\sum_r c_{jr}}$$

all nondirected graphs

$\bar{k}(\mathbf{c}) = \bar{k}(\mathbf{c}^\star)$

$\forall k$: $p(k|\mathbf{c}) = p(k|\mathbf{c}^\star)$

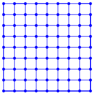
$\forall k,k'$: $W(k,k'|\mathbf{c}) = W(k,k'|\mathbf{c}^\star)$

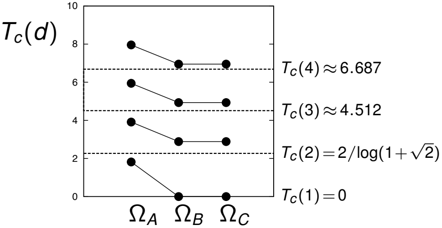
• $\mathbf{c}^\star$

critical temperatures of Ising spin models

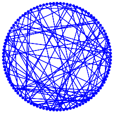
Ω_A: graphs with imposed $\bar{k} = \sum_k k\, p(k|\mathbf{c}^\star)$
Ω_B: graphs with imposed $p(k|\mathbf{c}^\star)$
Ω_C: graphs with imposed $p(k|\mathbf{c}^\star)$ and $W(k,k'|\mathbf{c}^\star)$

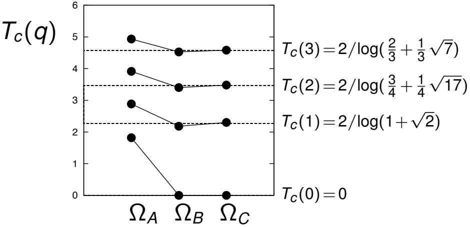
- $\mathbf{c}^\star$ = d-dim cubic lattice
  $p(k) = \delta_{k,2^d}$





- $\mathbf{c}^\star$ = 'small world' lattice
  $p(k \geq 2) = \mathrm{e}^{-q} q^{k-2}/(k-2)!$



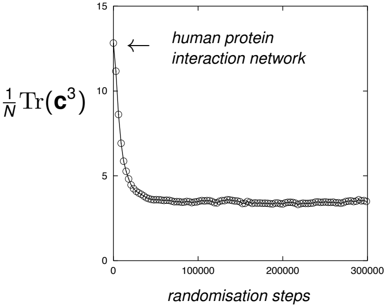


most informative
next observable $\omega(\mathbf{c})$?

- *random* graphs with prescribed $p(k|\mathbf{c}^\star)$ and $W(k,k'|\mathbf{c}^\star)$: locally tree-like ...

  protein interaction networks $\mathbf{c}^\star$:
  have many short loops ...

  geometric (eg lattice-like) networks $\mathbf{c}^\star$:
  have many short loops ...



- $\omega(\mathbf{c})$ must count short loops,
  but stat mech methods (replicas, GFA, cavity, belief prop) require locally tree-like graphs ...

simplest ensemble with controlled nr of triangles (Strauss):

$$p(\mathbf{c}) \sim \mathrm{e}^{u\sum_{ij} c_{ij} + v\sum_{ijk} c_{ij}c_{jk}c_{ki}}$$

let us <u>count</u> graphs first
(simpler than averaging over them?)

combine:

$$\sum_{ij} c_{ij} = N\int \mathrm{d}\mu\ \mu^2 \varrho(\mu|\mathbf{c}), \qquad \sum_{ijk} c_{ij}c_{jk}c_{ki} = N\int \mathrm{d}\mu\ \mu^3 \varrho(\mu|\mathbf{c})$$

$$\varrho(\mu|\mathbf{c}) = \frac{2}{N\pi}\lim_{\varepsilon\downarrow 0}\mathrm{Im}\frac{\partial}{\partial\mu}\log Z(\mu+\mathrm{i}\varepsilon|\mathbf{c}), \qquad Z(\mu|\mathbf{c}) = \int d\phi\ e^{-\frac{1}{2}\mathrm{i}\phi\cdot[\mathbf{c}-\mu\mathbb{1}]\phi}$$

$$\begin{aligned} S &= -\sum_{\mathbf{c}} p(\mathbf{c})\log p(\mathbf{c}) \\ &= \left(1 - u\frac{\partial}{\partial u} - v\frac{\partial}{\partial v}\right)\lim_{\varepsilon,\Delta\downarrow 0}\log\sum_{\mathbf{c}}\prod_{\mu}\left[Z(\mu+\mathrm{i}\varepsilon|\mathbf{c})^{-\mathrm{i}} Z^*(\mu+\mathrm{i}\varepsilon|\mathbf{c})^{\mathrm{i}}\right]^{\frac{\Delta}{\pi}(2u\mu+3v\mu^2)} \end{aligned}$$

replica analysis with finite
imaginary replica dimension?

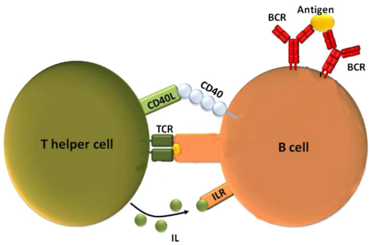
Model of Agliari and Barra

- B-cell *clones* b_μ

  each B-clone can recognise and attack *specific* antigen a_μ

- T-cell *clones* σ_i

  coordinate B-clones via cytokine signals $\xi_i^\mu = -1, 0, 1$ (-1: contract, $+1$: expand)

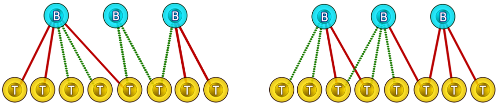


energy function:

$$p(\boldsymbol{\sigma}, \mathbf{b}) = \frac{\mathrm{e}^{-\sqrt{\beta} H(\boldsymbol{\sigma}, \mathbf{b})}}{Z} \qquad H(\boldsymbol{\sigma}, \mathbf{b}) = \frac{1}{2\sqrt{\beta}} \sum_{\mu=1}^{N_B} b_\mu^2 - \sum_{\mu=1}^{N_B} b_\mu \overbrace{\left(\sum_{i=1}^{N_T} \xi_i^\mu \sigma_i + \lambda_\mu a_\mu \right)}^{\text{expansion force on clone } \mu}$$

randomly drawn cytokine variables:
(bi-partite random graph)

$$p(\xi_i^\mu) = \frac{c}{2N}\left[\delta_{\xi_i^\mu,1} + \delta_{\xi_i^\mu,-1}\right] + (1-\frac{c}{N})\delta_{\xi_i^\mu,0} \qquad c: \ \textit{promiscuity}$$

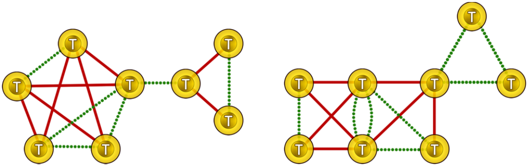


$N_B = \alpha N \sim 10^8$

$N \sim 2.10^8$

'integrate out' the B-clones,
gives system of interacting T-clones:

$$p(\boldsymbol{\sigma}) = \frac{\mathrm{e}^{-\beta H_{\rm eff}(\boldsymbol{\sigma})}}{Z_T} \qquad H_{\rm eff}(\boldsymbol{\sigma}) = -\frac{1}{2}\sum_{i,j=1}^{N}\sigma_i\sigma_j\sum_{\mu=1}^{\alpha N}\xi_i^\mu\xi_j^\mu - \sum_{i=1}^{N}\sigma_i\sum_{\mu=1}^{\alpha N}\lambda_\mu g_\mu \xi_i^\mu$$



Immune versus neural network models

mathematically very similar ...
both store and recall information ...

$$p(\boldsymbol{\sigma}) = \frac{\mathrm{e}^{-\beta H(\boldsymbol{\sigma})}}{Z_T} \qquad H(\boldsymbol{\sigma}) = -\frac{1}{2}\sum_{i,j=1}^{N} \sigma_i\sigma_j J_{ij} - \sum_{\mu=1}^{\alpha N} h_\mu \sum_{i=1}^{N} \sigma_i \xi_i^\mu$$

- Hopfield model: bond dilution
  c_{ij}: finitely connected tree-like graph

$$J_{ij} = c_{ij}\sum_{\mu=1}^{\alpha N} \xi_i^\mu \xi_j^\mu, \qquad h_\mu = \mathcal{O}(\frac{1}{N}), \qquad p(\xi_i^\mu) = \frac{1}{2}\Big[\delta_{\xi_i^\mu,1} + \delta_{\xi_i^\mu,-1}\Big]$$

recall of one N-bit pattern at a time

- Immune model: pattern dilution

$$J_{ij} = \sum_{\mu=1}^{\alpha N} \xi_i^\mu \xi_j^\mu, \qquad h_\mu = \mathcal{O}(1), \qquad p(\xi_i^\mu) = \frac{c}{2N}\Big[\delta_{\xi_i^\mu,1} + \delta_{\xi_i^\mu,-1}\Big] + (1 - \frac{c}{N})\delta_{\xi_i^\mu,0}$$

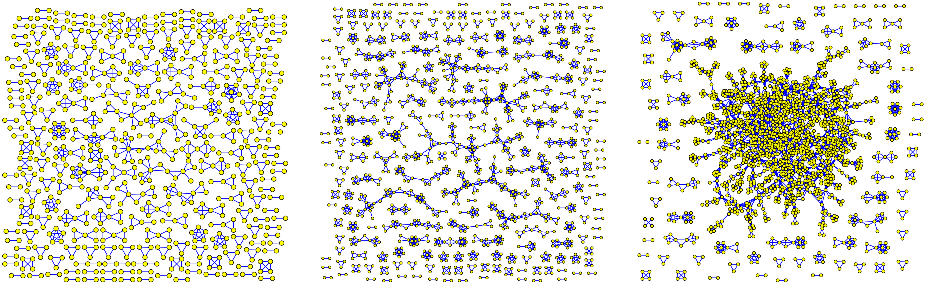
need recall of $\mathcal{O}(N)$ c-bit patterns ...

but analysis & solution *very* different!!

topological features
of the effective T-T graph

$J_{ij} = \sum_{\mu=1}^{\alpha N} \xi_i^\mu \xi_j^\mu$

$\alpha c^2 < 1$ $\alpha c^2 = 1$ $\alpha c^2 > 1$



percolation transition:
$\alpha c^2 = 1$

Statistical mechanical analysis

$$H(\boldsymbol{\sigma}) = -\frac{1}{2c}\sum_{\mu}^{\alpha N} M_\mu^2(\boldsymbol{\sigma}) - \sum_{\mu=1}^{\alpha N}\psi_\mu M_\mu(\boldsymbol{\sigma}), \qquad M_\mu(\boldsymbol{\sigma}) = \sum_{i=1}^{N}\xi_i^\mu \sigma_i$$

- To calculate:

$$f = -\lim_{N\to\infty}\frac{1}{\beta N}\log Z_N, \qquad Z_N = \sum_{\boldsymbol{\sigma}\in\{-1,1\}^N} \mathrm{e}^{\frac{\beta}{2c}\sum_\mu M_\mu^2(\boldsymbol{\sigma})+\beta\sum_\mu \psi_\mu M_\mu(\boldsymbol{\sigma})}$$

$M_\mu(\boldsymbol{\sigma}) > 0$: pos signal to B-clone, $b_\mu \uparrow$
$M_\mu(\boldsymbol{\sigma}) < 0$: neg signal to B-clone, $b_\mu \downarrow$

$$\mathcal{P}(M,\psi|\boldsymbol{\sigma}) = \frac{1}{\alpha N}\sum_{\mu=1}^{\alpha N}\delta_{M,M_\mu(\boldsymbol{\sigma})}\delta(\psi-\psi_\mu) \qquad \psi_\mu: \textit{ antigen trigger}$$

- Disorder:

αN^2 frozen random vars $\{\xi_i^\mu\}$

$$p(\xi_i^\mu) = \frac{c}{2N}\left[\delta_{\xi_i^\mu,1}+\delta_{\xi_i^\mu,-1}\right] + (1-\frac{c}{N})\delta_{\xi_i^\mu,0}$$

bookkeeping:

$$f = -\lim_{N\to\infty}\frac{1}{\beta N}\log\sum_{\boldsymbol{\sigma}} \mathrm{e}^{\frac{\beta}{2c}\sum_{\mu=1}^{\alpha N} M_\mu^2(\boldsymbol{\sigma})+\beta\sum_{\mu=1}^{\alpha N}\psi_\mu M_\mu(\boldsymbol{\sigma})}$$

$$= -\lim_{N\to\infty}\frac{1}{\beta N}\log\sum_{\boldsymbol{\sigma}} \mathrm{e}^{\alpha\beta N\int\mathrm{d}\psi\sum_M \mathcal{P}(M,\psi|\boldsymbol{\sigma})\left(M^2/2c+M\psi\right)}$$

insert:

$$1=\prod_{M,\psi}\int\mathrm{d}\mathcal{P}(M,\psi)\;\delta\Big[\mathcal{P}(M,\boldsymbol{\psi})-\frac{1}{\alpha N}\sum_{\mu=1}^{\alpha N}\delta_{M,M_\mu(\boldsymbol{\sigma})}\delta(\psi-\psi_\mu)\Big]$$

path integral form:

$$f=-\lim_{N\to\infty}\frac{1}{\beta N}\log\int\{\mathrm{d}\mathcal{P}\mathrm{d}\hat{\mathcal{P}}\}\;\mathrm{e}^{N\left\{\mathrm{i}\int\mathrm{d}\psi\sum_M\mathcal{P}(M,\psi)\hat{\mathcal{P}}(M,\psi)+\alpha\beta\int\mathrm{d}\psi\sum_M\mathcal{P}(M,\psi)\left(\frac{M^2}{2c}+M\psi\right)+\Omega[\hat{\mathcal{P}}|\{\xi\}]\right\}}$$

$$\Omega[\hat{\mathcal{P}}|\{\xi\}]=\lim_{N\to\infty}\frac{1}{N}\log\sum_{\boldsymbol{\sigma}}\mathrm{e}^{-\frac{\mathrm{i}}{\alpha}\sum_\mu\hat{\mathcal{P}}(M_\mu(\boldsymbol{\sigma}),\psi_\mu)}$$

steepest descent:

$$f=\mathrm{extr}_{\{\mathcal{P},\hat{\mathcal{P}}\}}\,f[\{\mathcal{P},\hat{\mathcal{P}}\}]$$

$$-\beta f[\{\mathcal{P},\hat{\mathcal{P}}\}]=\overbrace{\mathrm{i}\int\mathrm{d}\psi\sum_M\mathcal{P}(M,\psi)\hat{\mathcal{P}}(M,\psi)+\alpha\beta\int\mathrm{d}\psi\sum_M\mathcal{P}(M,\psi)\Big(\frac{M^2}{2c}+M\psi\Big)}^{\textit{harmless terms}}\;+\;\overbrace{\Omega[\hat{\mathcal{P}}|\{\xi\}]}^{\textit{the problem}}$$

Disorder average – replica method

focus on disorder-averaged free energy $\bar{f}$,
work out saddle-point eqns:

$$\bar{f} = f[\chi]\Big|_{\chi(M,\psi)=\frac{M^2}{2c}+M\psi}, \qquad \mathcal{P}(M,\psi) = -\frac{1}{\alpha}\frac{\delta f[\chi]}{\delta\chi(M,\psi)}\Big|_{\chi(M,\psi)=\frac{M^2}{2c}+M\psi}$$

$$f[\chi] = -\lim_{N\to\infty}\frac{1}{\beta N}\overline{\log\sum_{\boldsymbol{\sigma}} \mathrm{e}^{\beta\sum_{\mu=1}^{\alpha N}\chi(M_\mu(\boldsymbol{\sigma}),\psi_\mu)}}, \qquad M_\mu(\boldsymbol{\sigma}) = \sum_i \sigma_i\xi_i^\mu$$

replica identity (Kac):
$\overline{\log z} = \lim_{n\to 0} n^{-1}\log\overline{z^n}$

$$\overline{\log\sum_{\boldsymbol{\sigma}}\mathrm{e}^{G(\boldsymbol{\sigma})}} = \lim_{n\to 0}\frac{1}{n}\log\overline{\Big(\sum_{\boldsymbol{\sigma}}\mathrm{e}^{G(\boldsymbol{\sigma})}\Big)^n} = \lim_{n\to 0}\frac{1}{n}\log\sum_{\boldsymbol{\sigma}^1}\ldots\sum_{\boldsymbol{\sigma}^n}\overline{\mathrm{e}^{\sum_{\alpha=1}^n G(\boldsymbol{\sigma}^\alpha)}}$$

Hence

$$\begin{aligned} f[\chi] &= -\lim_{N\to\infty}\lim_{n\to 0}\frac{1}{\beta N n}\log\sum_{\boldsymbol{\sigma}^1\ldots\boldsymbol{\sigma}^n}\overline{\mathrm{e}^{\beta\sum_{\alpha=1}^n\sum_{\mu=1}^{\alpha N}\chi(M_\mu(\boldsymbol{\sigma}^\alpha),\psi_\mu)}} \\ &= -\lim_{N\to\infty}\lim_{n\to 0}\frac{1}{\beta N n}\log\Big\{\prod_{\alpha\mu}\Big[\sum_{M_{\alpha\mu}=-\infty}^{\infty}\int_{-\pi}^{\pi}\frac{\mathrm{d}\omega_{\alpha\mu}}{2\pi}\Big]\mathrm{e}^{\mathrm{i}\sum_{\alpha\mu}\omega_{\alpha\mu}M_{\alpha\mu}+\sum_{\alpha\mu}\beta\chi(M_\mu^\alpha,\psi_\mu)} \\ &\qquad\qquad \times\sum_{\boldsymbol{\sigma}^1\ldots\boldsymbol{\sigma}^n}\overline{\mathrm{e}^{-\mathrm{i}\sum_i\sum_{\alpha\mu}\omega_{\alpha\mu}\sigma_i^\alpha\xi_i^\mu}}\Big\} \end{aligned}$$

(i) carry out disorder average
(ii) manipulations, path integrals, steepest descent ...

$$f[\chi] = -\lim_{n\to 0}\frac{1}{\beta n}\mathrm{extr}_{\{Q,L\}}\ \Psi_n[\{Q,L\}|\chi], \qquad \Psi_n[\{Q,L\}|\chi] = \textit{complicated functional}$$

$$Q = \{Q(\mathbf{M})\}, \qquad \mathbf{M}\in\mathbb{Z}^n$$
$$L = \{L(\boldsymbol{\sigma})\}, \quad \boldsymbol{\sigma}\in\{-1,1\}^n$$

saddle point eqns:

$$Q(\mathbf{M}) = \int_{-\pi}^{\pi}\mathrm{d}\boldsymbol{\omega}\ \cos(\boldsymbol{\omega}\cdot\mathbf{M})\exp\left[c\,\frac{\sum_{\boldsymbol{\sigma}}\cos(\boldsymbol{\omega}\cdot\boldsymbol{\sigma})\mathrm{e}^{L(\boldsymbol{\sigma})}}{\sum_{\boldsymbol{\sigma}}\mathrm{e}^{L(\boldsymbol{\sigma})}}\right] \qquad \boldsymbol{\omega}\in[-\pi,\pi]^n$$

$$L(\boldsymbol{\sigma}) = \alpha c\,\mathrm{e}^{\frac{\beta n}{2c}}\int\mathrm{d}\psi\ P(\psi)\left\{\frac{\sum_{\mathbf{M}}Q(\mathbf{M})\mathrm{e}^{\beta\sum_\alpha\chi(M_\alpha,\psi)}\cosh[\beta(\frac{1}{c}\mathbf{M}\cdot\boldsymbol{\sigma}+\psi\sum_\alpha\sigma_\alpha)]}{\sum_{\mathbf{M}}Q(\mathbf{M})\mathrm{e}^{\beta\sum_\alpha\chi(M_\alpha,\psi)}}\right\}$$

next:
solve, then analytical
continuation $n\to 0$ in

$$P(M|\psi) = \lim_{n\to 0}\left.\frac{\sum_{\mathbf{M}}\left(\frac{1}{n}\sum_{\gamma=1}^{n}\delta_{M,M_\gamma}\right)\mathrm{e}^{\beta\sum_\alpha\chi(M_\alpha,\psi)}Q(\mathbf{M})}{\sum_{\mathbf{M}}\mathrm{e}^{\beta\sum_\alpha\chi(M_\alpha,\psi)}Q(\mathbf{M})}\right|_{\chi(M,\psi)=M^2/2c+M\psi}.$$

Replica symmetric solutions

replica symmetric (RS)
ansatz for saddle point:

$$L(\boldsymbol{\sigma}) = \alpha c \int \mathrm{d}h\ W(h) \prod_{\alpha=1}^{n} \mathrm{e}^{\beta h \sigma^\alpha}, \qquad Q(\mathbf{M}) = \mathrm{e}^{c} \int \{\mathrm{d}\pi\}\ W[\{\pi\}] \prod_{\alpha=1}^{n} \pi(M_\alpha),$$

$W(h)$: normalised distr, $W(h) = W(-h)$
$W[\pi]$: normalised functional distr, non-zero iff $\sum_{M\in\mathbb{Z}} \pi(M) = 1$

RS saddle point eqns,
for $n \to 0$:

$$W(h) = \int \{\mathrm{d}\pi\}\ W[\pi] \int \mathrm{d}\psi\ P(\psi) \sum_{\tau=\pm 1} \delta \left[h - \tau\psi - \frac{1}{2\beta} \log \left(\frac{\sum_M \pi(M) \mathrm{e}^{\beta(M^2/2c + M(\psi+\tau/c))}}{\sum_M \pi(M) \mathrm{e}^{\beta(M^2/2c + M(\psi-\tau/c))}} \right) \right]$$

$$W[\pi] = \mathrm{e}^{-c} \sum_{k\geq 0} \frac{c^k}{k!} e^{-\alpha c k} \sum_{r \geq 0} \frac{(\alpha c)^r}{r!} \int_{-\infty}^{\infty} \Big[\prod_{s\leq r} \mathrm{d}h_s W(h_s) \Big] \sum_{\ell_1 \ldots \ell_r \leq k}$$

$$\times \prod_M \delta \left[\pi(M) - \frac{\sum_{\sigma_1 \ldots \sigma_k = \pm 1} \mathrm{e}^{\beta \sum_{s\leq r} h_s \sigma_{\ell_s}} \delta_{M, \sum_{\ell \leq k} \sigma_\ell}}{\sum_{\sigma_1 \ldots \sigma_k = \pm 1} \mathrm{e}^{\beta \sum_{s\leq r} h_s \sigma_{\ell_s}}} \right]$$

Eliminate $W[\pi]$:

$$W(h) = \mathrm{e}^{-c}\sum_{k\geq 0}\frac{c^k}{k!}\mathrm{e}^{-\alpha ck}\sum_{r\geq 0}\frac{(\alpha c)^r}{r!}\int_{-\infty}^{\infty}\Big[\prod_{s\leq r}\mathrm{d}h_s W(h_s)\Big]\sum_{\ell_1\ldots\ell_r\leq k}\int\!\mathrm{d}\psi\, P(\psi)$$
$$\times\sum_{\tau=\pm 1}\delta\left[h-\tau\psi-\frac{1}{2\beta}\log\left(\frac{\sum_{\sigma_1\ldots\sigma_k=\pm 1}\mathrm{e}^{\beta(\sum_{\ell\leq k}\sigma_\ell)^2/2c+\beta(\sum_{\ell\leq k}\sigma_\ell)(\psi+\tau/c)+\beta\sum_{s\leq r}h_s\sigma_{\ell_s}}}{\sum_{\sigma_1\ldots\sigma_k=\pm 1}\mathrm{e}^{\beta(\sum_{\ell\leq k}\sigma_\ell)^2/2c+\beta(\sum_{\ell\leq k}\sigma_\ell)(\psi-\tau/c)+\beta\sum_{s\leq r}h_s\sigma_{\ell_s}}}\right)\right]$$

$$P(M|\psi) = \sum_{k\geq 0}p(k)P(M|k,\psi),\qquad p(k)=\mathrm{e}^{-c}c^k/k!$$

$$P(M|k,\psi) = \mathrm{e}^{-\alpha ck}\sum_{r\geq 0}\frac{(\alpha c)^r}{r!}\int_{-\infty}^{\infty}\Big[\prod_{s\leq r}\mathrm{d}h_s W(h_s)\Big]\sum_{\ell_1\ldots\ell_r\leq k}$$
$$\times\left\{\frac{\sum_{\sigma_1\ldots\sigma_k=\pm 1}\delta_{M,\sum_{\ell\leq k}\sigma_\ell}\;\mathrm{e}^{\beta(\sum_{\ell\leq k}\sigma_\ell)^2/2c+\beta\psi\sum_{\ell\leq k}\sigma_\ell+\beta\sum_{s\leq r}h_s\sigma_{\ell_s}}}{\sum_{\sigma_1\ldots\sigma_k=\pm 1}\mathrm{e}^{\beta(\sum_{\ell\leq k}\sigma_\ell)^2/2c+\beta\psi\sum_{\ell\leq k}\sigma_\ell+\beta\sum_{s\leq r}h_s\sigma_{\ell_s}}}\right\}$$

h: clonal interference field

state without clonal cross-talk

$W(h) = \delta(h)$,
always a soln, for any (α, T, c)

$k > 0$:

$$P(M|k,\psi) = \mathrm{e}^{-\alpha ck} \sum_{r\geq 0} \frac{(\alpha c)^r}{r!} \sum_{\ell_1 \ldots \ell_r \leq k} \left\{ \frac{\sum_{\sigma_1 \ldots \sigma_k = \pm 1} \delta_{M, \sum_{\ell \leq k} \sigma_\ell} \mathrm{e}^{\beta(\sum_{\ell \leq k} \sigma_\ell)^2/2c + \beta\psi \sum_{\ell \leq k} \sigma_\ell}}{\sum_{\sigma_1 \ldots \sigma_k = \pm 1} \mathrm{e}^{\beta(\sum_{\ell \leq k} \sigma_\ell)^2/2c + \beta\psi \sum_{\ell \leq k} \sigma_\ell}} \right\}$$

at $T = 0$:

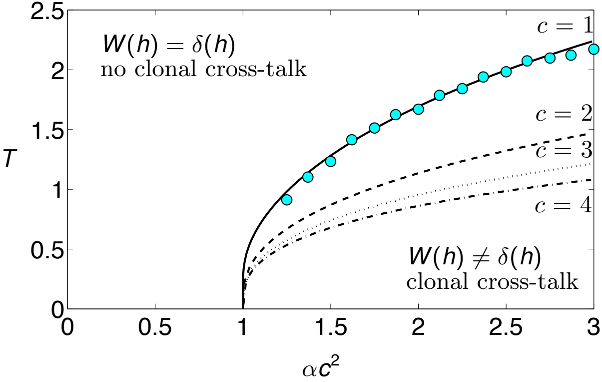
$\psi \neq 0$: $P(M|k,\psi) = \delta_{M, k\,\mathrm{sgn}(\psi)}$
i.e. error free activation or inhibition
of stored strategy with k nonzero entries

$\psi = 0$: $P(M|k,\psi) = \frac{1}{2}[\delta_{M,k} + \delta_{M,-k}]$
weak ergodicity breaking,
clone oscillates randomly between $M_\mu > 0$ *and* $M_\mu < 0$ *states*,
important for homeostasis!

Phase diagram

continuous bifurcations
away from $W(h)=\delta(h)$:

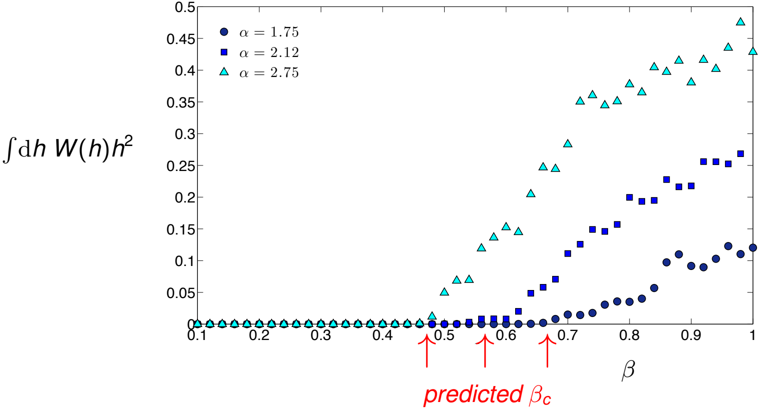
$$1=\alpha c^2\sum_{k\geq 0}\mathrm{e}^{-c}\frac{c^k}{k!}\left\{\frac{\int\mathrm{d}z\;\mathrm{e}^{-\frac{1}{2}z^2}\tanh(z\sqrt{\beta/c}+\beta/c)\cosh^{k+1}(z\sqrt{\beta/c}+\beta/c)}{\int\mathrm{d}z\;\mathrm{e}^{-\frac{1}{2}z^2}\cosh^{k+1}(z\sqrt{\beta/c}+\beta/c)}\right\}^2$$



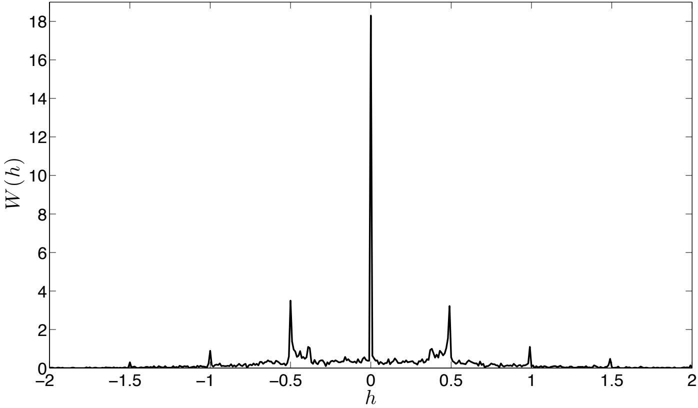
circles: numerical soln of $W(h)$ eqn for $c=1$

Simulations and population dynamics

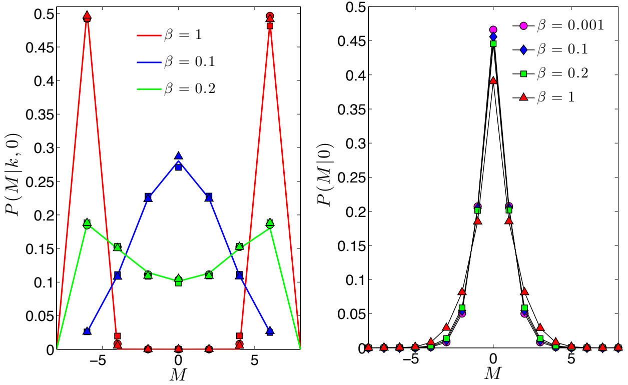
numerical soln of eqn for $W(h)$
via population dynamics algorithm
(here $c = 1$)



clonal cross-talk interference field distribution $W(h)$ below T_c (here $c = 2$, $\alpha = 2$ and $\beta = 6.2$)



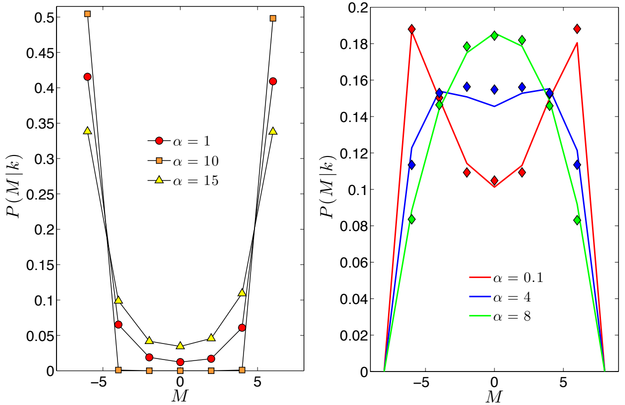
overlap statistics in $W(h) = \delta(h)$ regime
(here $k = 6$, $c = 1$)



lines: theoretical predictions
markers: Monte-Carlo simulations with $N = 3.10^4$

left: bullets/squares/triangles for different α
right: bullets/squares/triangles for different β

overlap statistics:
$W(h) = \delta(h)$ regime vs $W(h) \neq \delta(h)$ regime
(here $k = 6$, $\beta = 0.8$)



lines: theoretical predictions
markers: Monte-Carlo simulations with $N = 3.10^4$

left: $c = 1$; right: $c = 3$

Summary

Processes on finitely connected graphs

- some spin models on graphs with many short loops are solvable

- here: $\mathbf{c} = \mathbf{A}^\dagger \mathbf{A}$
  A: $p \times N$ matrix with indep distributed $\{A_{\mu i}\}$

  allows for Hubbard-Stratonovich type transformation to equivalent theory with spins + scalar Gaussian fields, and for doing disorder average

$$Z = \sum_{\boldsymbol{\sigma}} \mathrm{e}^{\beta \sum_{i<j} c_{ij}\sigma_i\sigma_j} = \int \frac{\mathrm{d}\mathbf{z}}{(2\pi)^{p/2}} \sum_{\boldsymbol{\sigma}} \mathrm{e}^{\sqrt{\beta}\sum_{\mu i} z_\mu A_{\mu i}\sigma_i - \frac{1}{2}\sum_\mu z_\mu^2}$$

- further work:

  – systematic approximation of arbitrary 'loopy' graphs by graphs of the type $\mathbf{c} = \mathbf{A}^\dagger \mathbf{A}$, with indep $\{A_{ij}\}$?

  – entropy of Strauss model via imaginary replicas?

Immune system modelling

- promiscuous T-cells can coordinate an extensive number of B-cells effectively

- two phases, separated by continuous phase transition (within RS):
  $W(h) = \delta(h)$, phase without clonal cross-talk
  $W(h) \neq \delta(h)$, phase with clonal cross-talk

- without antigen triggers:

  weak ergodicity breaking,
  stochastic clonal oscillation between activation and suppression
  (important for homeostasis)

- further work:

  – replica symmetry breaking?

  – nonequilibrium statistical mechanics (GFA)

  – more realistic models, including dendritic cells,
  B-lymphocyte families, hypersomatic mutation etc

  – immune-tumour interaction

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paper

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