UNITED NATIONS EDUCATIONAL, SCIENTIFIC AND CULTURAL ORGANIZATION
INTERNATIONAL ATOMIC ENERGY AGENCY
INTERNATIONAL CENTRE FOR THEORETICAL PHYSICS
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SPRING COLLEGES IN COMPUTATIONAL PHYSICS

19 May - 27 June 1997

ADVANCED CLASSICAL MONTE CARLO SIMULATIONS

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1. Cluster Monte Carlo

2. Histograms

3. Bayesian analysis
   Transition matrix MC

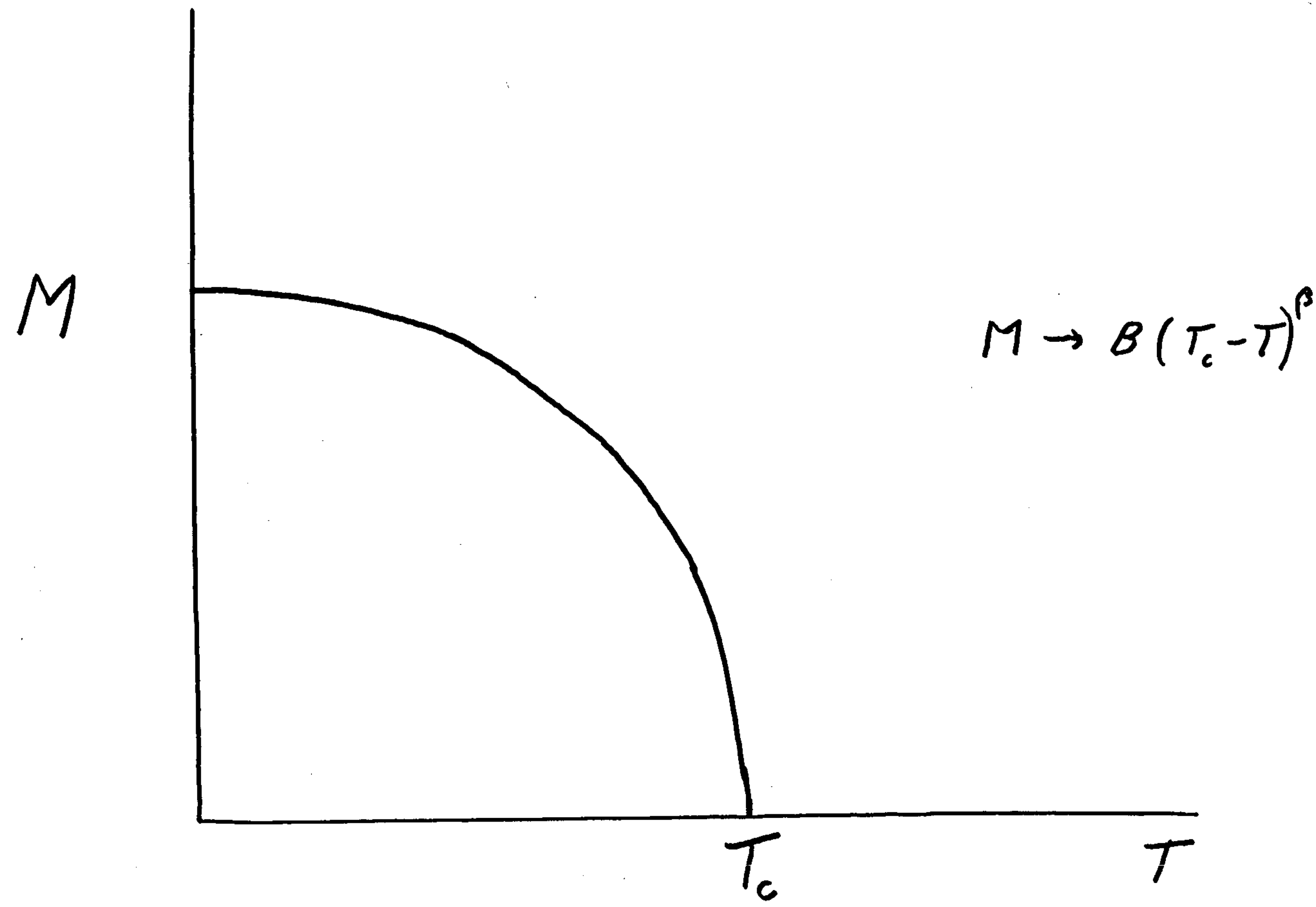
4. Simulation of
   biological molecules

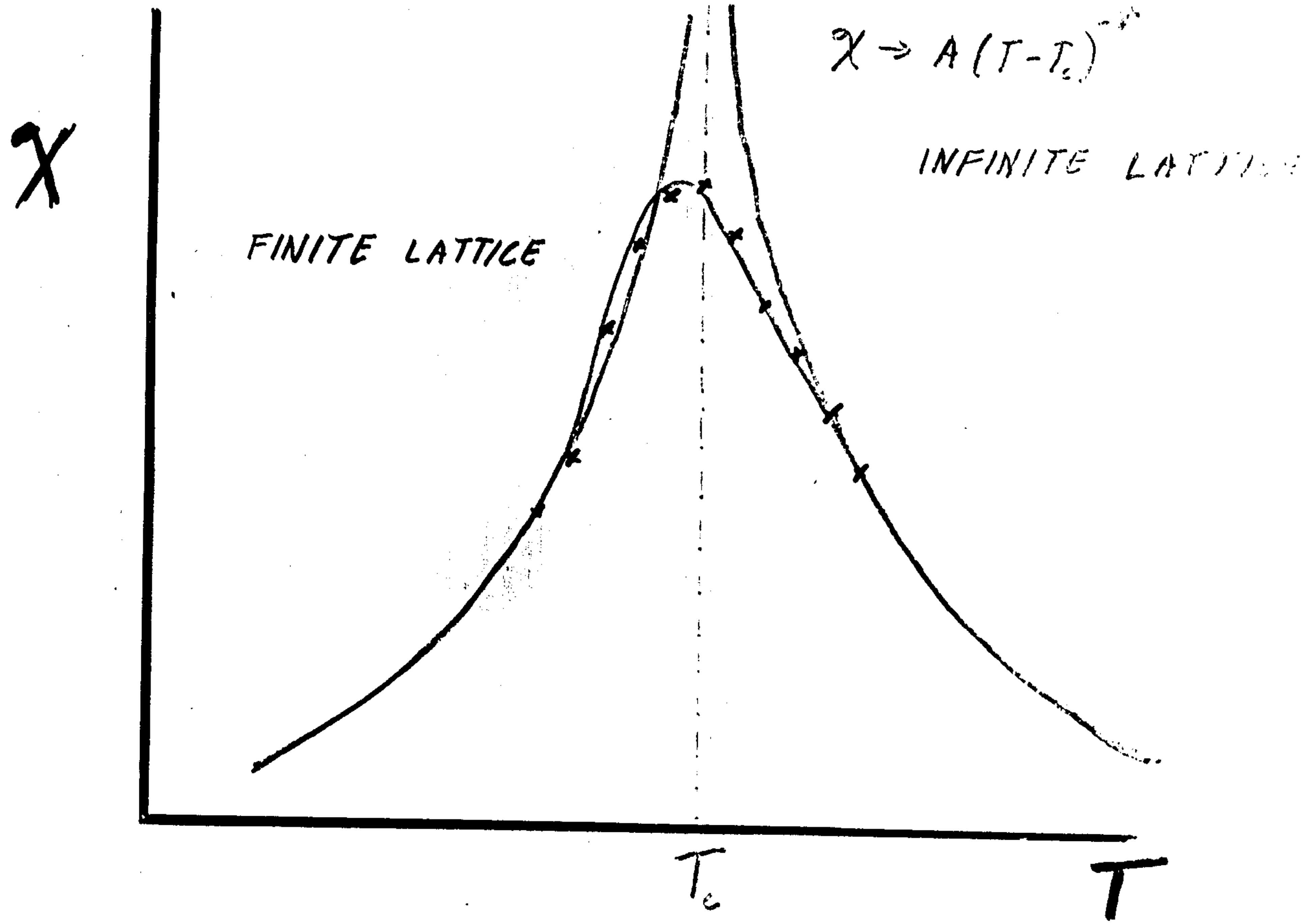
   Dynamically Optimized MC

Emancipation of
computer simulations
from experimental paradigm

Non-physical dynamics
for greater efficiency
- MC, cluster methods

Measurement of quantities
not available to experiment
MCRG
Histograms
Improved estimators


M
T_c
T
$M \to B(T_c - T)^{\beta}$



$\chi \to A(T-T_c)^{-\gamma}$
INFINITE LATTICE
FINITE LATTICE
χ
T_c
T

Monte Carlo Strategy

1) Test your program!

2) Think small

   small lattices
   short runs
   fast scan of parameters
   find "interesting" region
   vary the initial conditions

3) Concentrate on "interesting" region

   small lattices
   longer runs (but <<< budget)
   calculate errors
   estimate errors vs. run time
   for larger lattices

4) Increase lattice size

   compare
   look for size effects
   extrapolate
   calculate errors

Equilibrium Probability Density

$$P_{eq}(\sigma) = \frac{1}{Z} \exp[-E(\sigma)/k_B T]$$

$$Z = \mathrm{Tr}_{\sigma} \exp[-E(\sigma)/k_B T]$$

$$\langle E \rangle = \mathrm{Tr}_{\sigma} E(\sigma) P_{eq}(\sigma)$$

Markov Process

New state depends on old state

but <u>not</u>

on previous states.

Master Equation:

$$P(\sigma, t+\Delta t) - P(\sigma, t) =$$

$$\sum_{\sigma'} \left[W(\sigma' \to \sigma) P(\sigma', t) - W(\sigma \to \sigma') P(\sigma, t) \right]$$

$$P(\sigma, t+\delta t) - P(\sigma, t) =$$
$$\sum_{\sigma'} \left[W(\sigma' \to \sigma) P(\sigma', t) - W(\sigma \to \sigma') P(\sigma, t) \right]$$

Necessary condition for $P(\sigma,t) \longrightarrow P_{eq}(\sigma)$

$$\sum_{\sigma'} \left[W(\sigma' \to \sigma) P_{eq}(\sigma') - W(\sigma \to \sigma') P_{eq}(\sigma) \right] = 0$$

Stronger condition

Detailed Balance

$$W(\sigma' \to \sigma) P_{eq}(\sigma') = W(\sigma \to \sigma') P_{eq}(\sigma)$$

Detailed Balance

$$W(\sigma' \to \sigma) P_{eq}(\sigma') = W(\sigma \to \sigma') P_{eq}(\sigma)$$

$$P_{eq}(\sigma) = \frac{1}{Z} \exp[-E(\sigma)/k_B T]$$

$$\frac{W(\sigma' \to \sigma)}{W(\sigma \to \sigma')} = \exp[(E(\sigma') - E(\sigma))/kT]$$

Theorem for Markov Processes

IF:

1) For any two states, σ_A and σ_B, there exists a sequence of states, $\sigma_1 \dots \sigma_n$, such that

$$W(\sigma_A \to \sigma_1)\, W(\sigma_1 \to \sigma_2) \dots W(\sigma_n \to \sigma_B) \neq 0$$

and

2) Detailed Balance

THEN:

$$P(\sigma, t) \xrightarrow[t \to \infty]{} P_{eq}(\sigma)$$

ISING MODEL

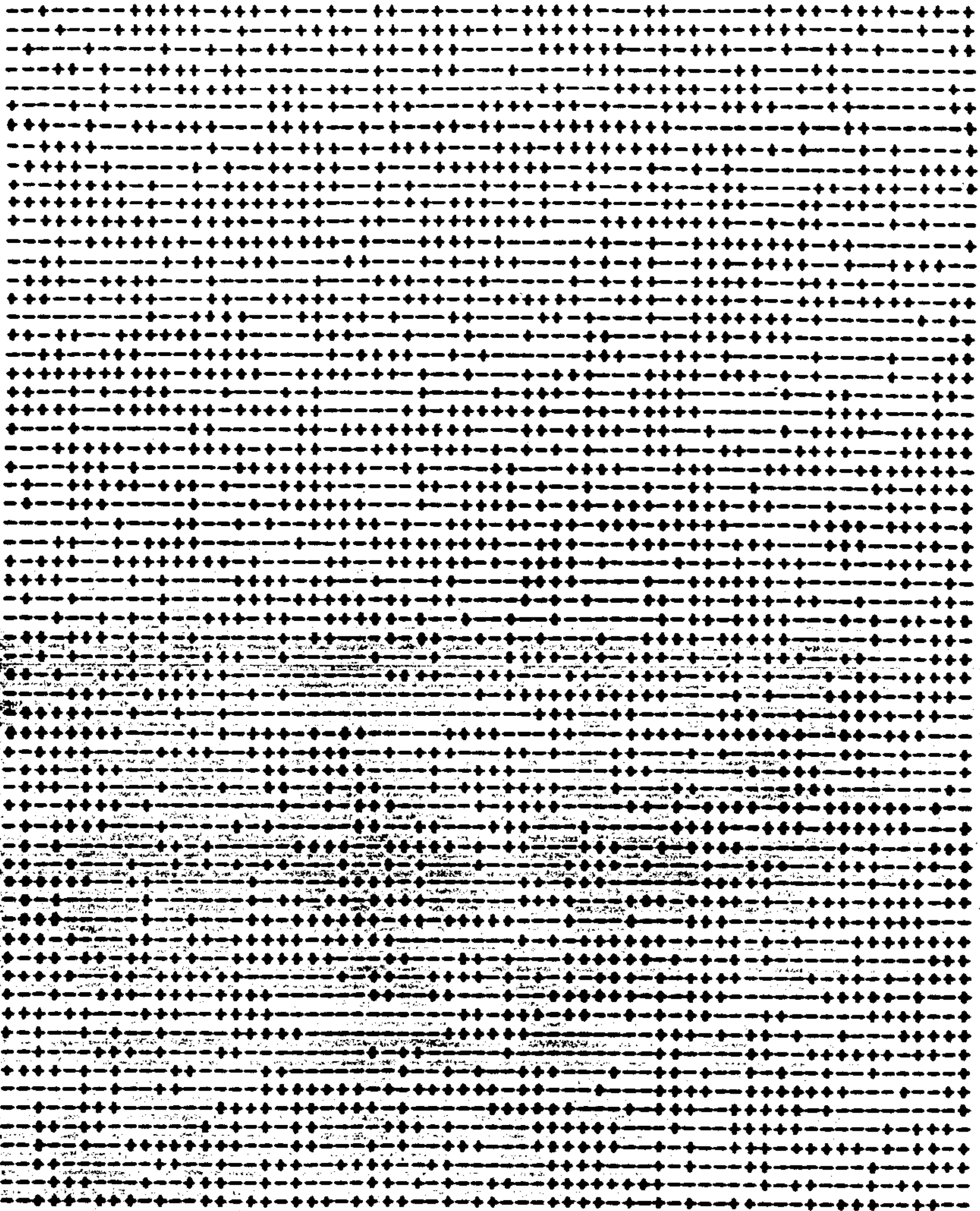
"Spins" σ_i on lattice sites

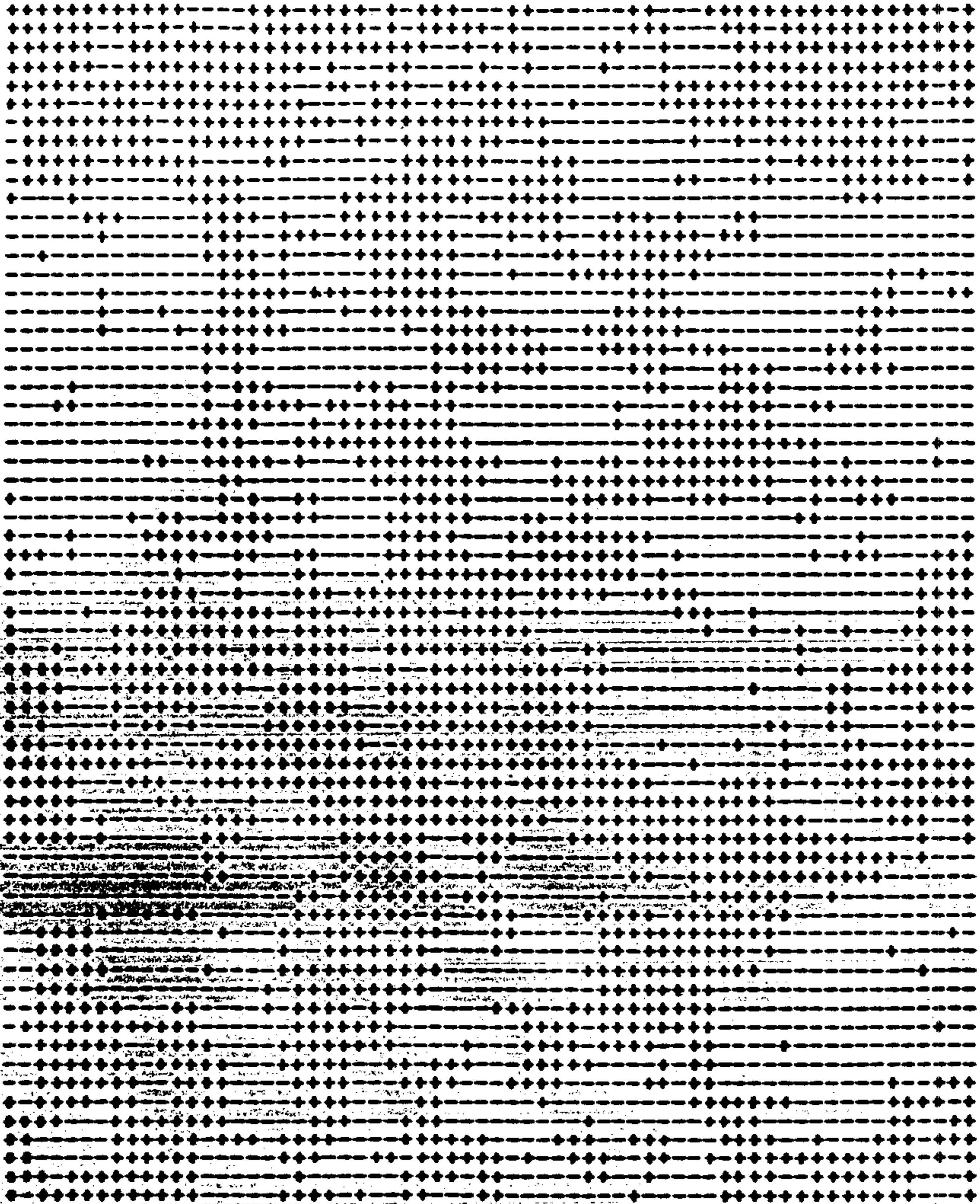
$$\sigma_i = +1 \quad \text{or} \quad -1$$

$$H = -J \sum_{\langle ij \rangle} \sigma_i \sigma_j$$

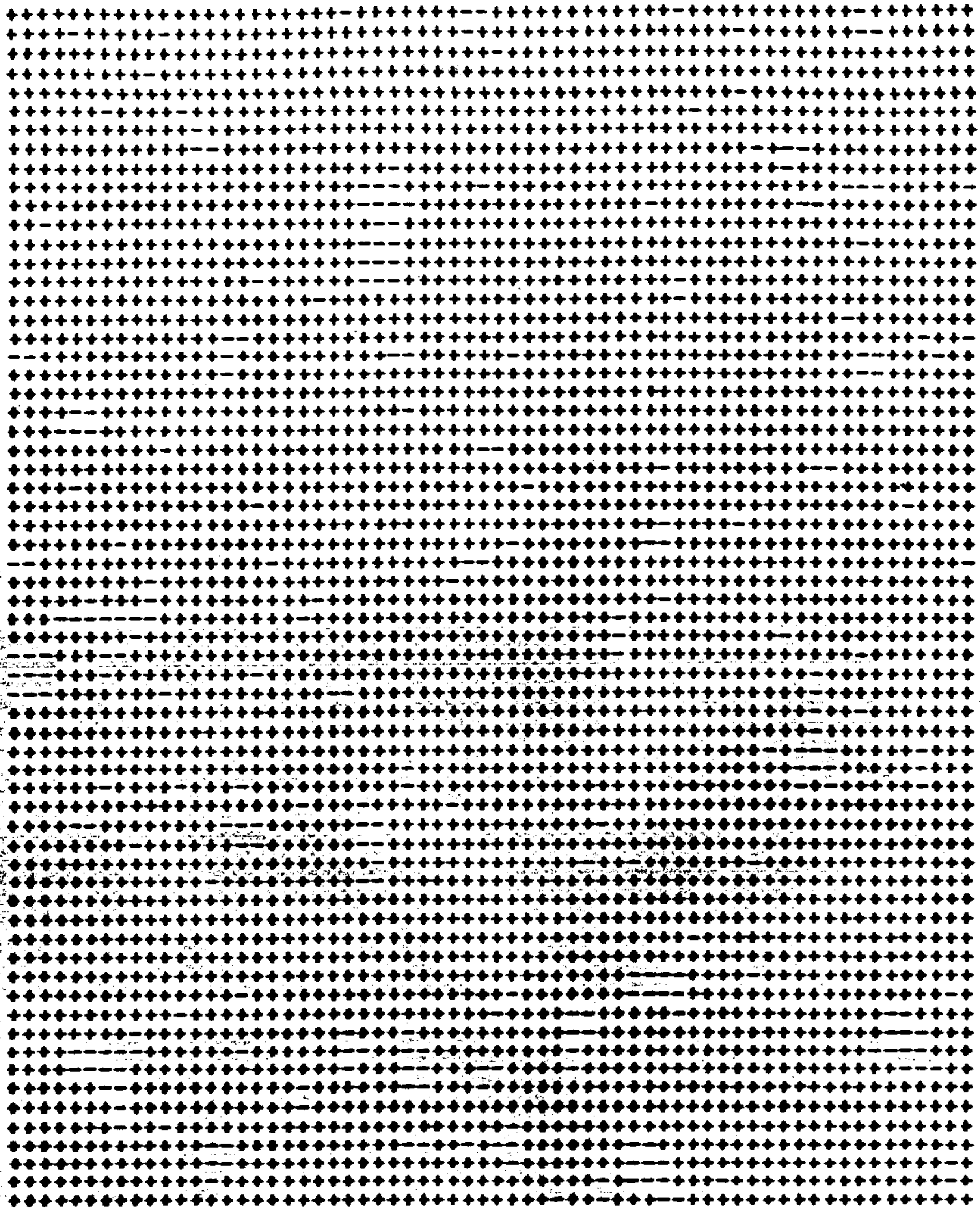
sum on nearest neighbors

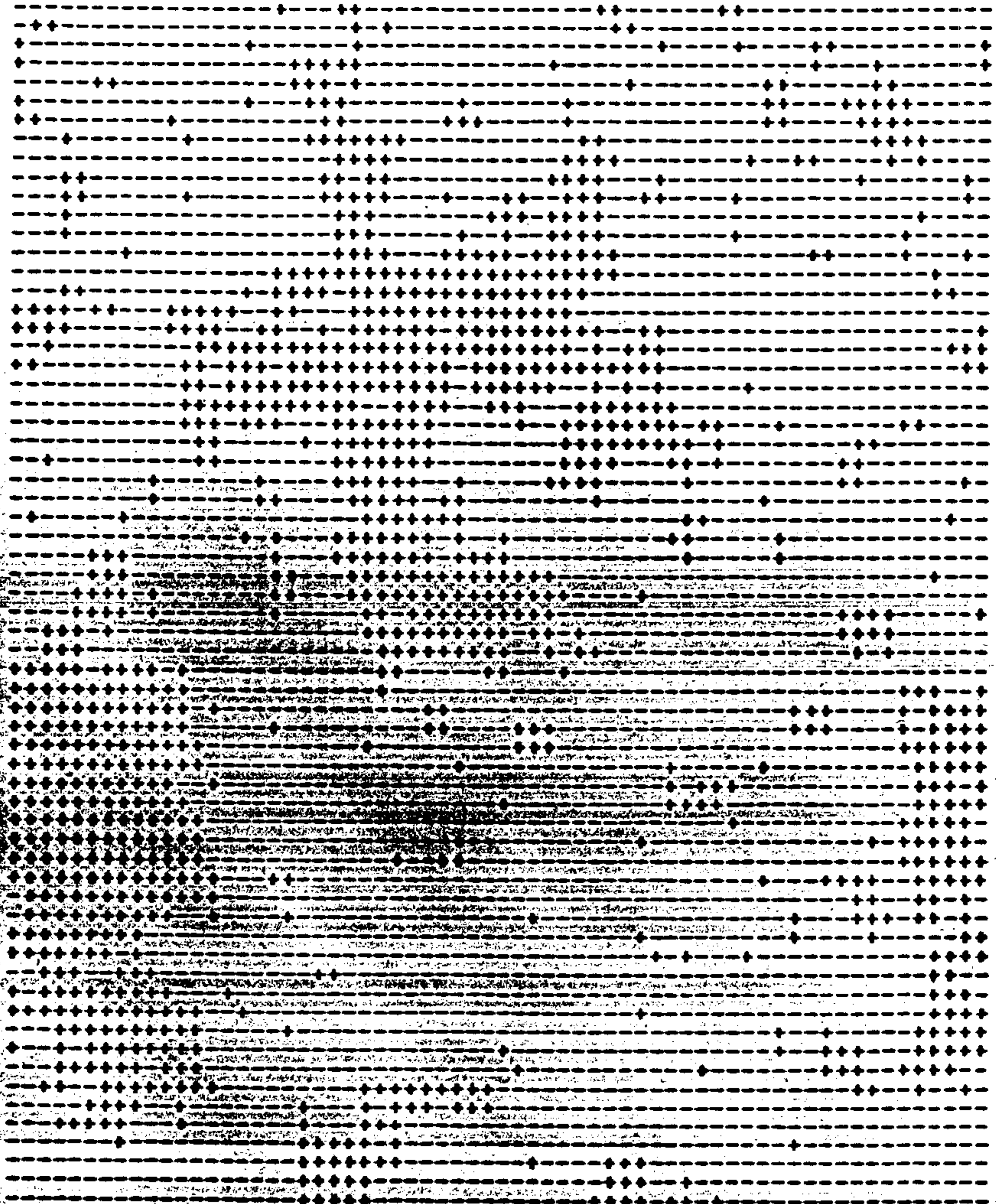
Neighbors	Energy
$+\,+$ or $-\,-$	$-J$
$+\,-$ or $-\,+$	$+J$





1.1 T_0





Critical Slowing Down

$$\tau \sim \xi^{z}$$

$z \equiv$ dynamical critical exponent

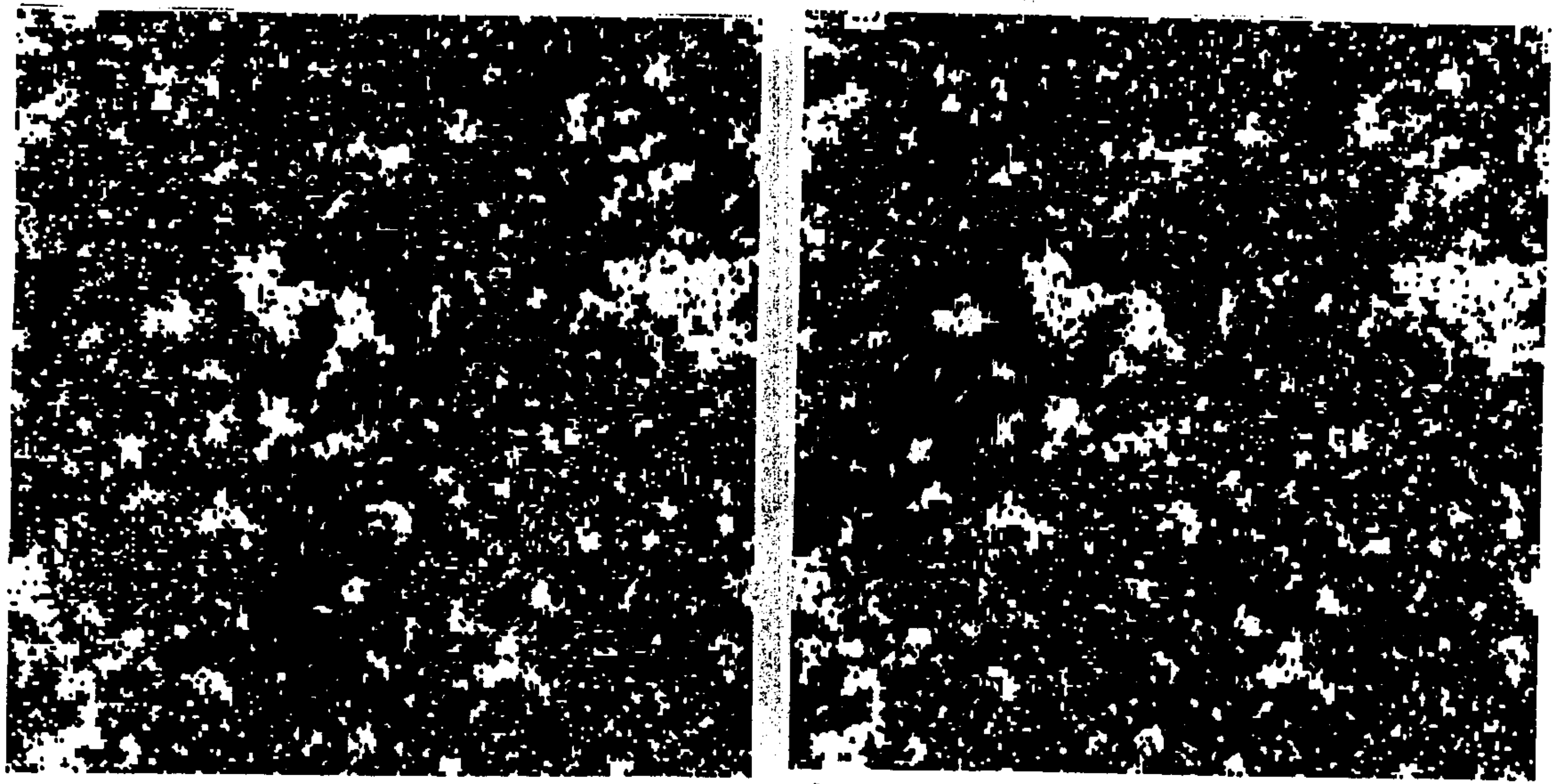
$$\xi \sim |T - T_c|^{-\nu}$$

$$\tau \sim |T - T_c|^{-z\nu}$$

For finite systems [L × L]

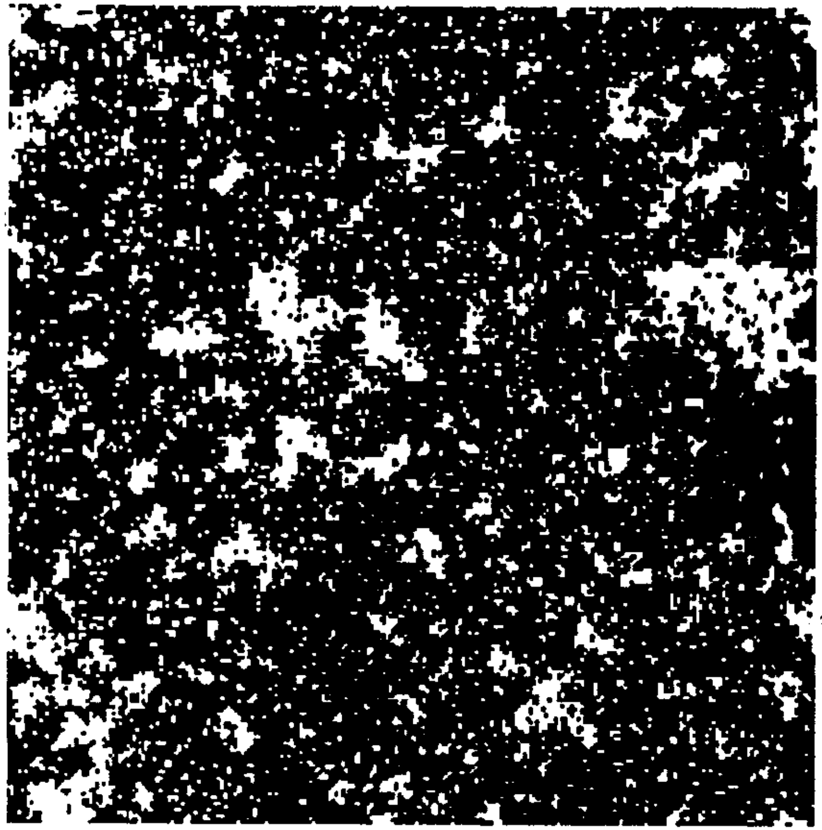
Maximum $\xi \sim L$

Maximum $\tau \sim L^{z}$



1. 2.

Standard Monte Carlo $T = T_c$ 256^2



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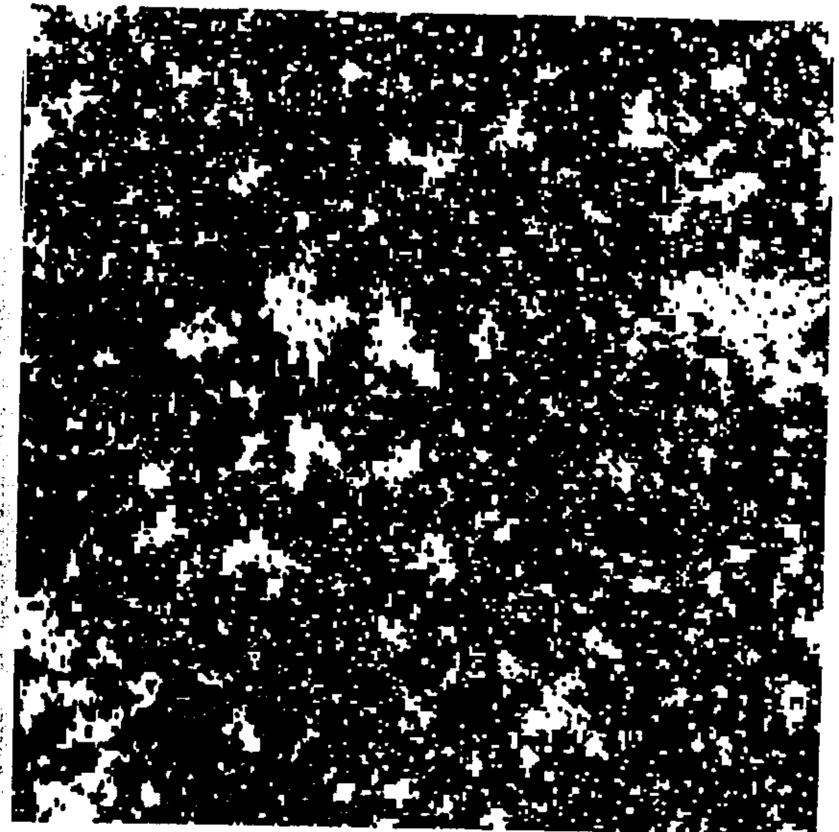
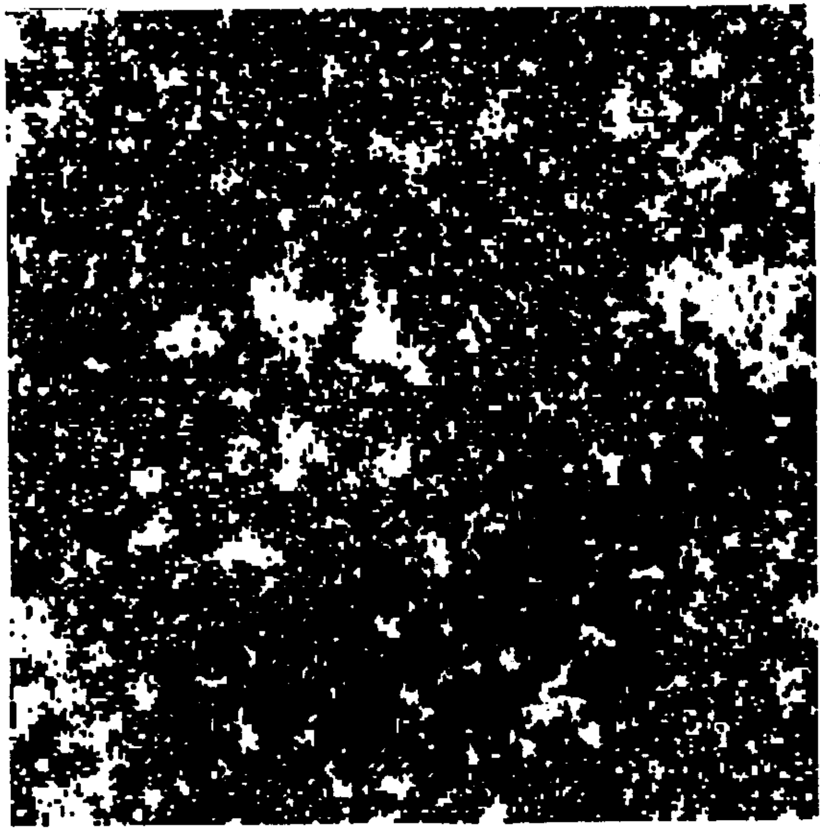


4

IIC $T = T_1$ 256^2



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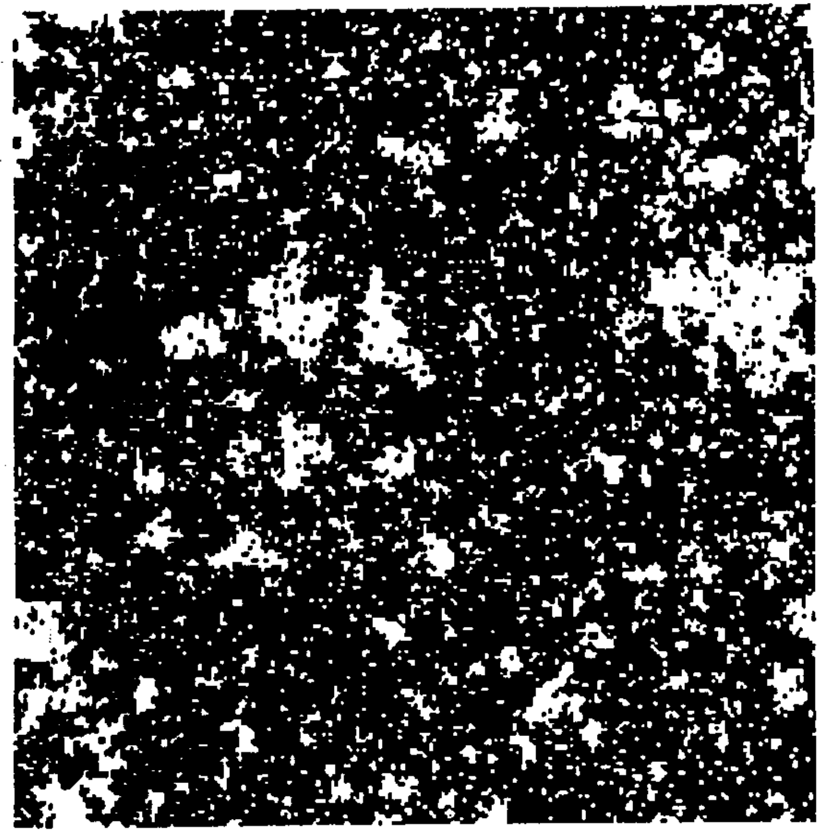


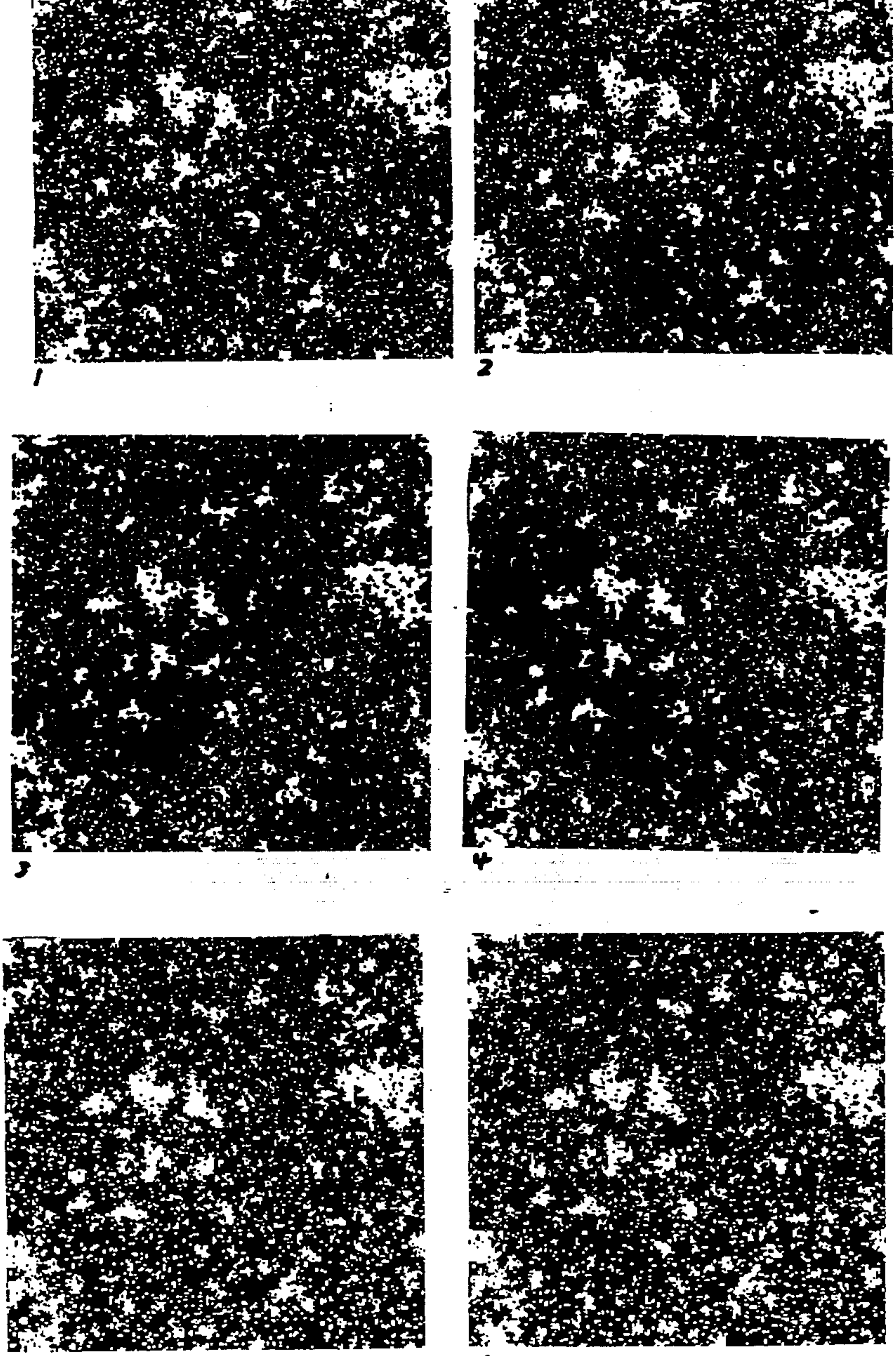
6

MC $T = T_c$ 256²

MC 5 6

$T = T_c$

56 x 256



1 2 3 4 5 6

Monte Carlo

Simulation of

Bond Percolation

X(J,K) : bond in x-direction
at site (J,K)

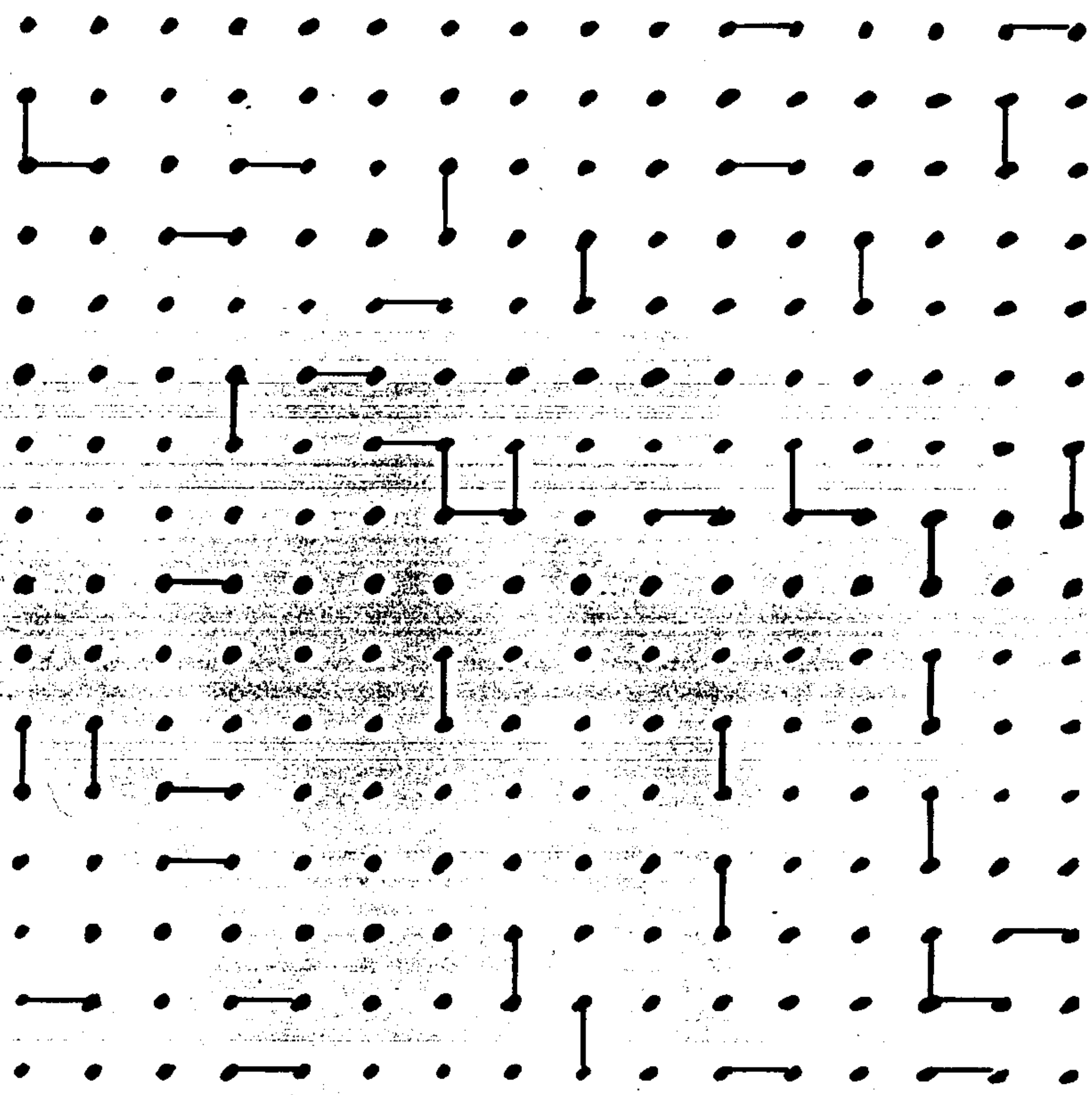
Y(J,K) : bond in y-direction

X, Y = 0 or 1

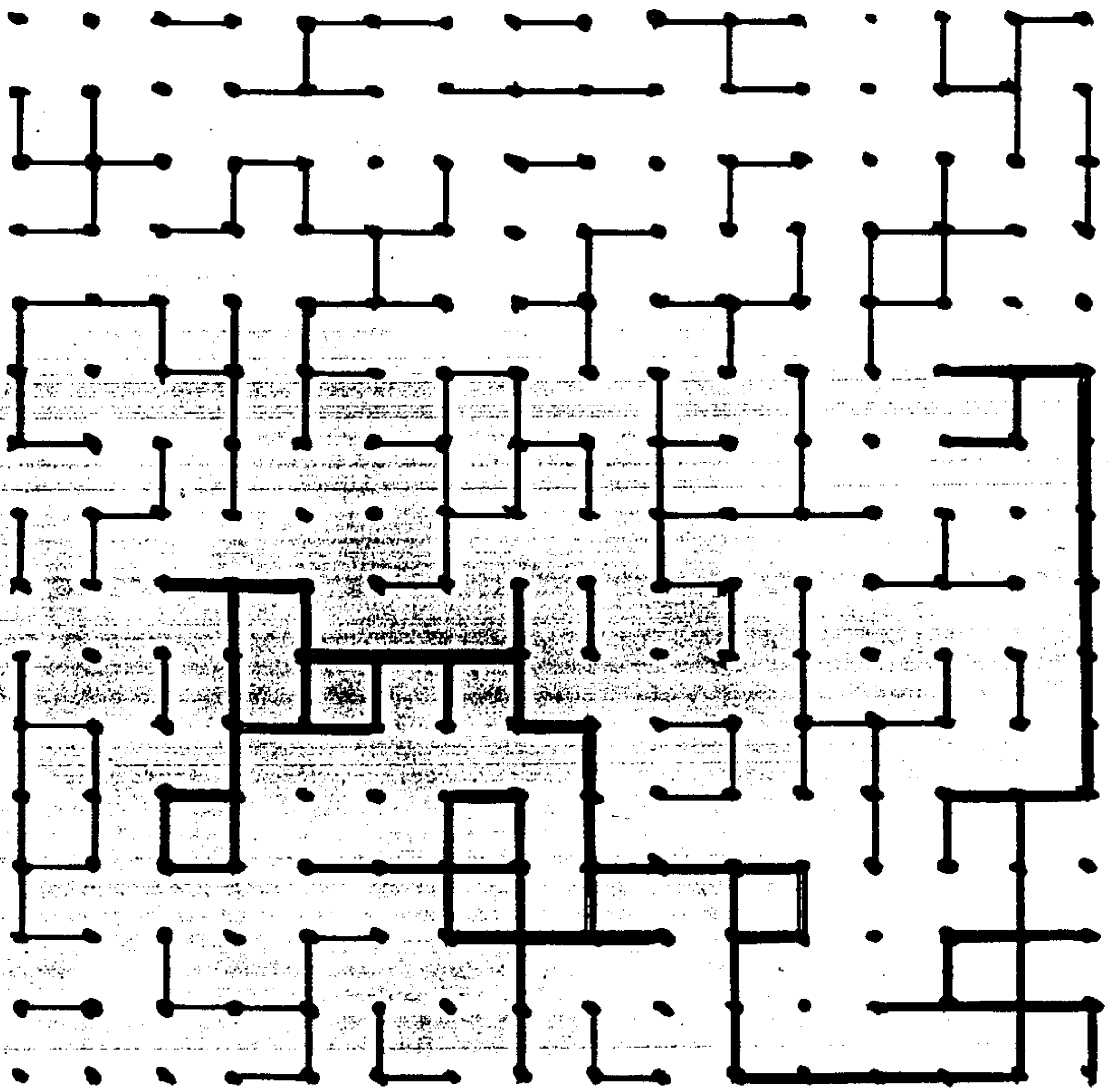
Essential part of program:

```
X(J,K) = 0
IF(RANX(J,K).LT.P) X(J,K)=1
```

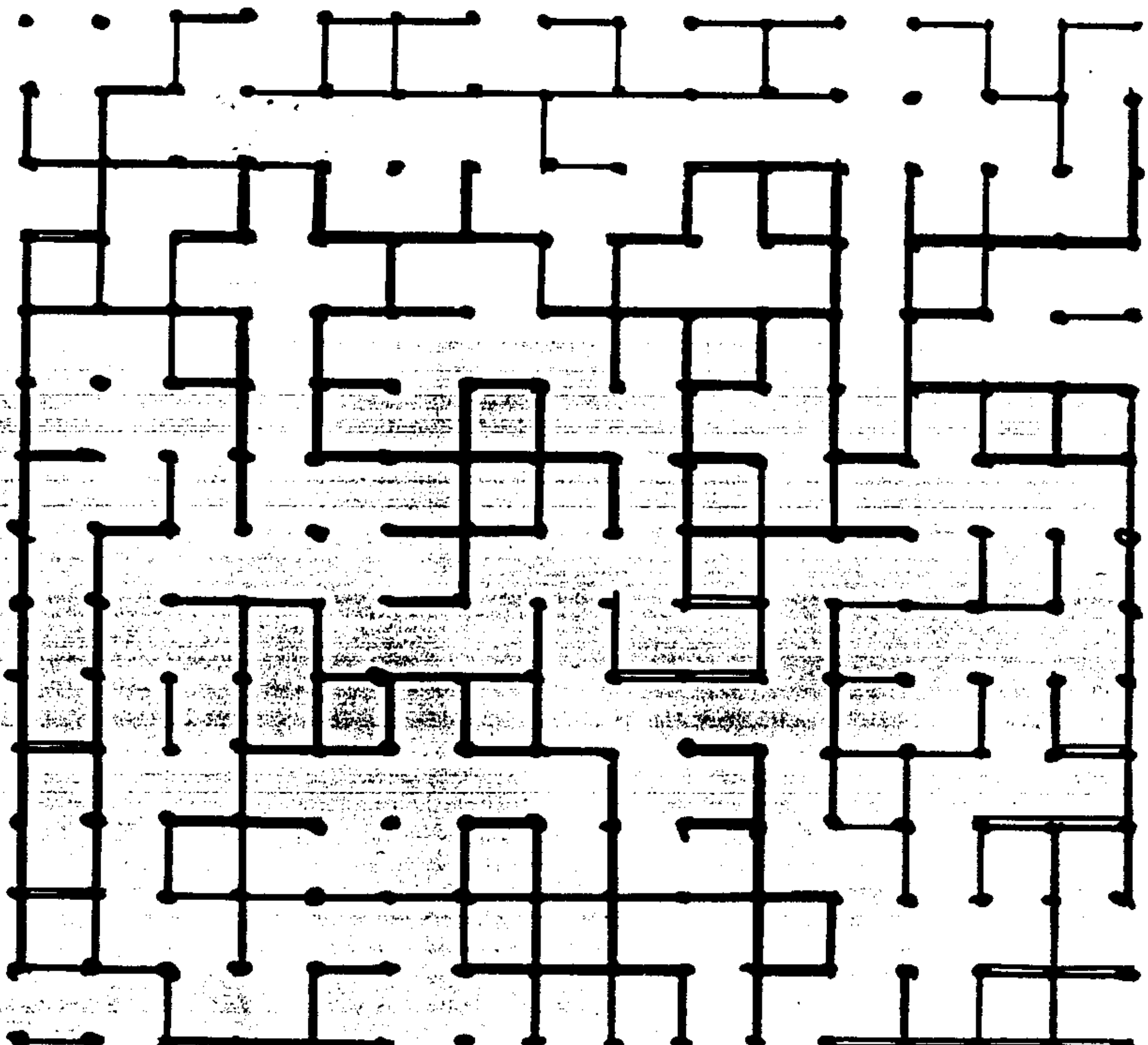
$p = 0.10$



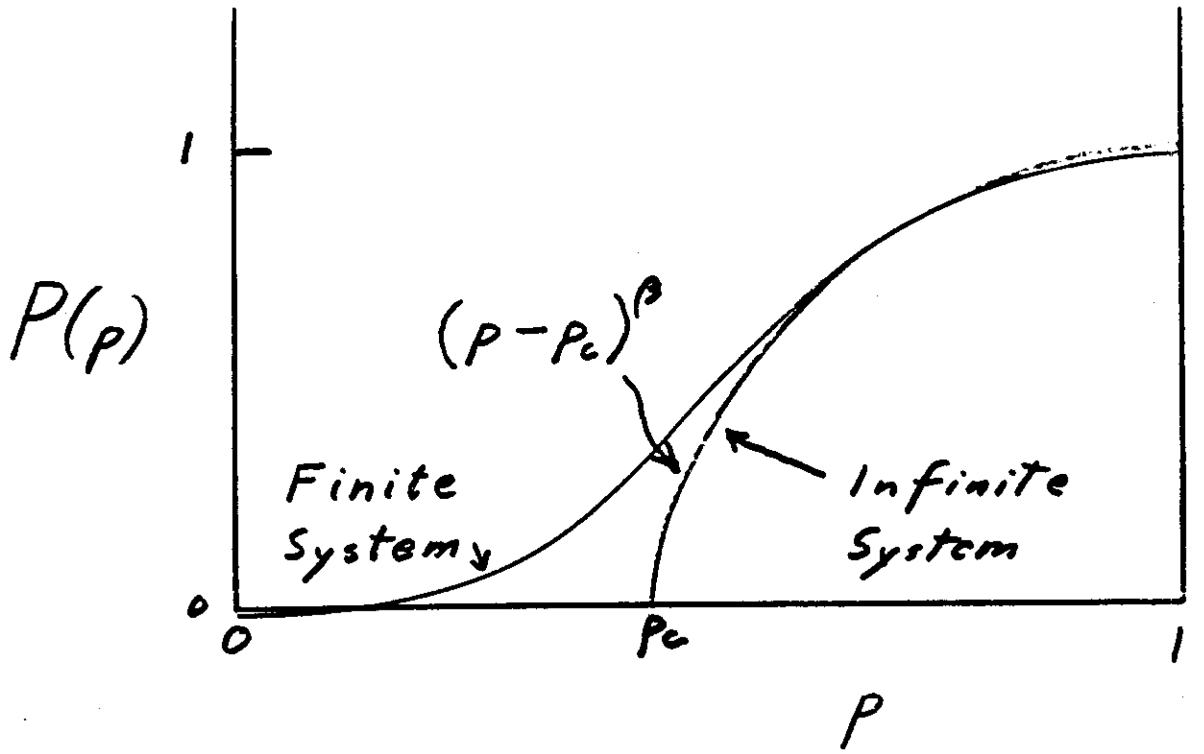
$p = 0.40$



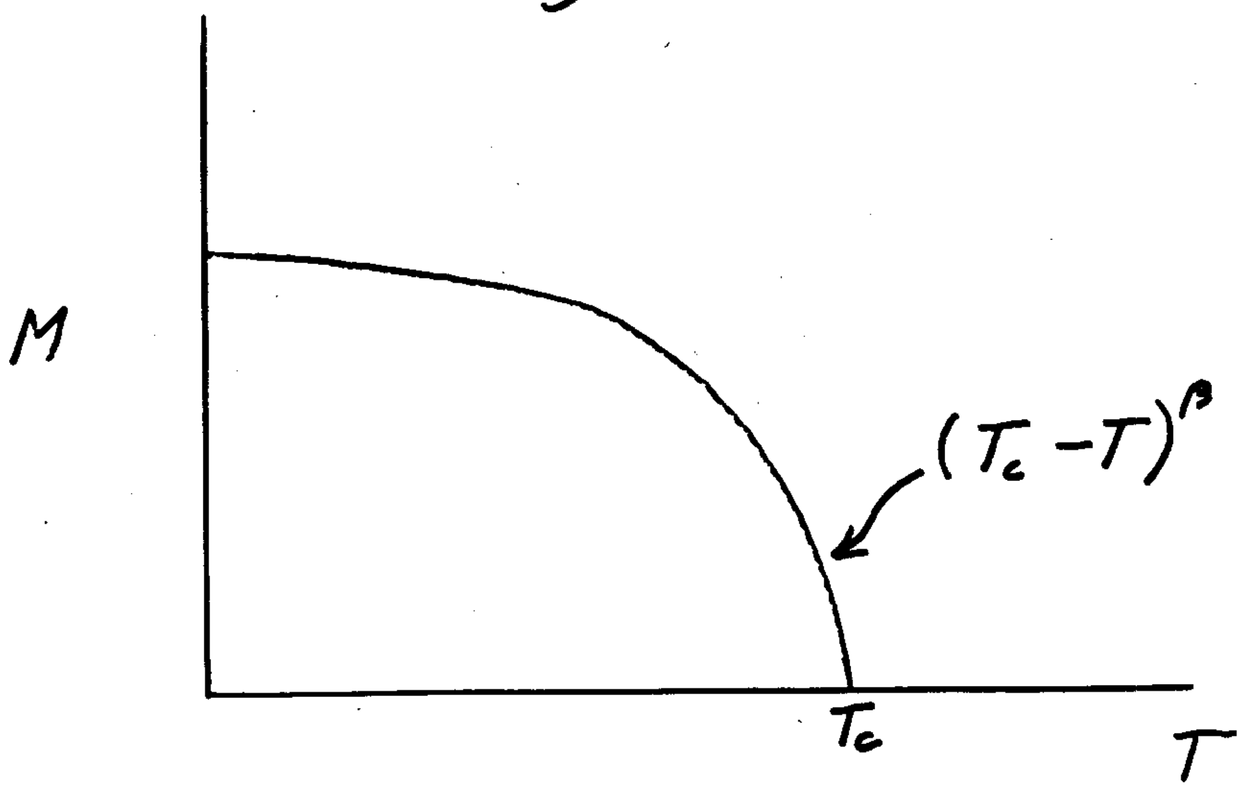
$p = 0.55$



Percolation



Magnetization



Ising Model

$$H = K \sum_{\langle i,j \rangle} \delta_{\sigma_i, \sigma_j}$$

$\sigma_i = +1$ or -1

or

$\sigma_i = 1$ or 2

Potts Model

$$\sigma_i = 1, 2, 3 \ldots q$$

Potts $\rightarrow$ Percolation

$$H = K \sum_{\langle ij \rangle} \left(\delta_{\sigma_i, \sigma_j} - 1 \right)$$

$$Z = \mathop{Tr}_{\sigma} \; e^{H}$$

$$H_{\langle \ell m \rangle} = K \sum_{\substack{\langle ij \rangle \\ \neq \langle \ell m \rangle}} \left(\delta_{\sigma_i, \sigma_j} - 1 \right)$$

$$Z^{same}_{\langle \ell m \rangle} \equiv \mathop{Tr}_{\sigma} \; e^{H_{\langle \ell m \rangle}} \; \delta_{\sigma_\ell, \sigma_m}$$

$$Z^{diff}_{\langle \ell m \rangle} \equiv \mathop{Tr}_{\sigma} \; e^{H_{\langle \ell m \rangle}} \left(1 - \delta_{\sigma_\ell, \sigma_m} \right)$$

$$Z = Z^{same}_{\langle \ell m \rangle} + e^{-K} \; Z^{diff}_{\langle \ell m \rangle}$$

Potts → Percolation

$$Z = Z^{same}_{\langle \ell m \rangle} + e^{-K} Z^{diff}_{\langle \ell m \rangle}$$

$$Z^{indep}_{\langle \ell m \rangle} \equiv \underset{\sigma}{Tr}\; e^{H_{\ell m}}$$

$$Z^{indep}_{\langle \ell m \rangle} = Z^{same}_{\langle \ell m \rangle} + Z^{diff}_{\langle \ell m \rangle}$$

$$Z = \underbrace{(1 - e^{-K})}_{p} Z^{same}_{\langle \ell m \rangle} + \underbrace{e^{-K}}_{(1-p)} Z^{indep}_{\langle \ell m \rangle}$$

Potts → Percolation

$$Z = p\, Z^{same}_{\langle \ell m \rangle} + (1-p)\, Z^{indep}_{\langle \ell m \rangle}$$

$$p = 1 - e^{-K}$$

$$Z = \mathop{Tr}_{\{links\}} p^{b} (1-p)^{\bar{b}} s^{N_c}$$

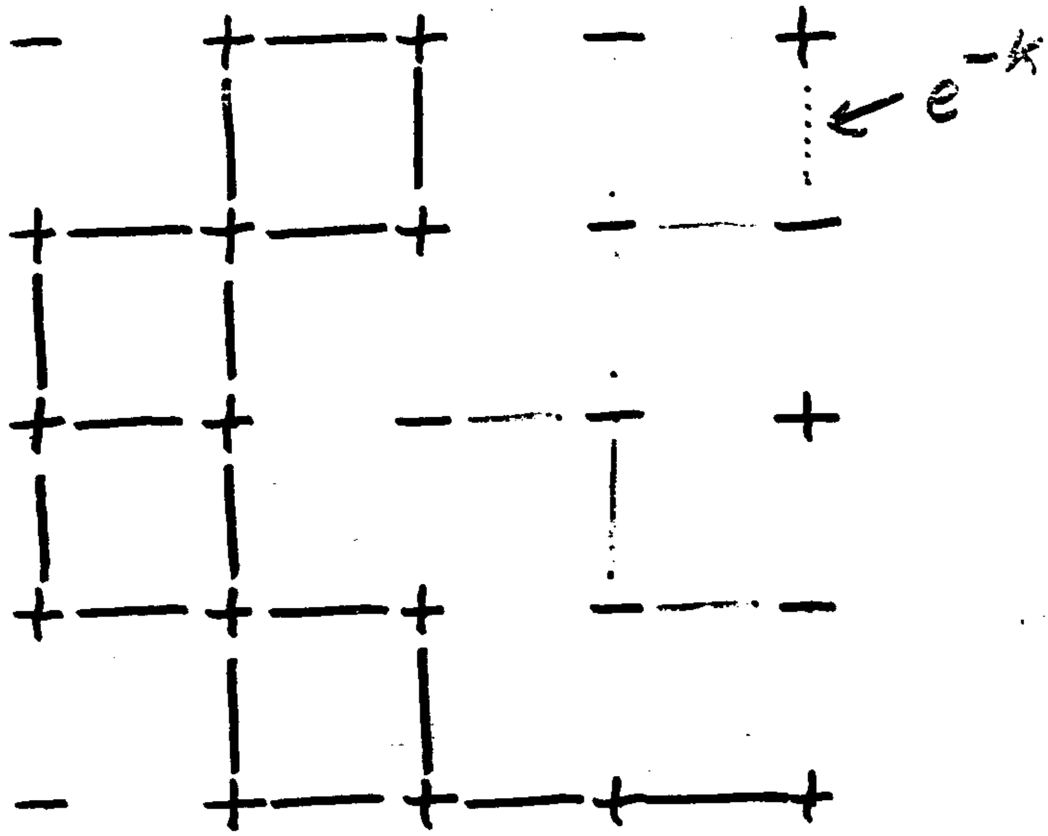
$$Z = \langle s^{N_c} \rangle_{\{links\}}$$

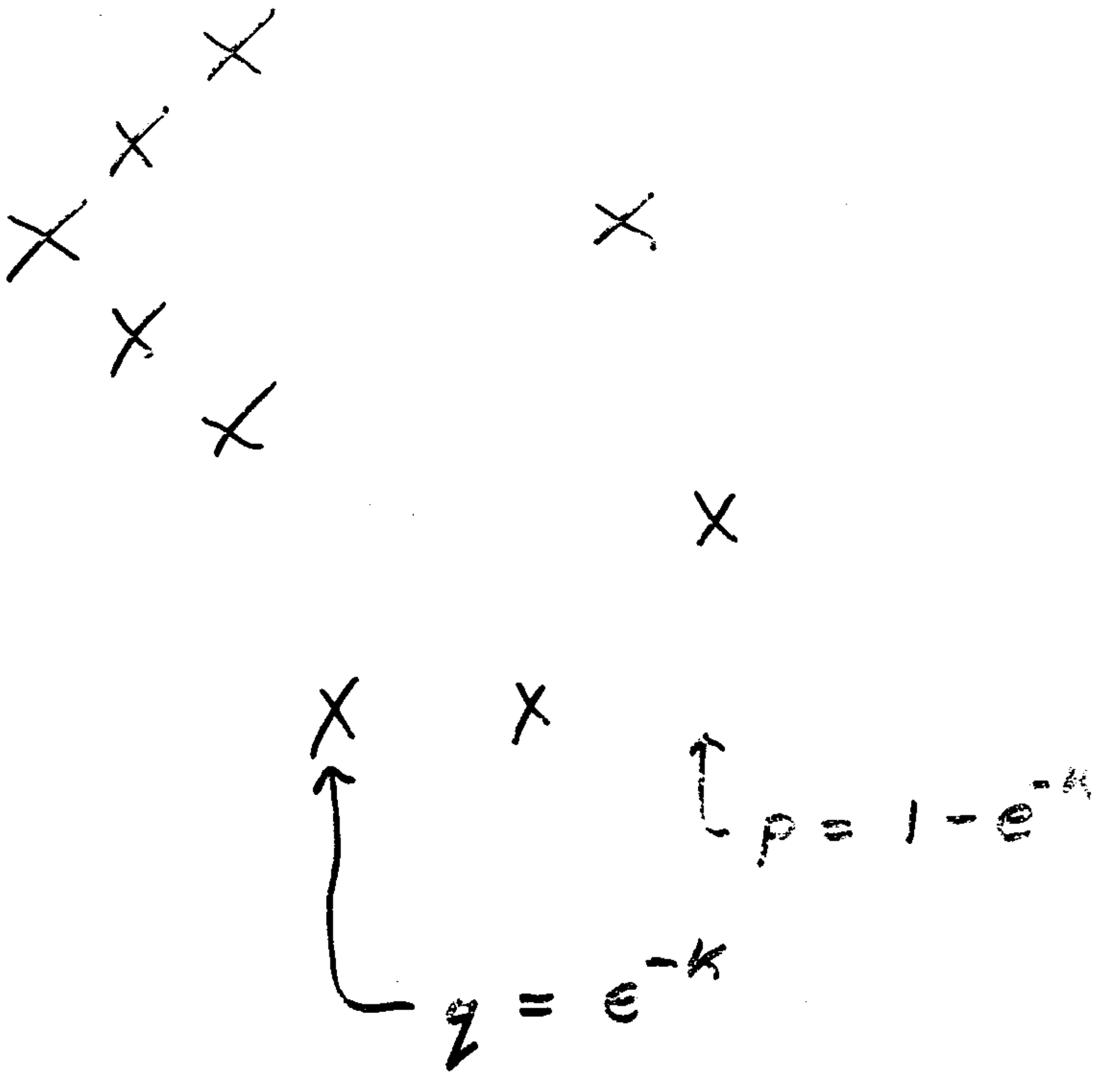
$$\langle N_c \rangle = \lim_{s \to 1} \left[\frac{\partial}{\partial s} \ln Z \right]$$

Kasteleyn + Fortuin, 1969

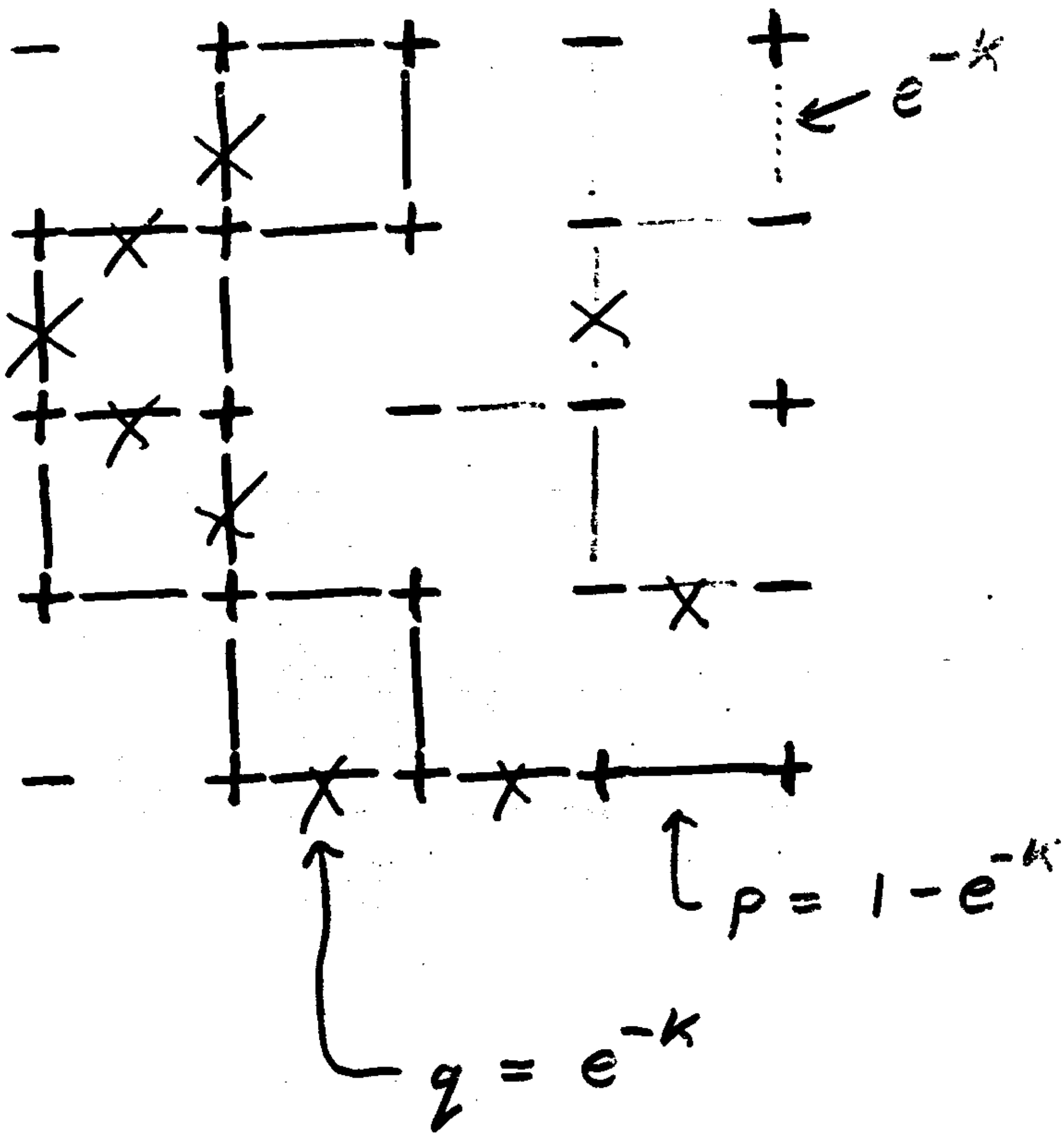
−	+	+	−	+
+	+	+	−	−
+	+	−	−	+
+	+	+	−	−
−	+	+	+	+

Potts Clusters



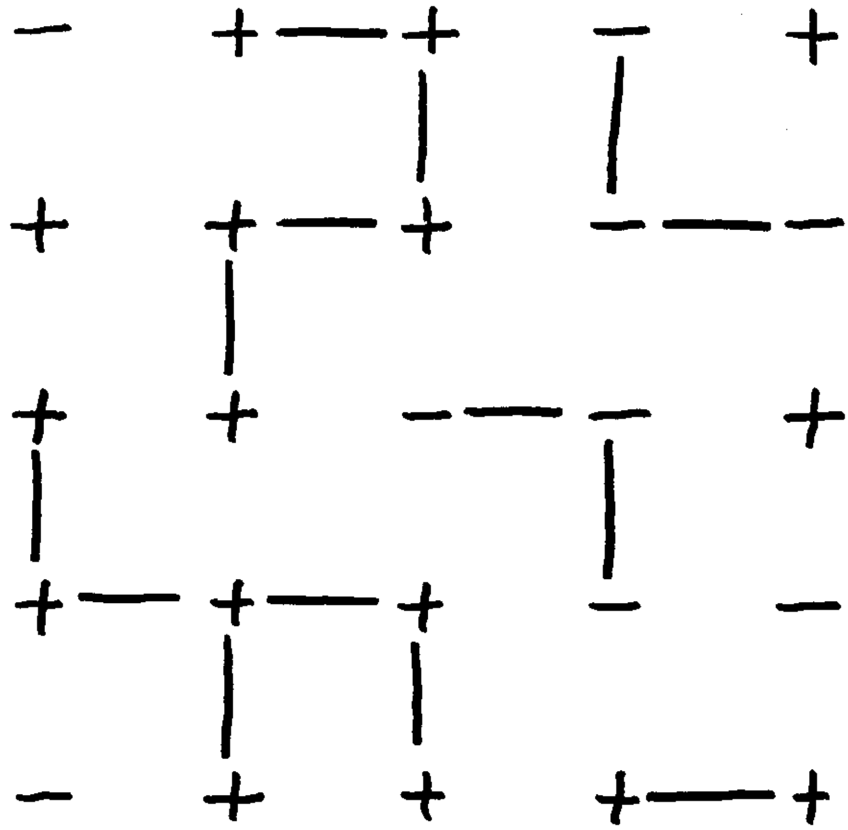

$p = 1 - e^{-K}$
$z = e^{-K}$

Potts Clusters

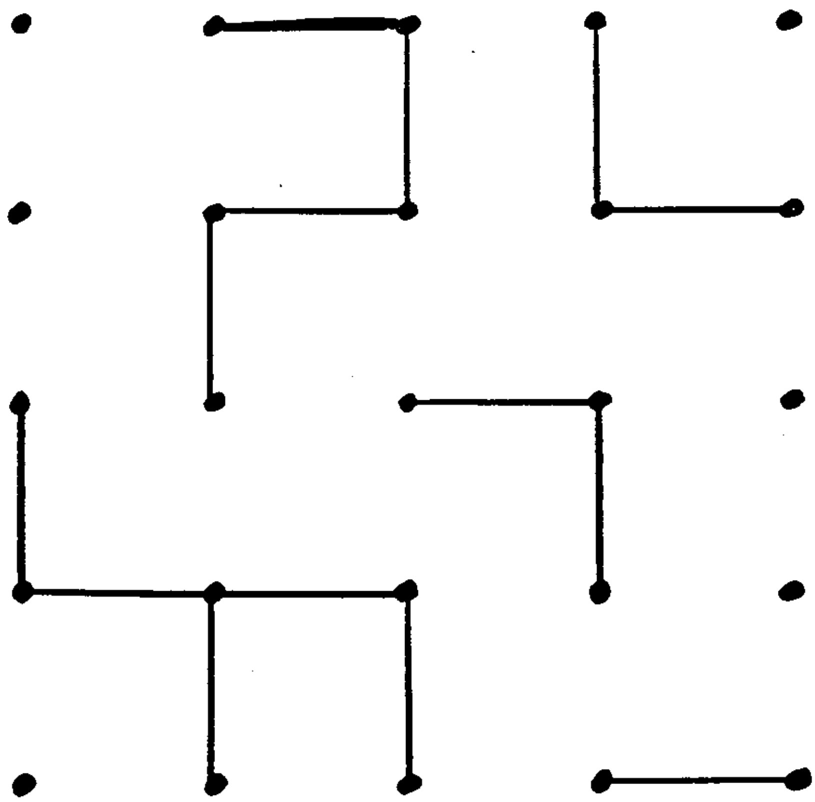


Site - Bond

Correlated Percolation



Percolation Clusters



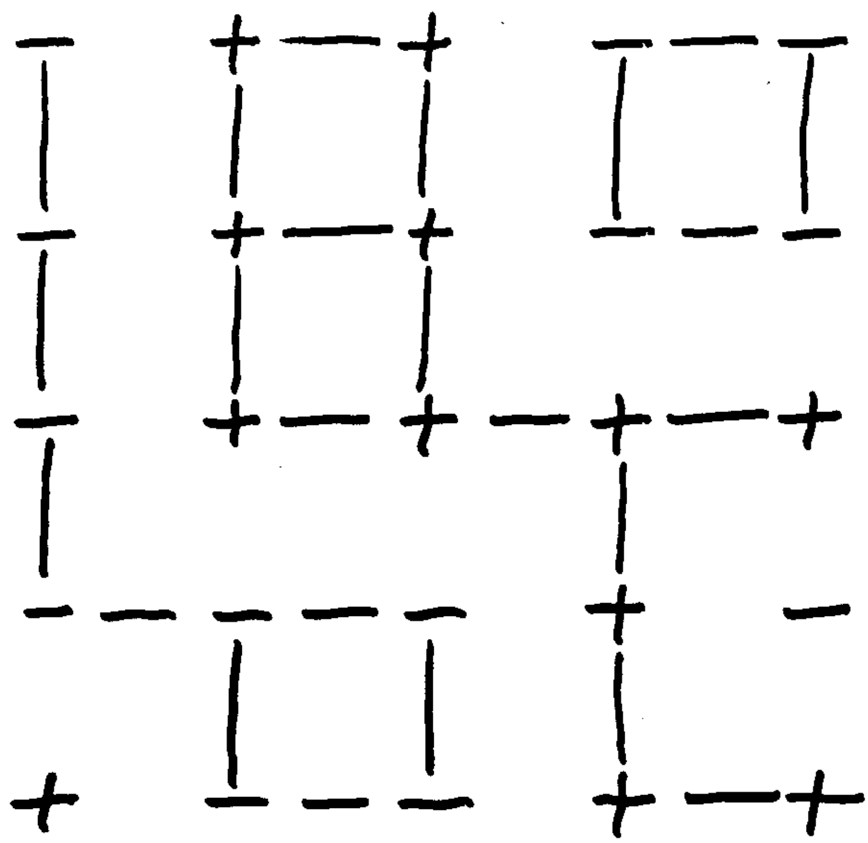
$p^{B} \quad q^{E-B} \quad s^{N_c}$

s = # of Potts states

$q = e^{-K} = 1 - p$

−	+	+	−	−
−	+	+	−	−
−	+	+	+	+
−	−	−	+	−
+	−	−	+	+

New Potts Clusters



Order Parameter

Ising Ferromaget

$$M = \lim_{H \to 0^+} \lim_{L \to \infty} L^{-d} \langle \sum_i \sigma_i \rangle$$

$$= \lim_{H \to 0^+} \lim_{L \to \infty} L^{-d} \langle \sum_n C_n \sigma_n \rangle$$

sum on clusters

$$M = \lim_{H \to 0^+} \lim_{L \to \infty} L^{-d} \langle C_{largest} \rangle$$

Magnetic Susceptibility

$$\chi = L^{-d} \left\langle \sum_{i,j} \sigma_i \sigma_j \right\rangle$$

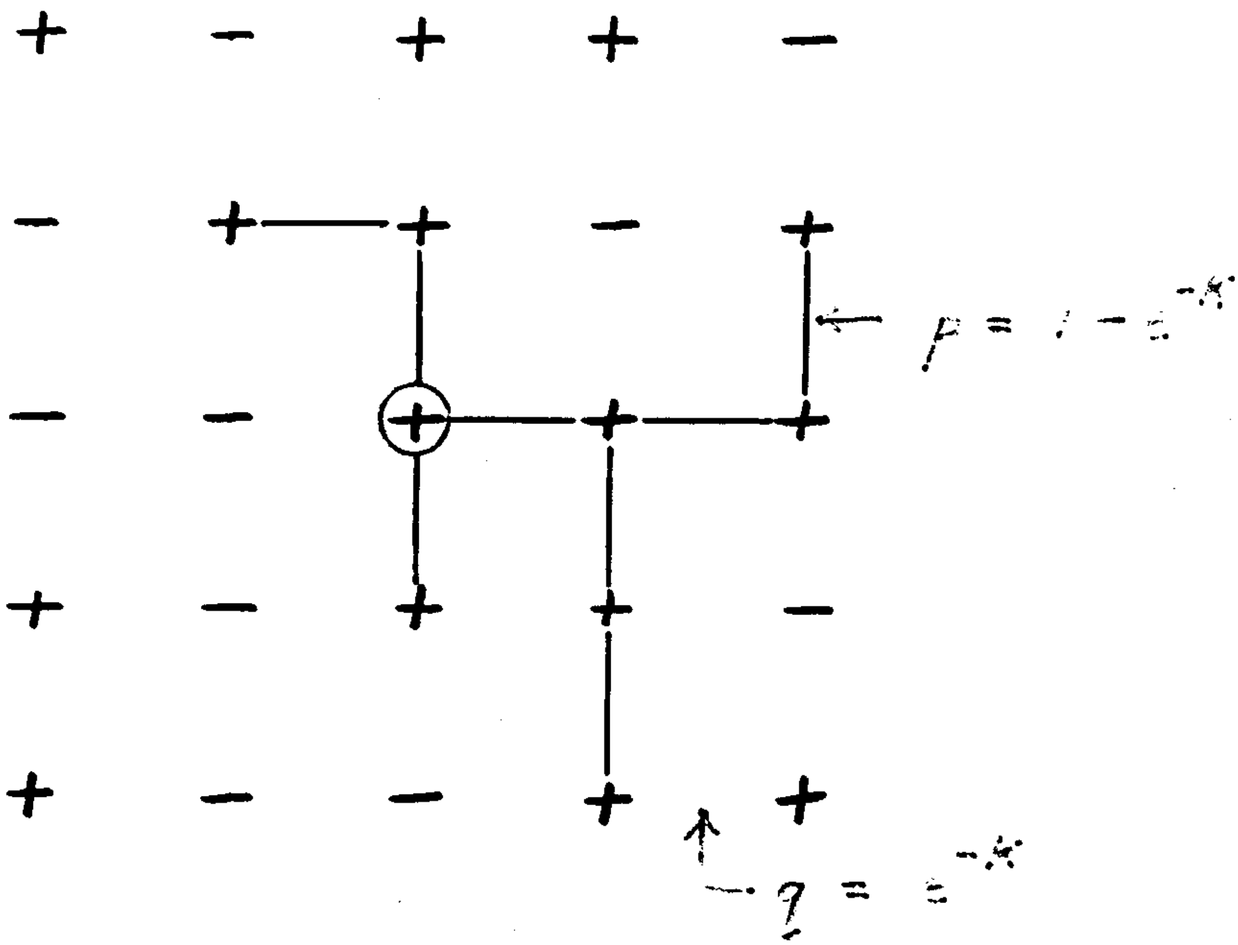
$$\chi = L^{-d} \left\langle \sum_{n,m} c_n c_m \sigma_n \sigma_m \right\rangle$$

$$\langle \sigma_n \sigma_m \rangle = \delta_{n,m}$$

$$\chi = L^{-d} \left\langle \sum_{n} c_n^2 \right\rangle$$

Single-Cluster Algorithm

U. Wolff

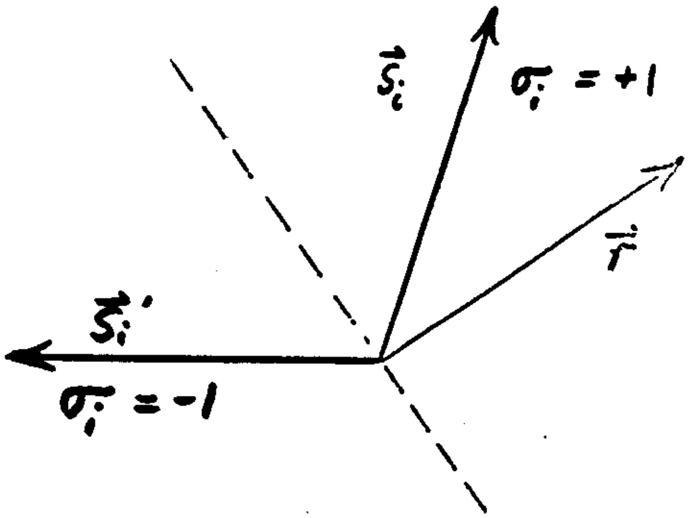


Embedded Ising Variables

U. Wolff

For $O(n)$ models

Example: $\vec{s}_i = (s_{ix}, s_{iy})$, $|\vec{s}_i| = 1$



$|\vec{r}| = 1$

$$\vec{s}_i\,' = \vec{s}_i + (\sigma_i - 1)(\vec{r} \cdot \vec{s}_i)\,\vec{r}$$

Application to

Anti ferromagnet

$K < 0$

PROBLEM:

$$p = 1 - e^{-K} < 0$$

$$q = e^{-K} > 1$$

Ising Antiferromagnet

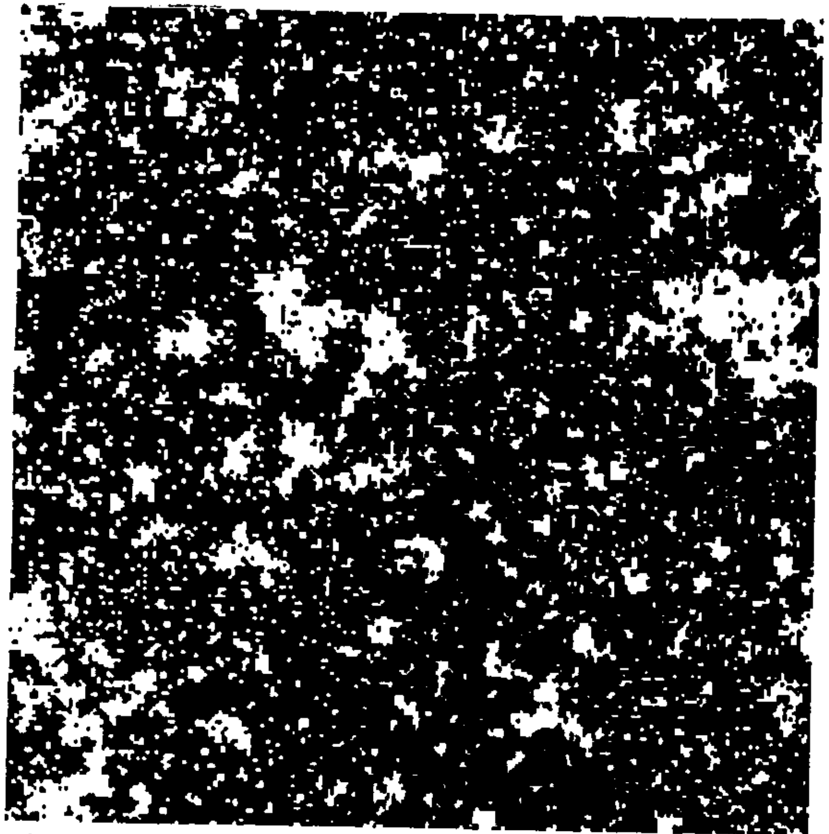
$$K < 0$$

Eliminate $Z^{same}_{\langle \ell m \rangle}$

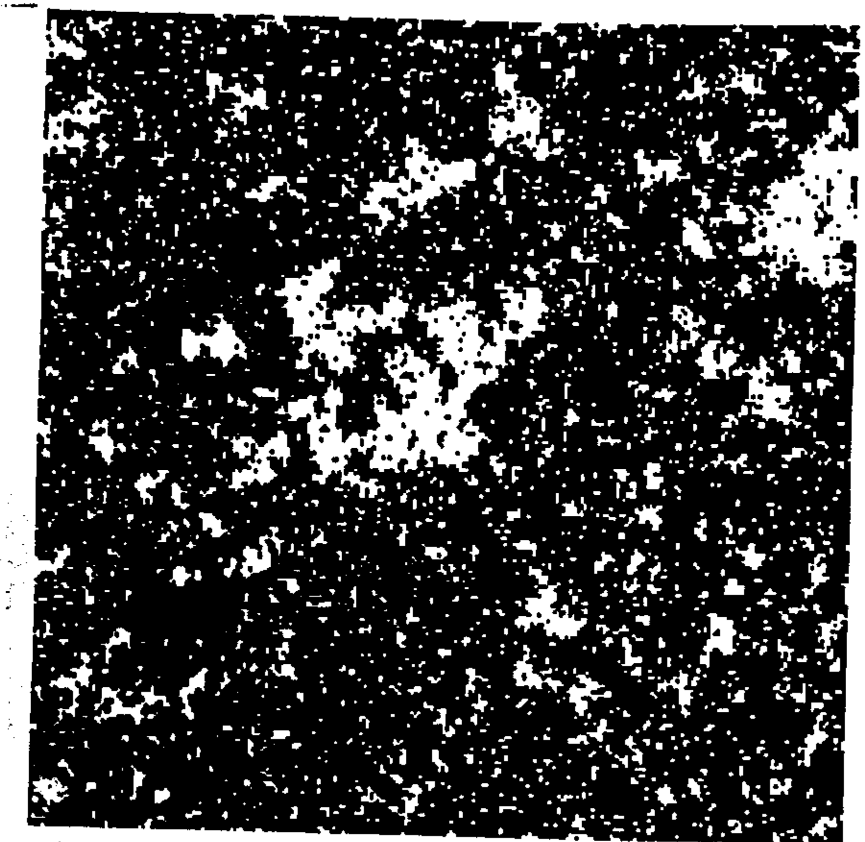
$$e^K Z = \underbrace{(1 - e^K)}_{p} Z^{diff}_{\langle \ell m \rangle} + \underbrace{e^K}_{1-p} Z^{IND}_{\langle \ell m \rangle}$$

$1 - e^K$ = Probability of antibond

$\Rightarrow$ Anticlusters

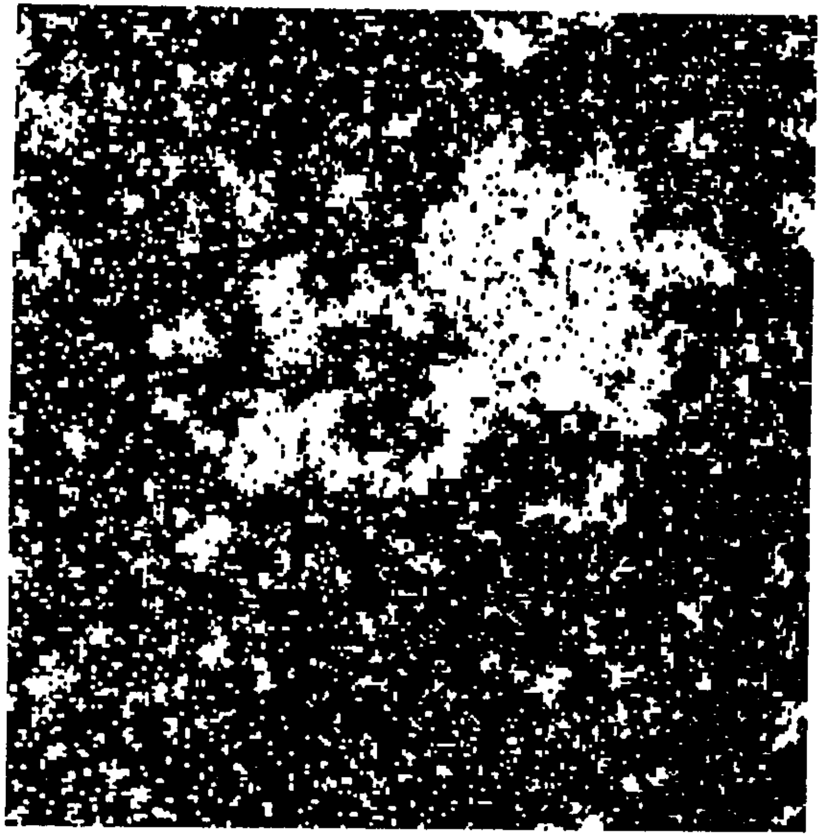


1



2

[illegible]lation $T = T_c$ 2.56²



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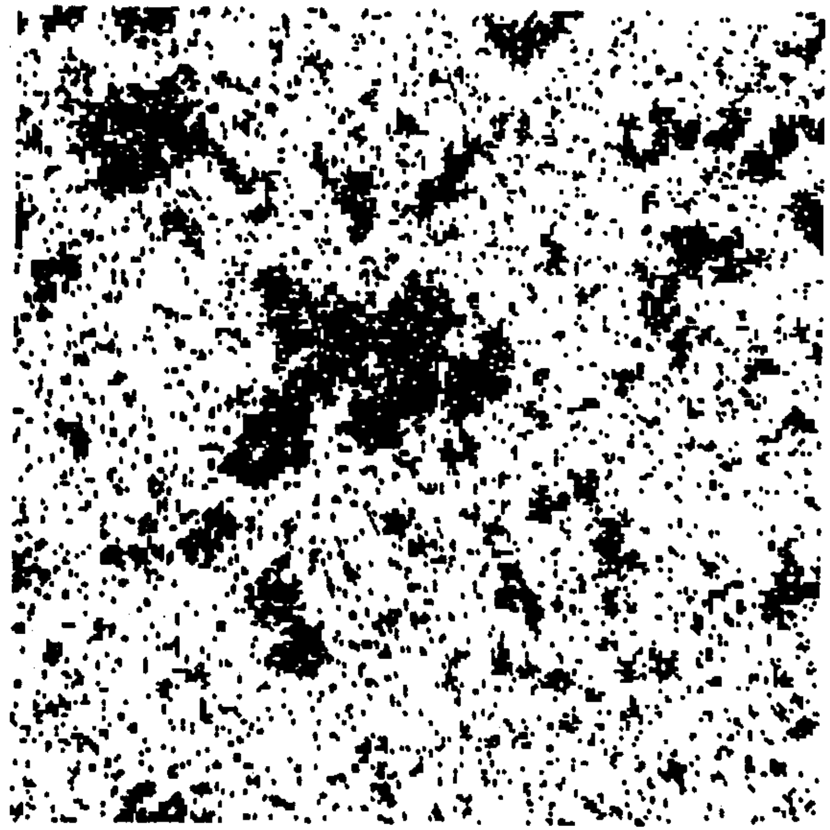
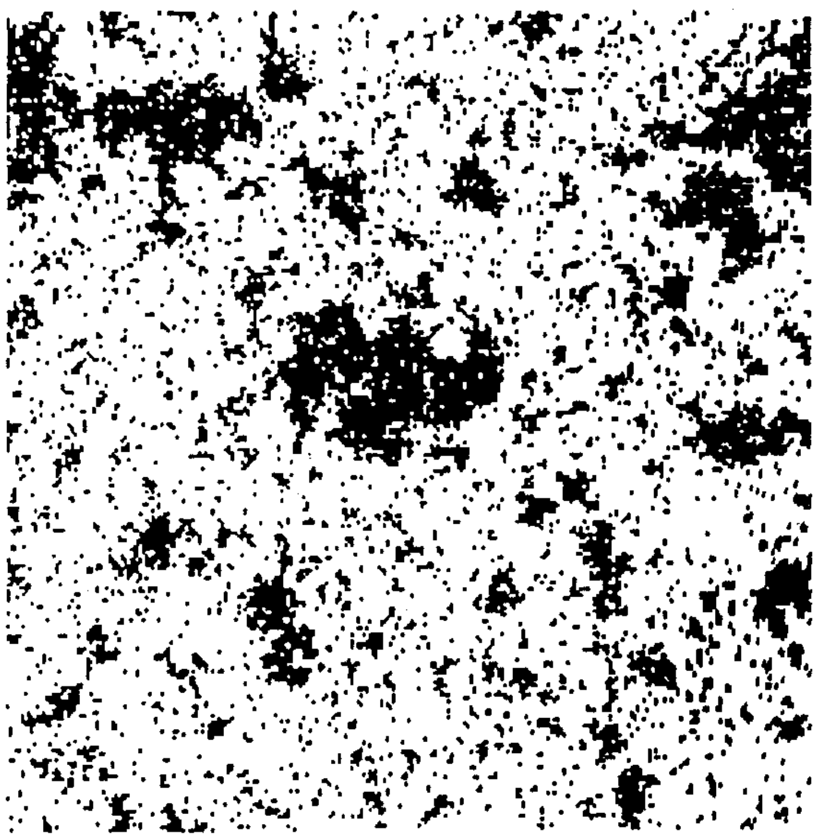
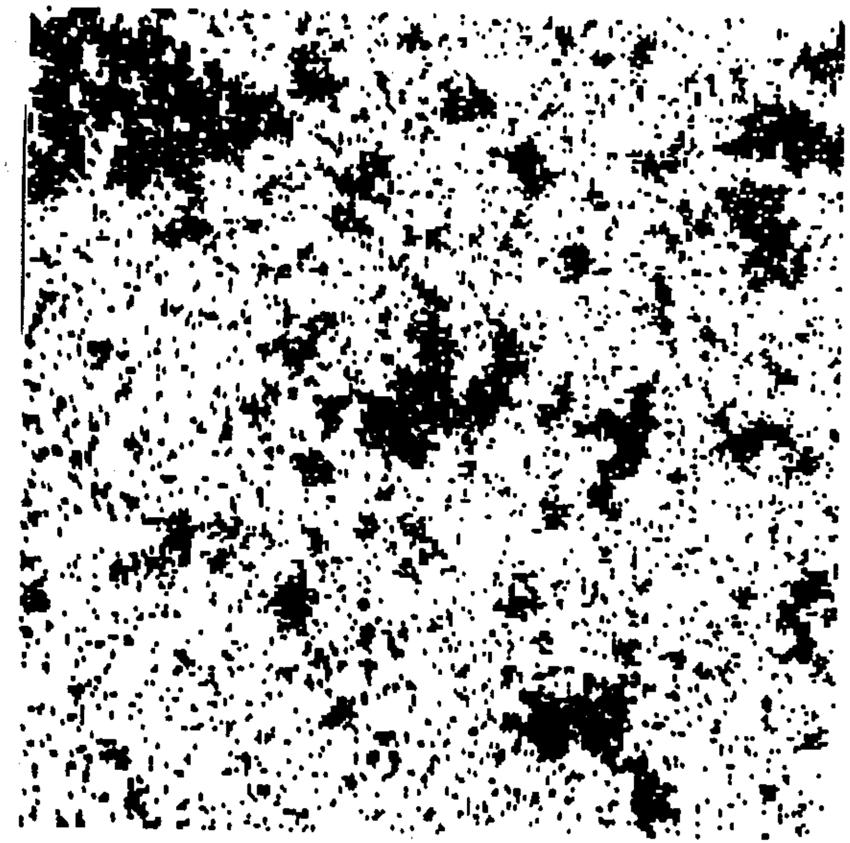


4

Potts-Percolation $T=T_c$ 256^2



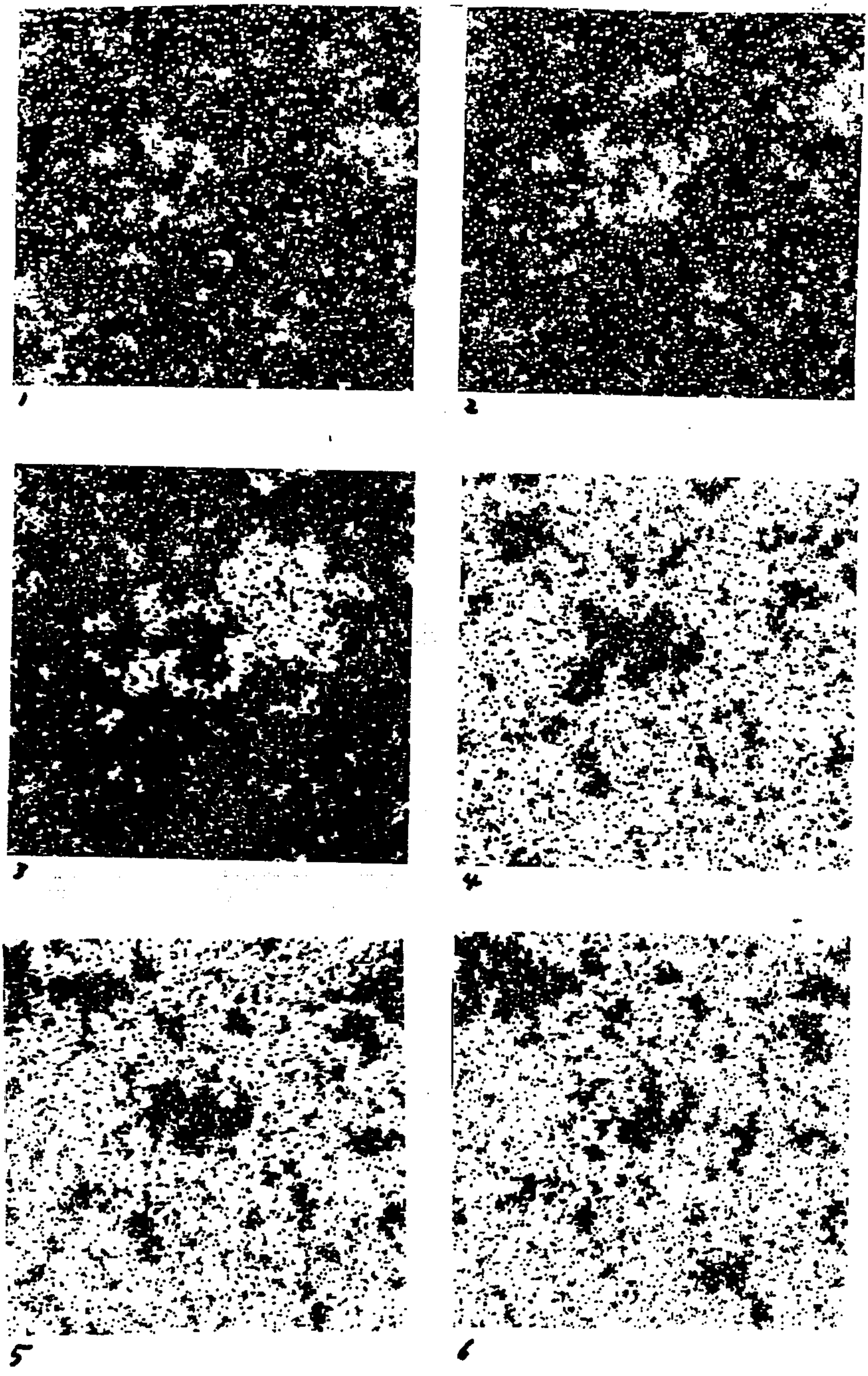
a



b

Potts simulation $T = T_c$ 256^2

H.S-
evolution
·x254
T_4



"Density of States"

$W(E)$ is the number of states with energy E

$$Z = \sum_{\{\sigma\}} \exp[-\beta E(\sigma)]$$

$$= \sum_{E} W(E)\, e^{-\beta E}$$

$$P(E) = \frac{1}{Z} W(E)\, e^{-\beta E}$$

Partition Function

$$Z = e^{-\beta F} = \mathop{Tr}_{\{\sigma\}} \exp[-\beta \mathcal{H}(\sigma)]$$

$$= \sum_E W(E) \exp[-\beta E]$$

$$\beta = 1/k_B T$$

Monte Carlo simulation at β_i

$\Rightarrow$ histogram $\quad N_i(E)$

$$\sum_E N_i(E) = n_i$$

$$\overline{N_i(E)} = n_i \; W(E) \; e^{-\beta_i E} \; e^{f_i}$$

$$f_i \equiv \beta_i F(\beta_i)$$

Approximation for $W(E)$

$$W(E) \approx n_i^{-1} N_i(E) e^{\beta_i E} e^{-f_i}$$

Then for other values of β

$$\langle A(E) \rangle = \sum_E A(E)\, W(E)\, e^{-\beta E} / Z(\beta)$$

$$Z(\beta) = \sum_E W(E)\, e^{-\beta E}$$

Single-Histogram Equation

$$\langle A(E) \rangle_\beta = \frac{\sum_E A(E)\, N_i(E) \exp[-(\beta - \beta_i) E]}{\sum_E N_i(E) \exp[-(\beta - \beta_i) E]}$$

Ising Model
d=2 16×16

Fig. 1

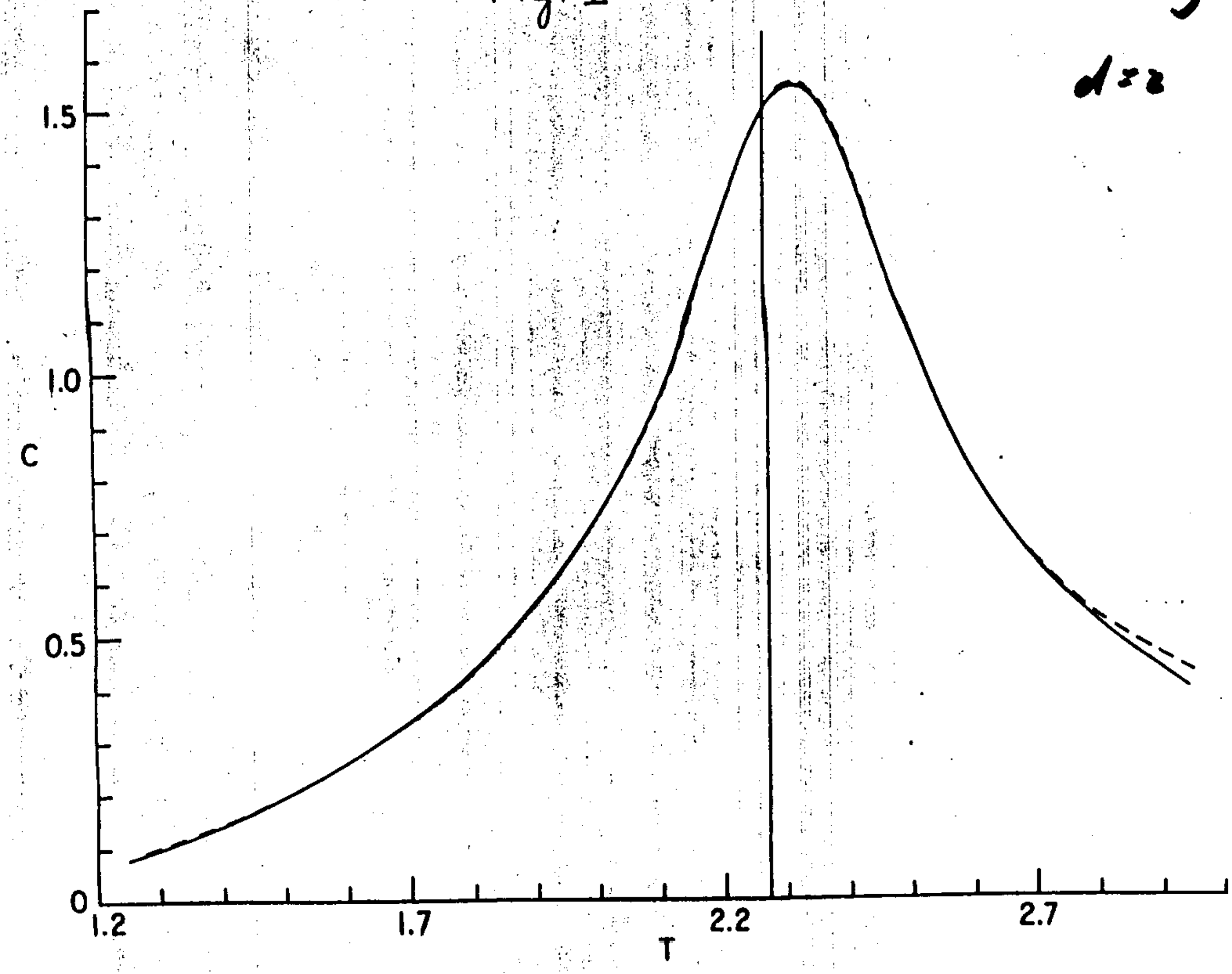
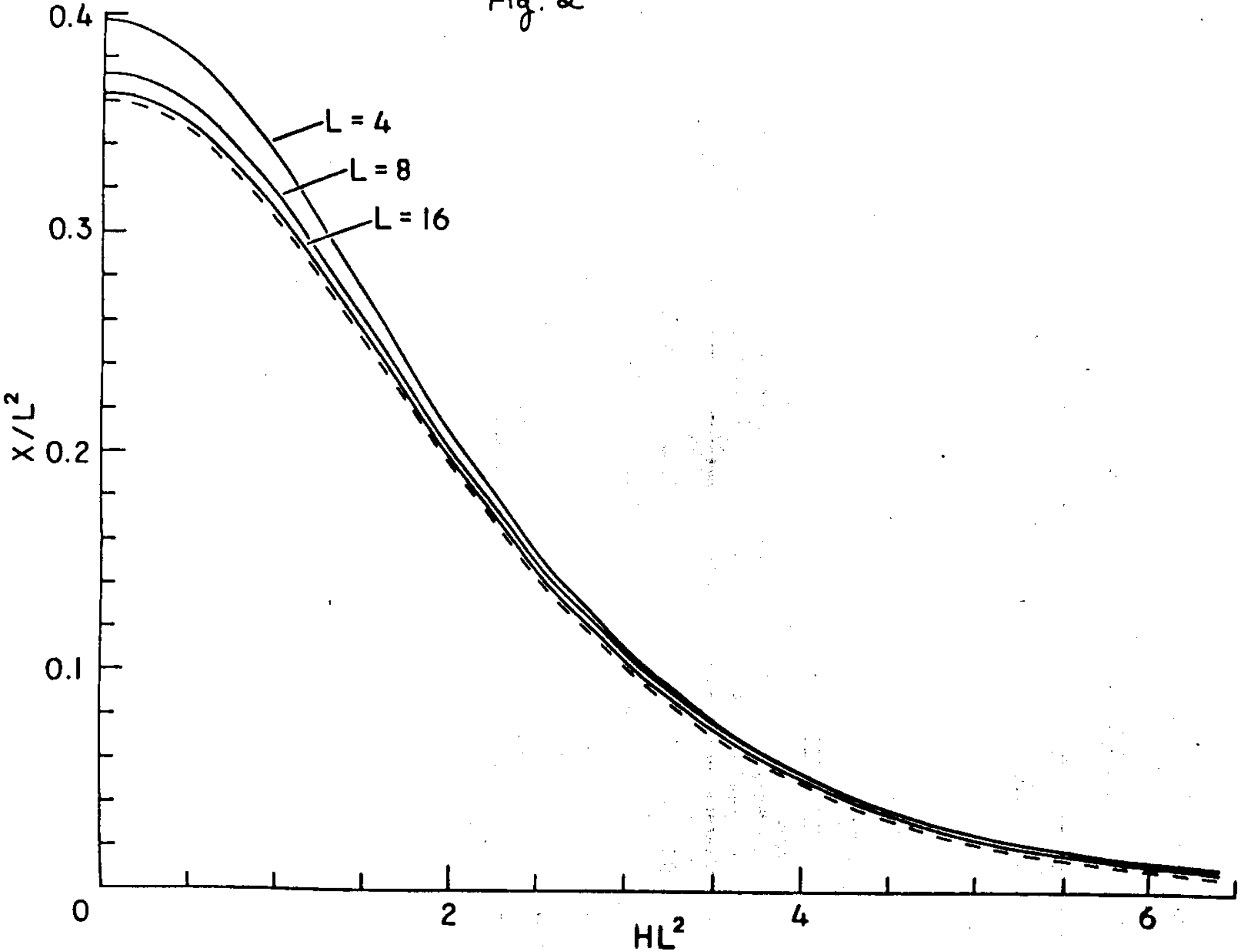


Fig. 2



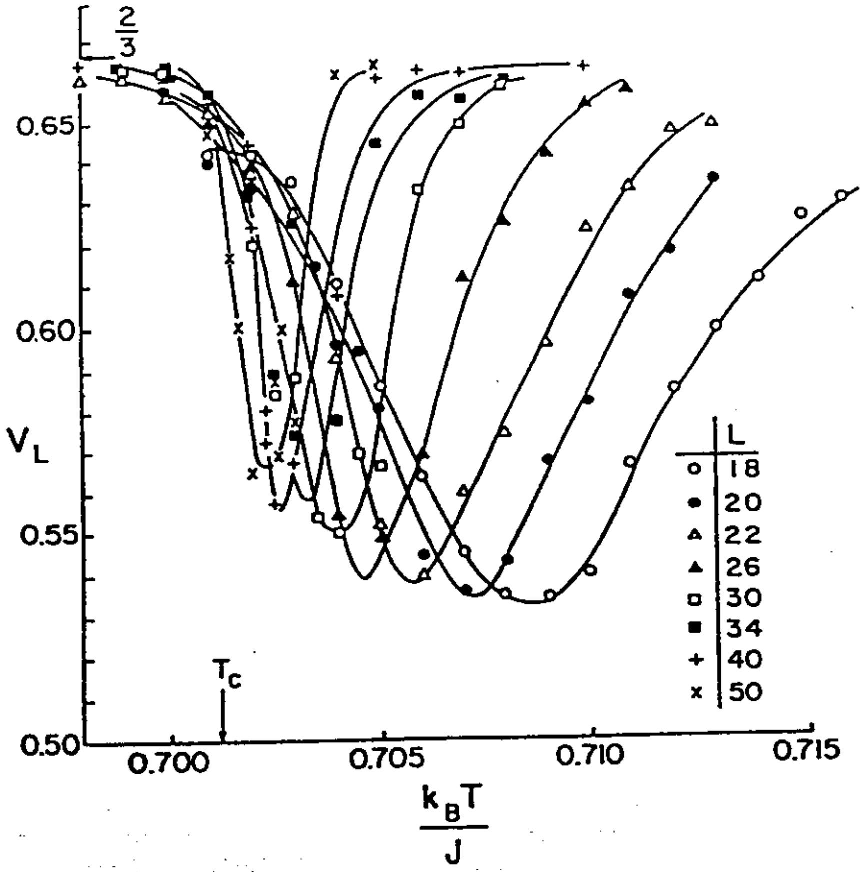


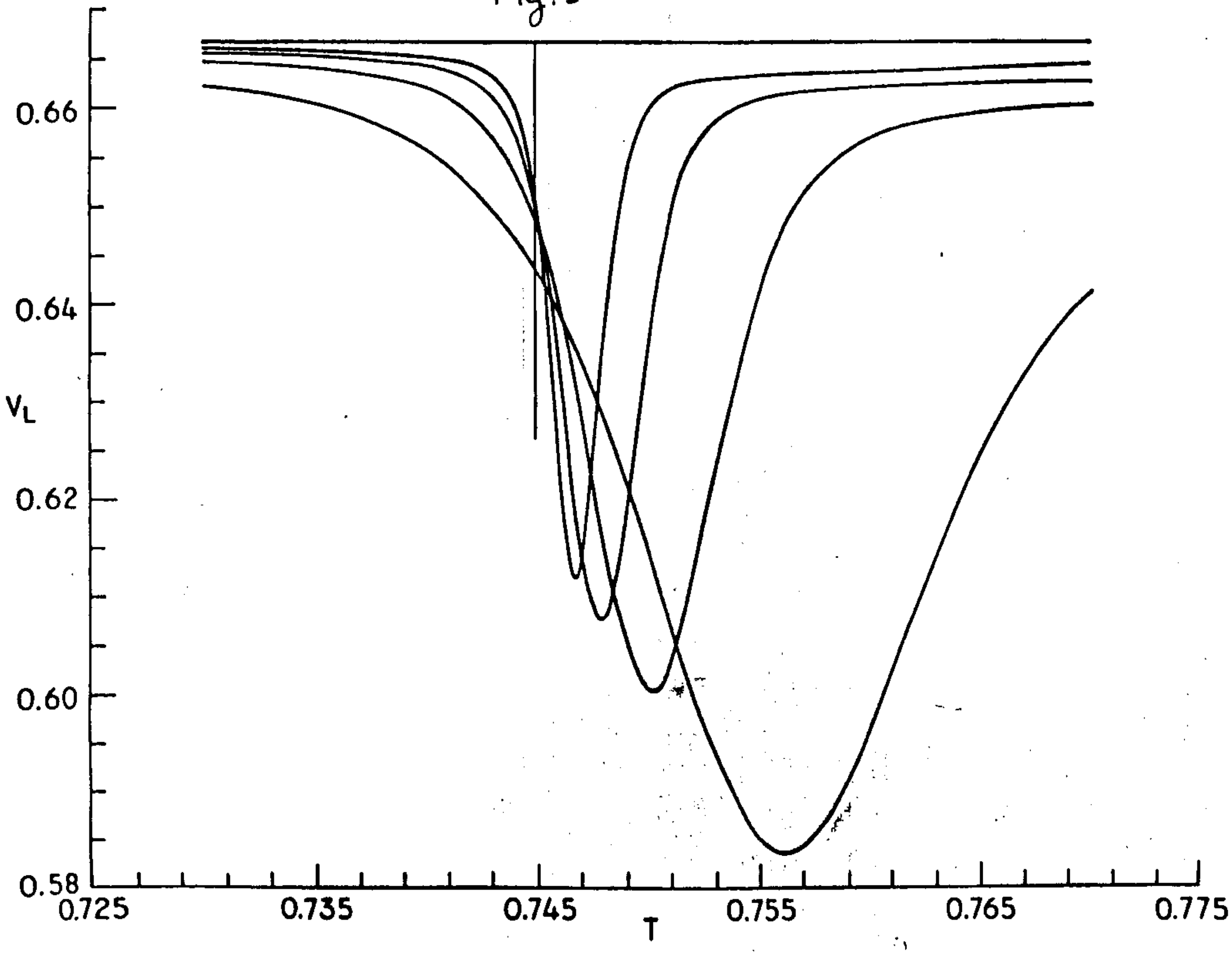
Fig. 1.4. Temperature variation of V_L, Eq. (1.11), of the two-dimensional 10-state Potts model for various lattice sizes. The transition temperature T_c and the trivial limit (2/3) for $V_L \to \infty$ are indicated. The nontrivial limit $[V_L|_{min} \to 0.559$, Eq. (1.18)] is consistent with the data. (From [1.48])

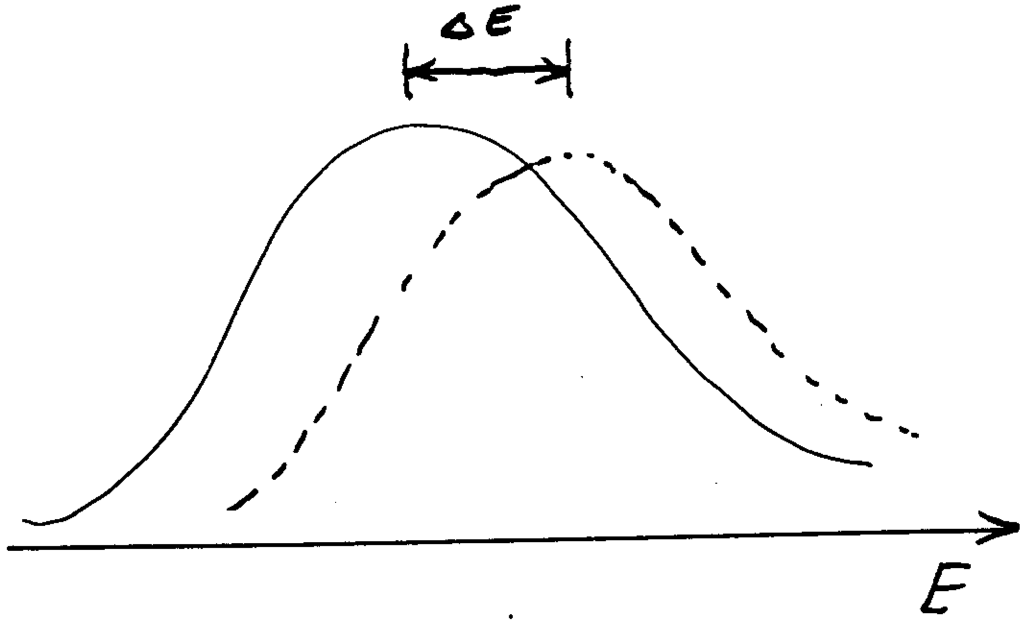
$$V_L = 1 - \frac{\langle E^4 \rangle_L}{3 \langle E^2 \rangle_L^2}$$

$$V_L^{min} \to \begin{cases} 2/3 & 2^{nd} \text{ order} \\ \frac{2}{3} - \frac{1}{3}\left(\frac{E_+^2 - E_-^2}{2E_+E_-}\right)^2 & 1^{st} \text{ order} \end{cases}$$

$q = 8$ [illegible]
$d = 2$

Fig. 3





$$\Delta E \approx \left[\langle (E - \langle E \rangle)^2 \rangle\right]^{\frac{1}{2}} = \left[L^d C \right]^{\frac{1}{2}}$$

$$\Delta E = \frac{\partial E}{\partial K} \Delta K = L^d C \, \Delta K$$

$$\Delta K \approx L^{-d/2} \, C^{-\frac{1}{2}}$$

At K_c $\quad C \sim L^{\alpha/\nu}$

$$\Delta K \sim L^{-\frac{1}{2}(d+\alpha/\nu)} = L^{-1/\nu} = L^{-y_t}$$

$\alpha = 2 - d\nu$

$d + \alpha/\nu = 2/\nu$

General Ensembles

$$P(E) \sim W(E)\, f(E)$$

Boltzmann

$$f(E) = e^{-\beta E}$$

$\beta = 1/k_B T$

"Multicanonical"

Berg + Neuhaus

$$f(E) \sim 1/W(E)$$

$$\Rightarrow \quad P(E) \sim \text{constant}$$

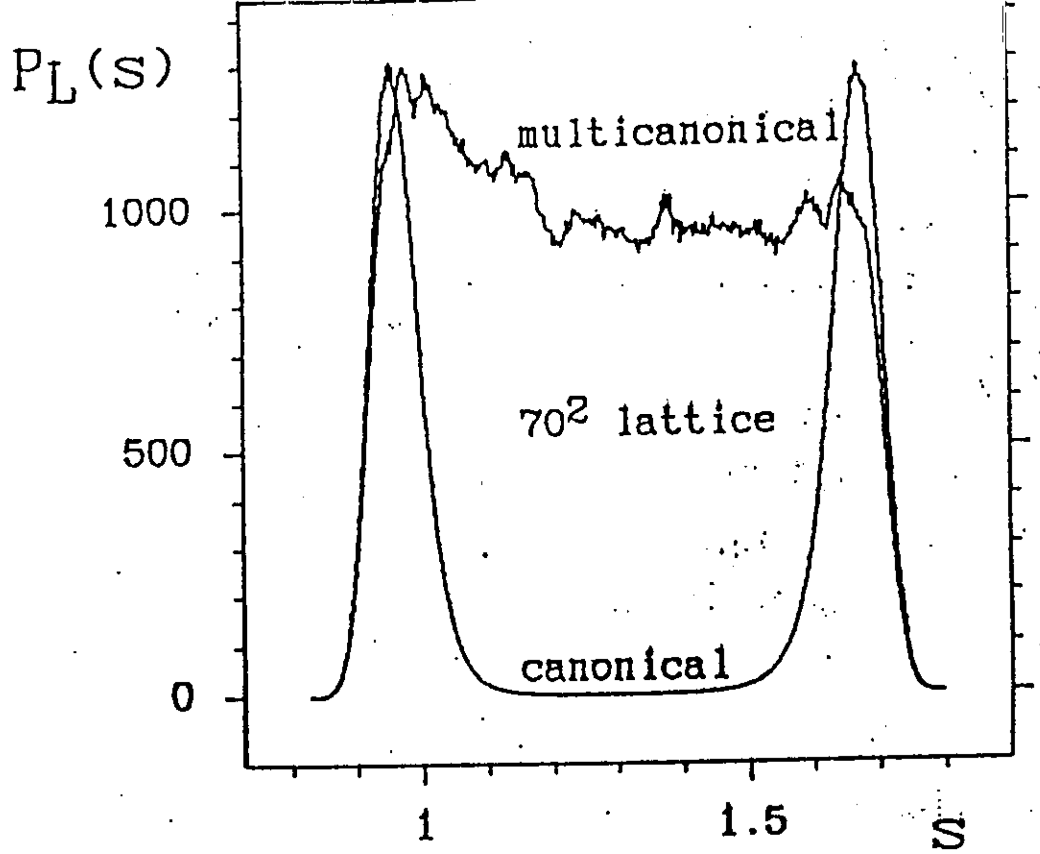
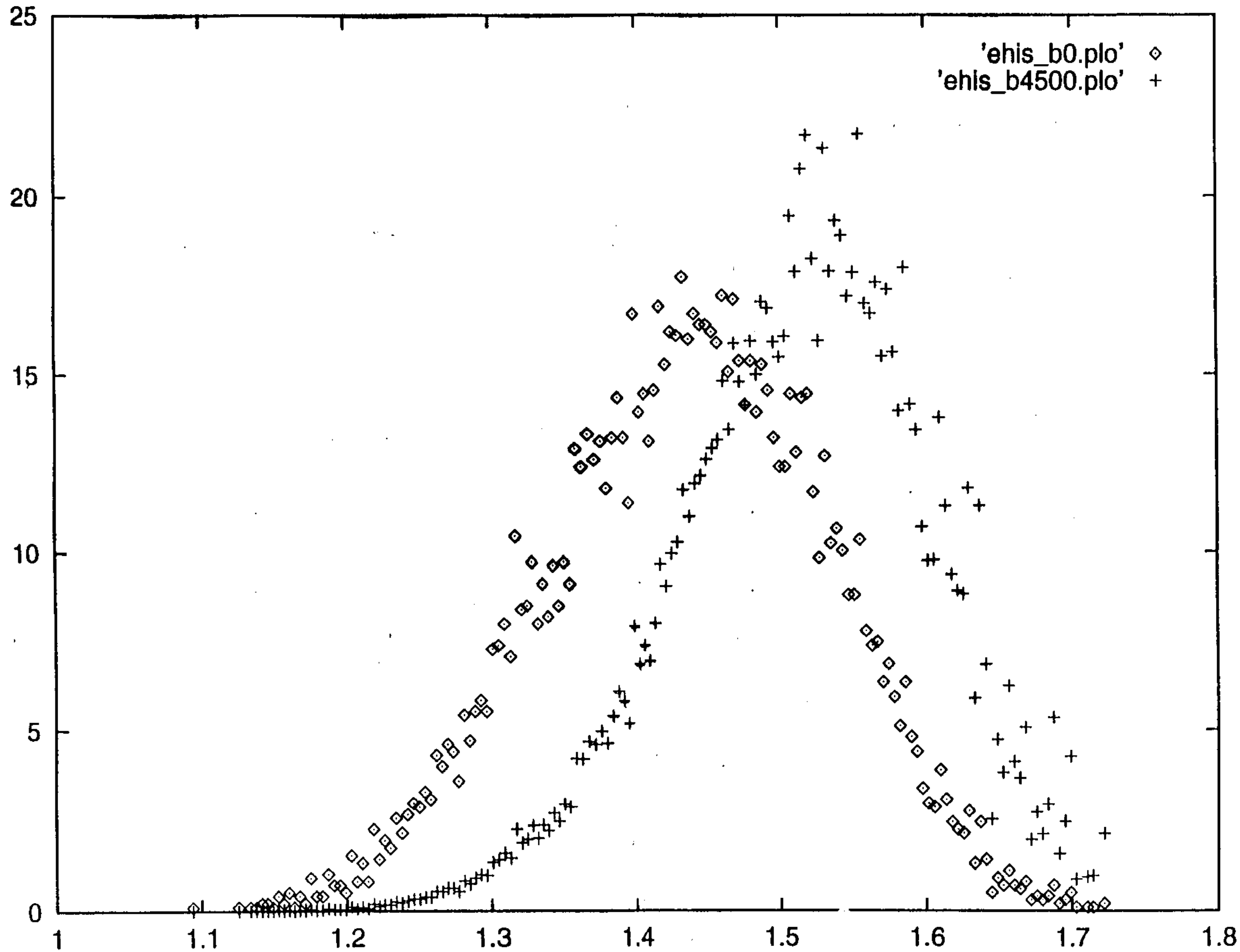


FIG. 2. Multicanonical action density distribution $\mathcal{P}_{70}(s)$ together with its reweighted distribution $P_{70}(s)$.

B. A. Berg and T. Neuhaus

Phys. Rev. Lett. 68, 9 (1992)


'ehis_b0.plo'
'ehis_b4500.plo'
25
20
15
10
5
0
1
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8

Multiple Histograms

$$W(E) = \sum_i p_i(E)\, n_i^{-1} N_i(E) \exp[\beta_i E - f_i]$$

$$f_i \equiv \beta_i F(\beta_i)$$

$$\sum_i p_i(E) = 1$$

Statistical error in $W(E)$

from statistical error in $\{N_i(E)\}$

Choose $\{p_i(E)\}$ to minimize error

Statistical Errors in Histograms

$N_i(E)$ independent of $N_j(E')$, $i \neq j$

Ferrenberg + Swendsen assume:

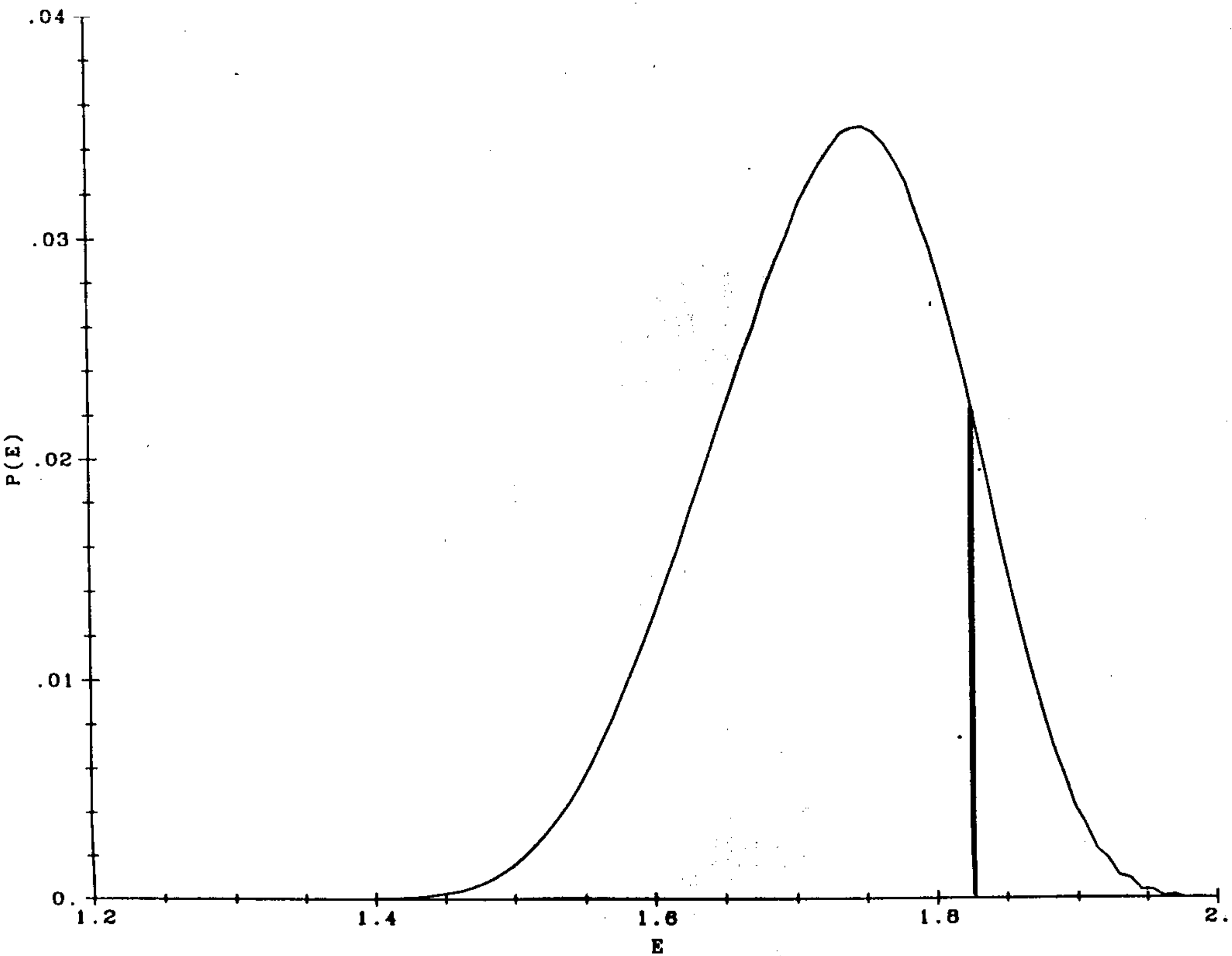
1) $N_i(E)$ independent of $N_i(E')$, $E \neq E'$

2) $\delta^2 N_i(E) = g_i \overline{N_i(E)}$

$$= g_i \, W(E) \, n_i \exp[-\beta_i E + f_i]$$

where $g_i = 1 + 2\tau_i$

16×16



Multiple Histogram Equations

$$W(E) = \frac{\sum_i g_i^{-1} N_i(E)}{\sum_j g_j^{-1} n_j \exp[-\beta_j E + f_j]}$$

$$e^{-f_i} = e^{-\beta_i F(\beta_i)} = \sum_E W(E)\, e^{-\beta_i E}$$

Error in density of states

$$\frac{\delta W(E)}{W(E)} = \left[\sum_i g_i^{-1} N_i(E)\right]^{-\frac{1}{2}}$$

Alternative treatment of error in $\{N_i(E)\}$

Huang, Moriarity, Myers, Potvin

Z. Phys. C **50**, 221 (1991)

used $\qquad \delta^2 N_i(E) = g_i N_i(E)$

instead of

5) $\qquad \delta^2 N_i(E) = g_i W(E) n_i \exp[-\beta_i E + f_i]$

$N_i(E) = 0$ required special treatment

Using $W(E)$ includes information from all histograms

Alternative treatment of error in $\{N_i(E)\}$

Alves, Berg, Villanova, PRB 41, 383 ('90)

64 replicas at each temperature

$\Rightarrow$ correct error for $\delta N_i(E)$

(very nearly $\delta^2 N_i(E) = N_i(E)$)

But ignored correlations between $N_i(E)$ and $N_i(E')$

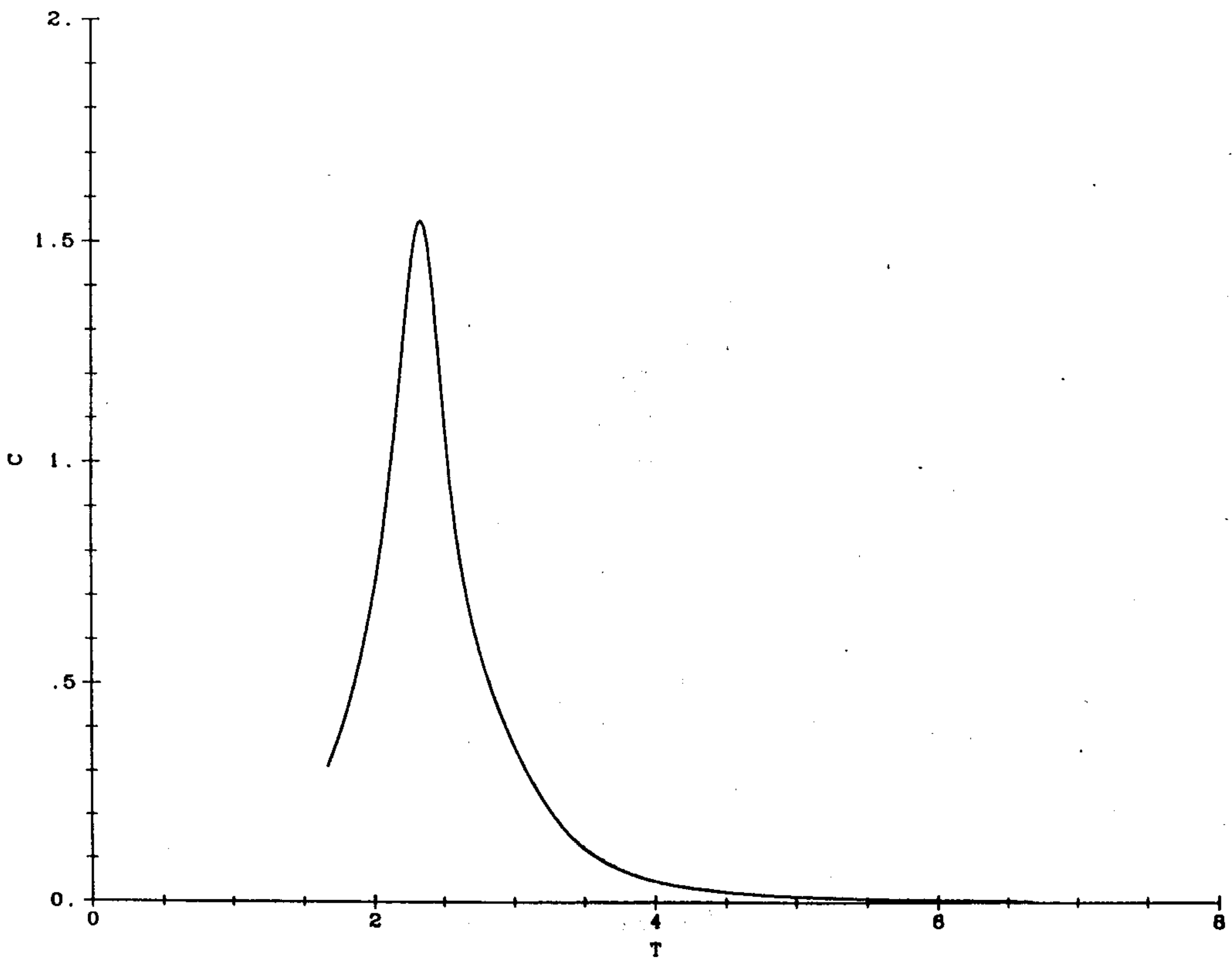
$\Rightarrow$ Total error underestimated

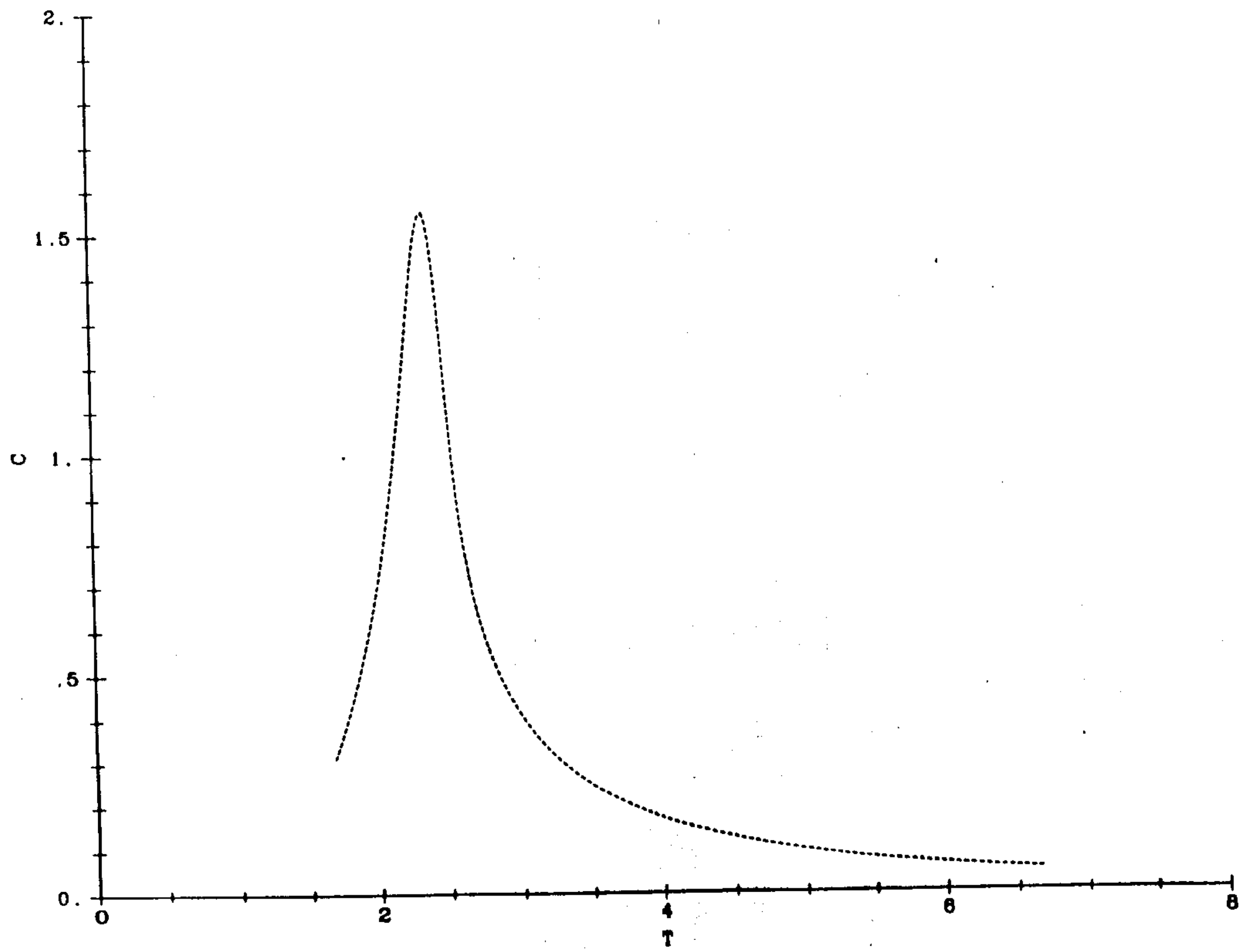
Different way of combining histograms

f_i's determined separately for each E

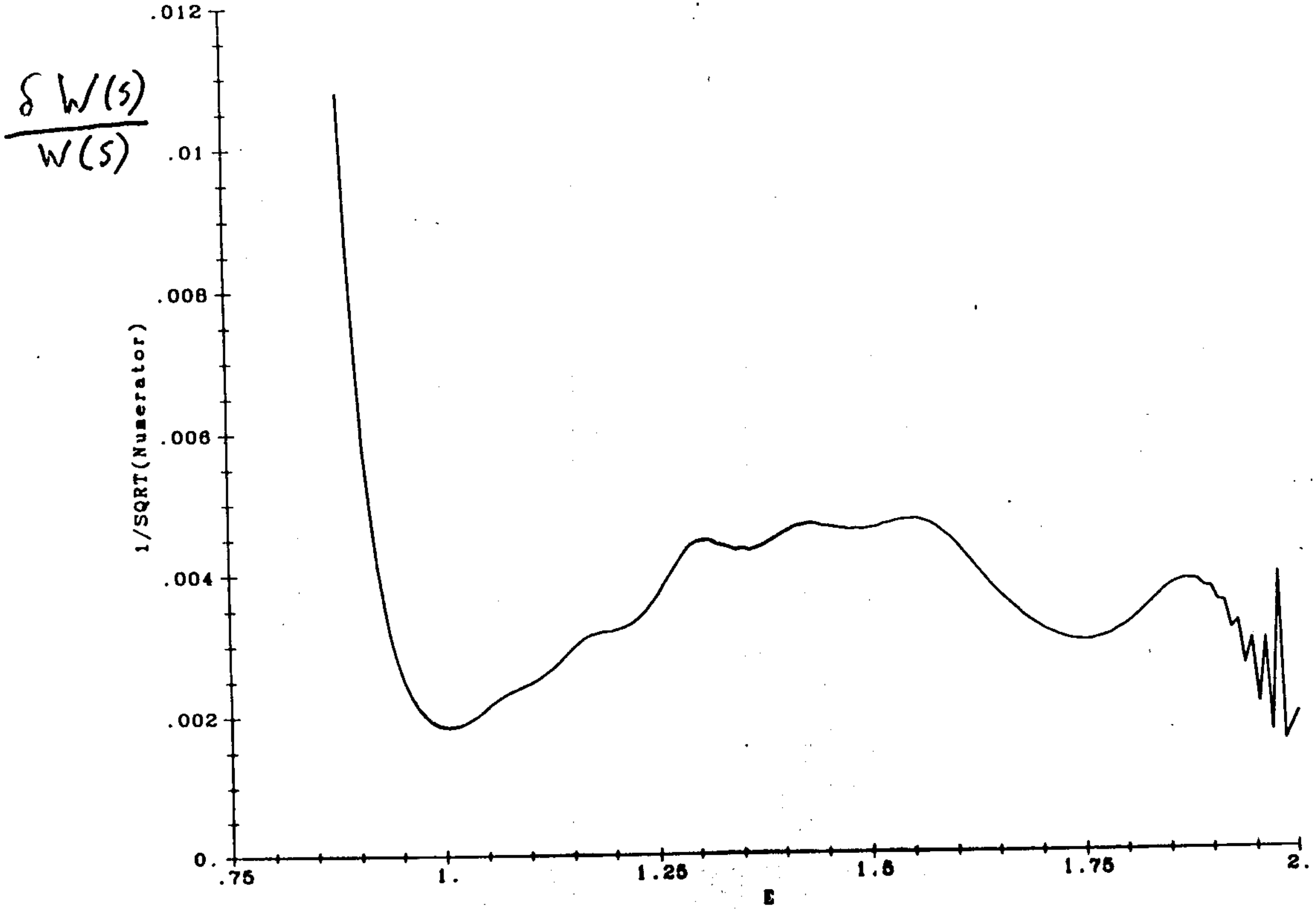
(not self consistently)

$\{K_\ell\} = \{K_c\}$



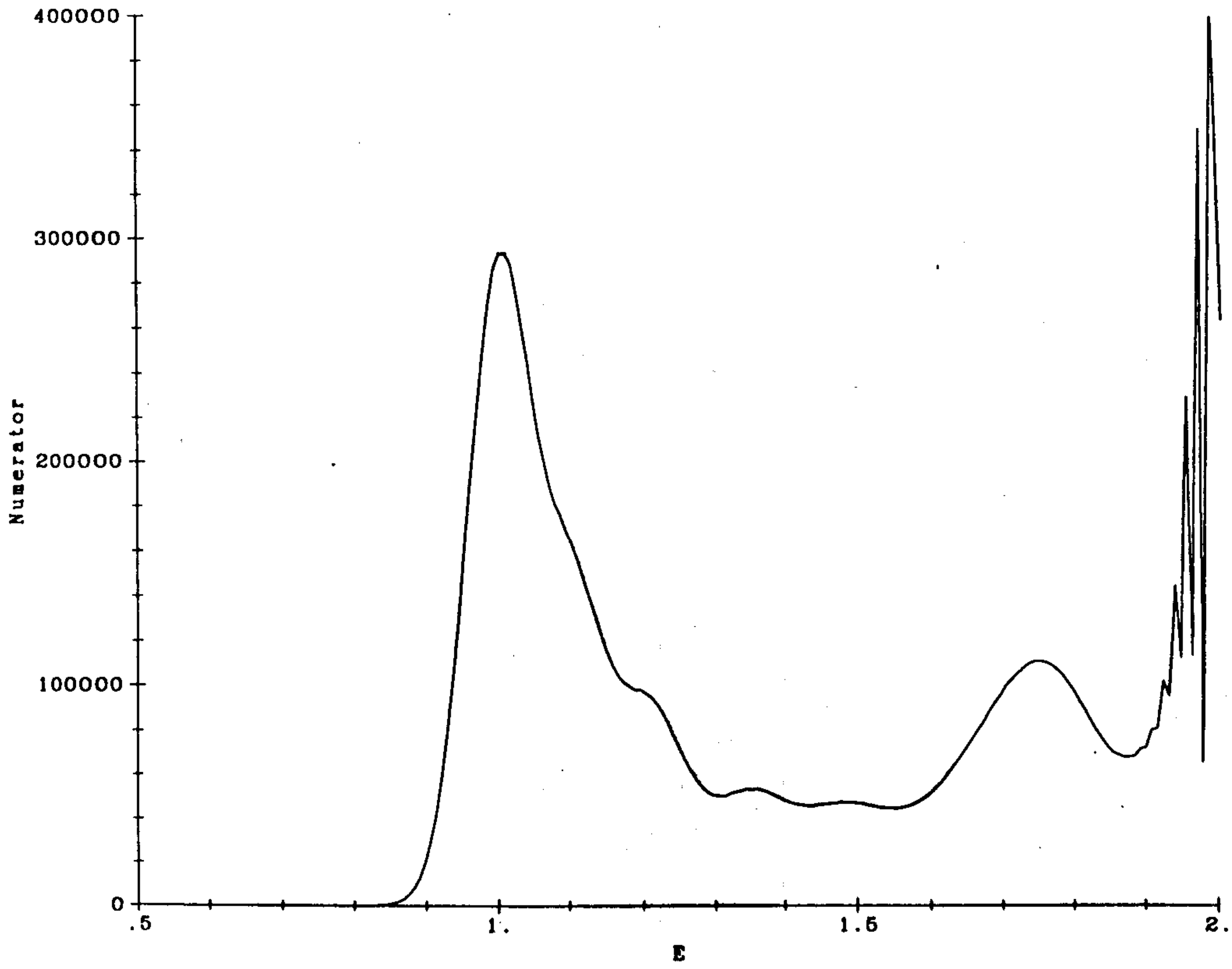


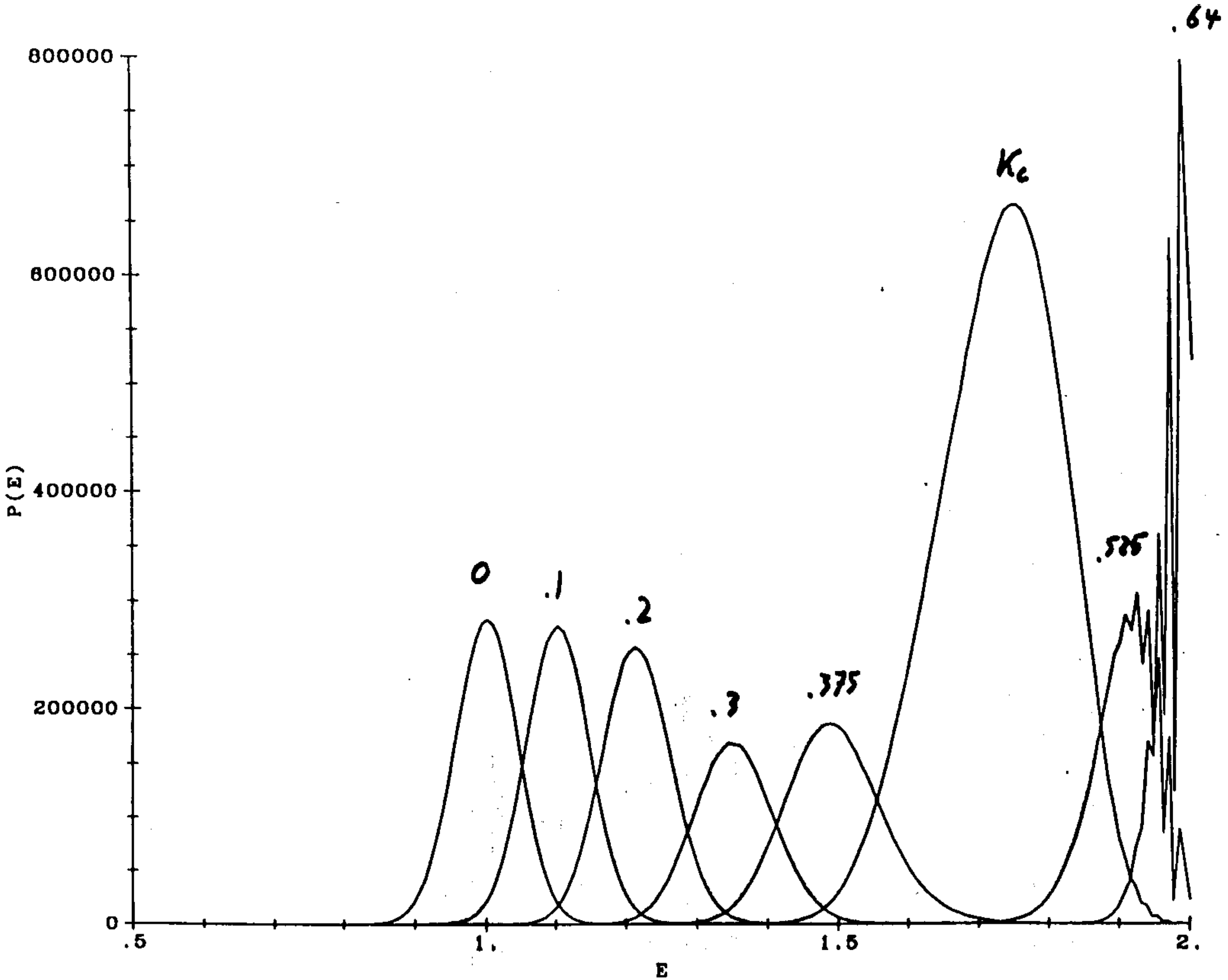
EXACT



$\frac{\delta W(s)}{W(s)}$
1/SQRT(Numerator)
.012
.01
.008
.006
.004
.002
0.
.75
1.
1.25
1.5
1.75
2.
E

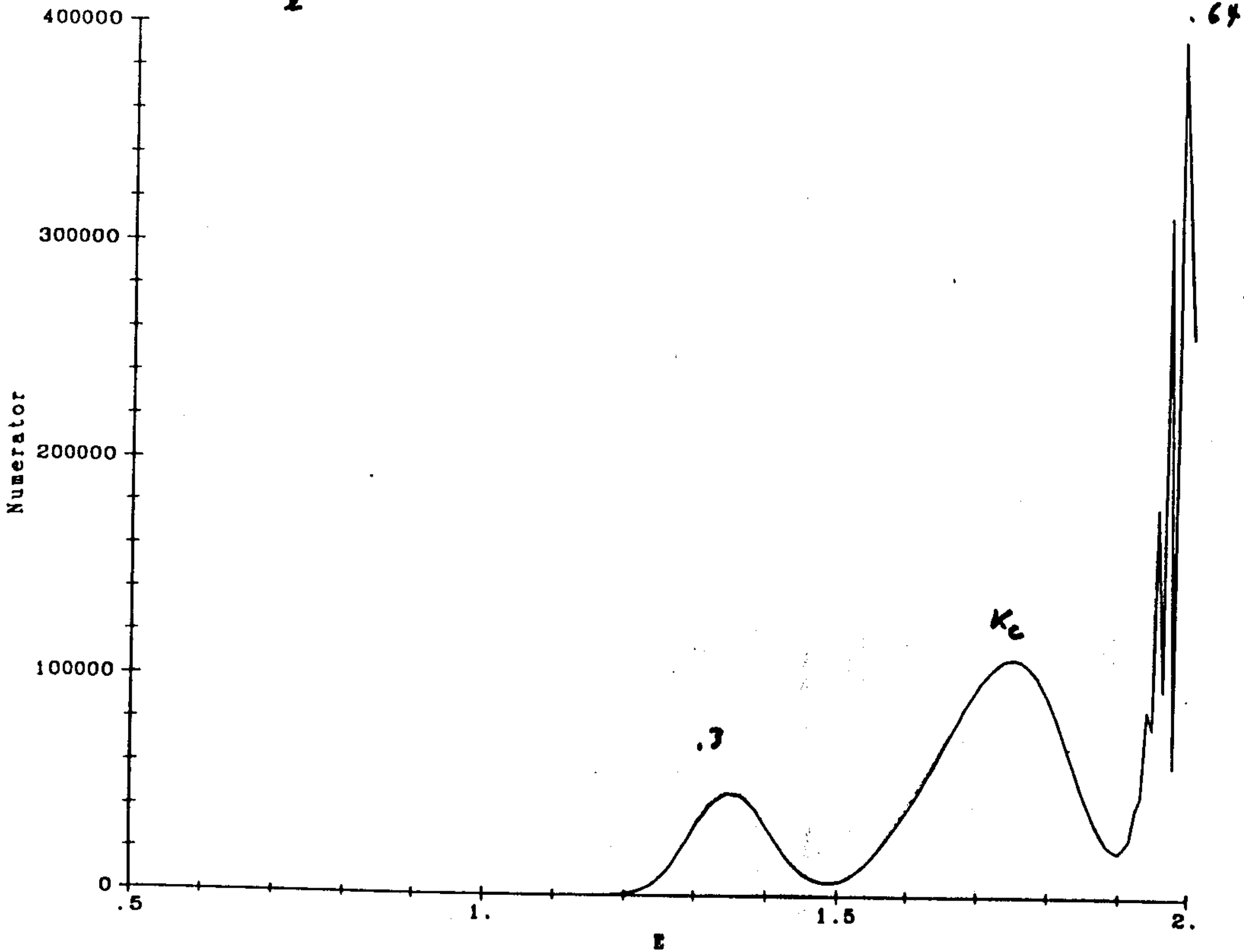
$$\sum_{\ell=1}^{8} g_\ell^{-1} H_\ell(s)$$

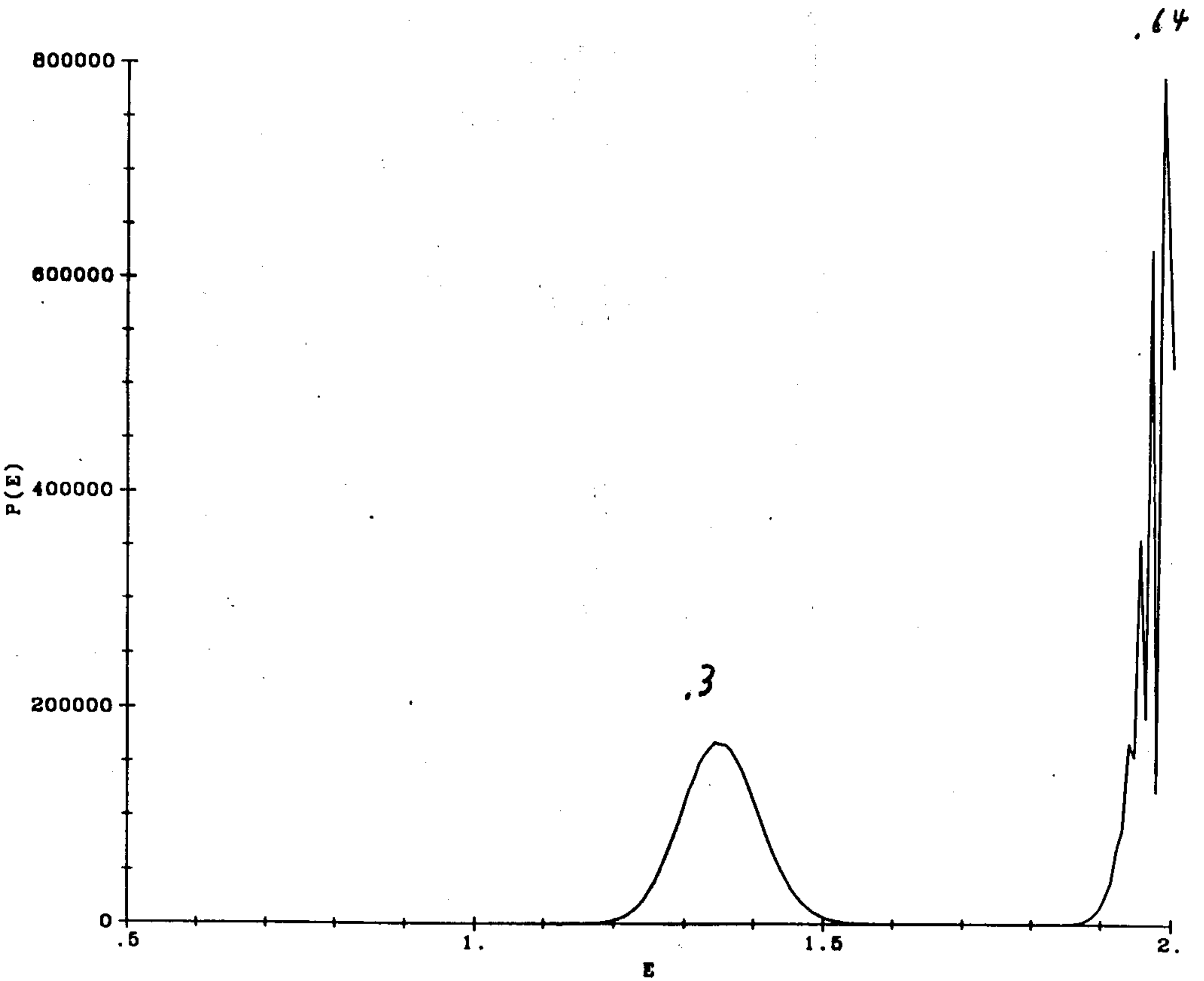




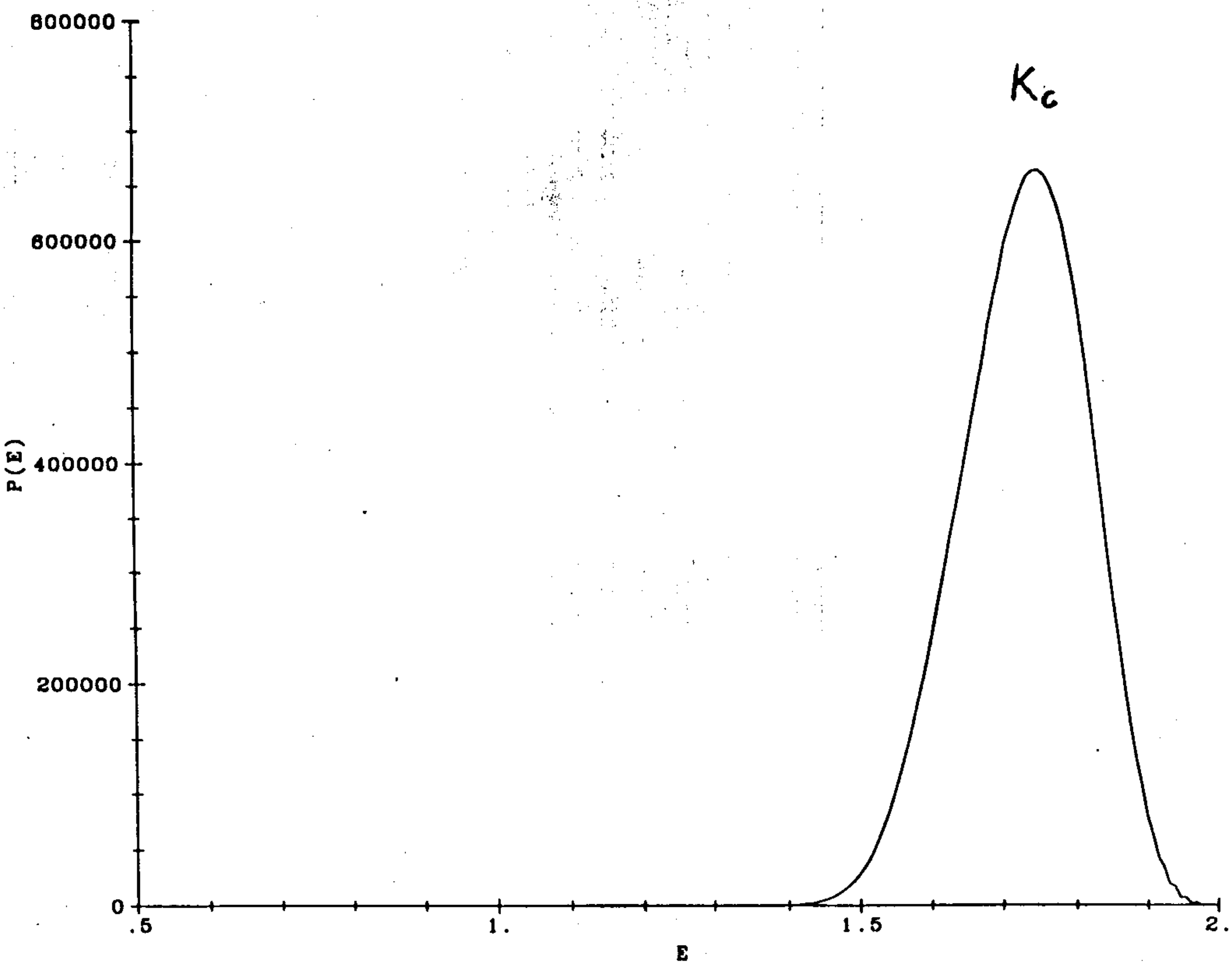
P(E)
800000
600000
400000
200000
0
.5
1.
1.5
2.
E
0
.1
.2
.3
.375
K_c
.525
.64

$\sum_{l} g_l^{-1} H_l(s)$



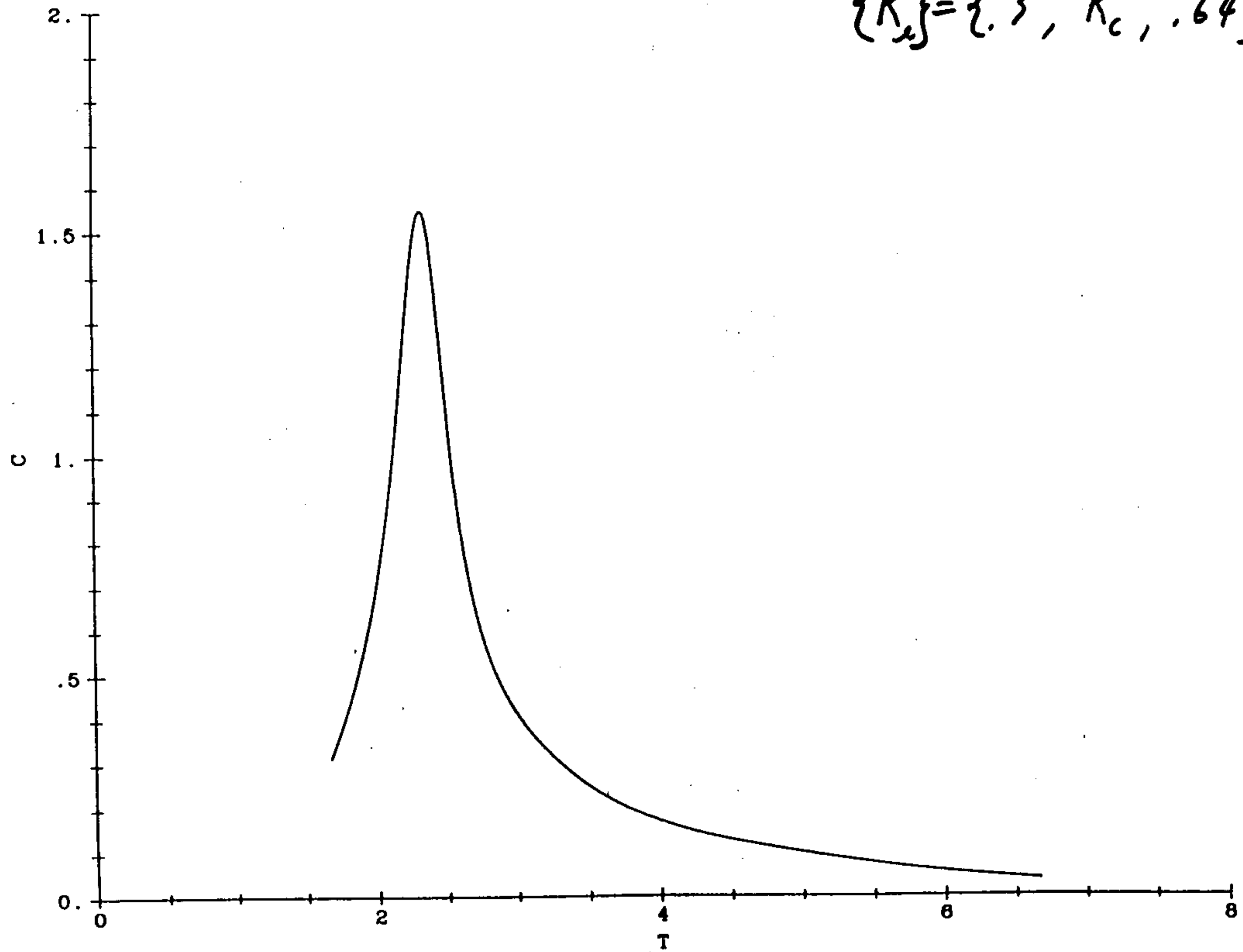


2

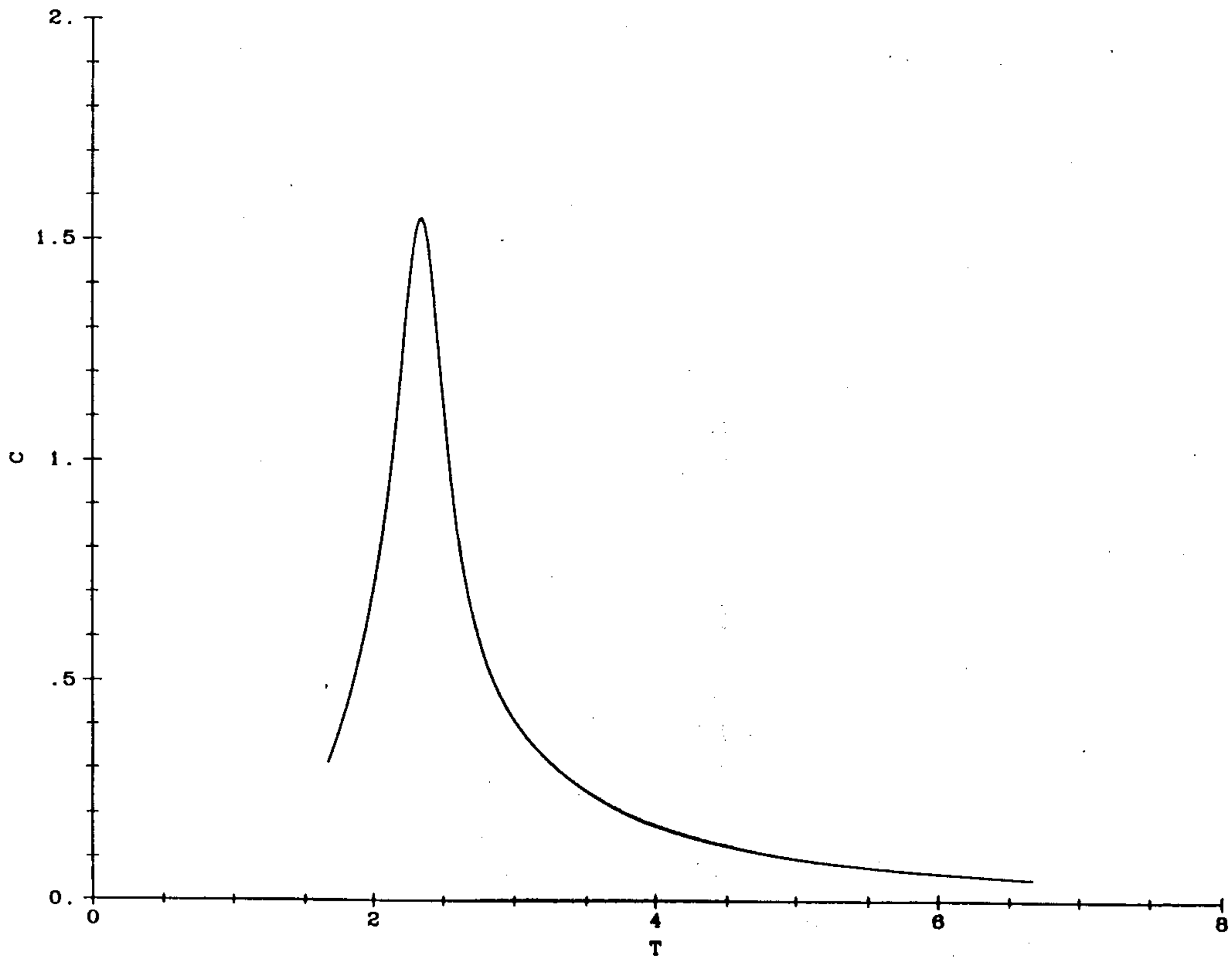


Kc
800000
600000
400000
200000
0
P(E)
.5
1.
1.5
2.
E

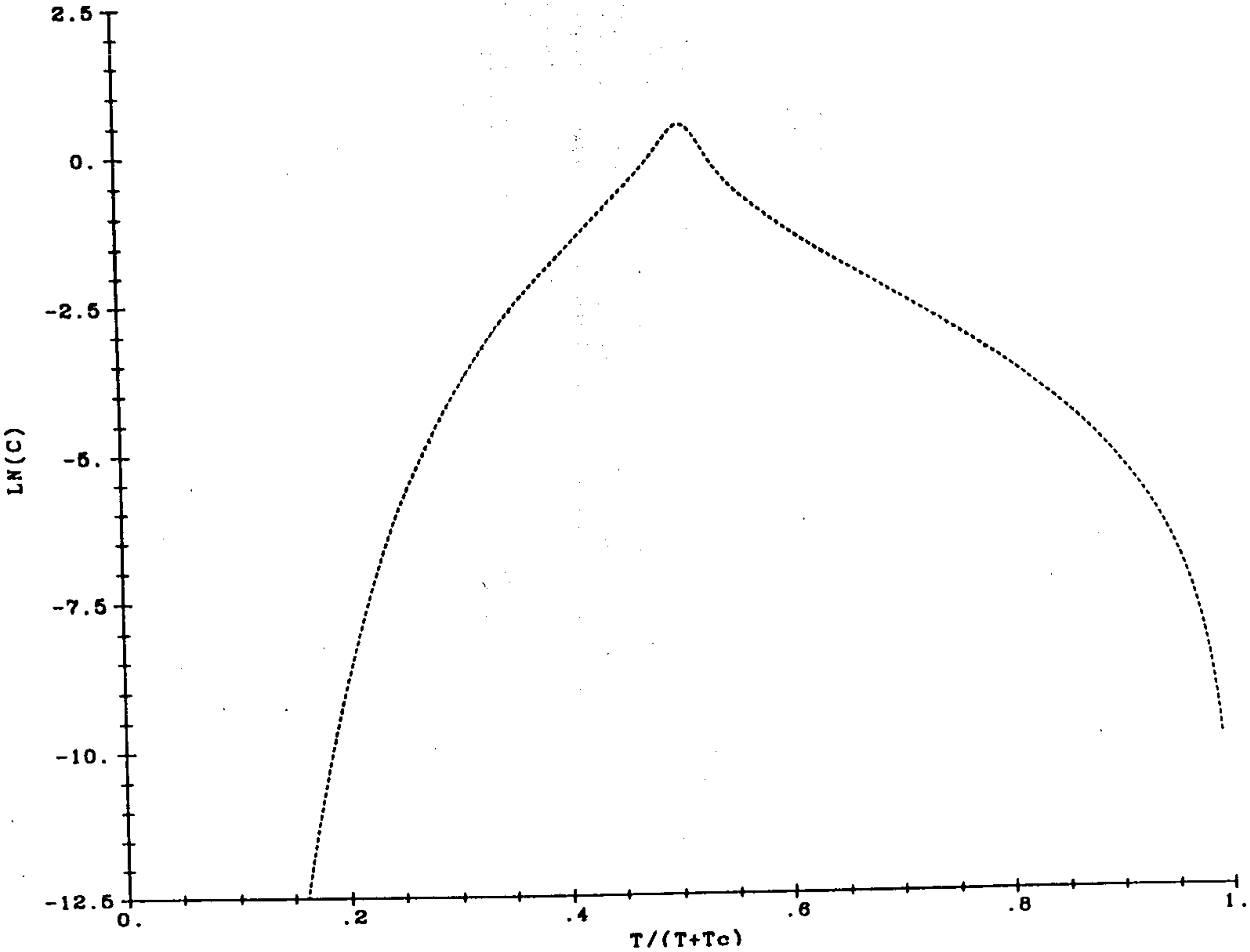
$\{K_i\} = \{.3,\ K_c,\ .64\}$



$\{K_\ell \mid \ell = 1,\dots 8\}$

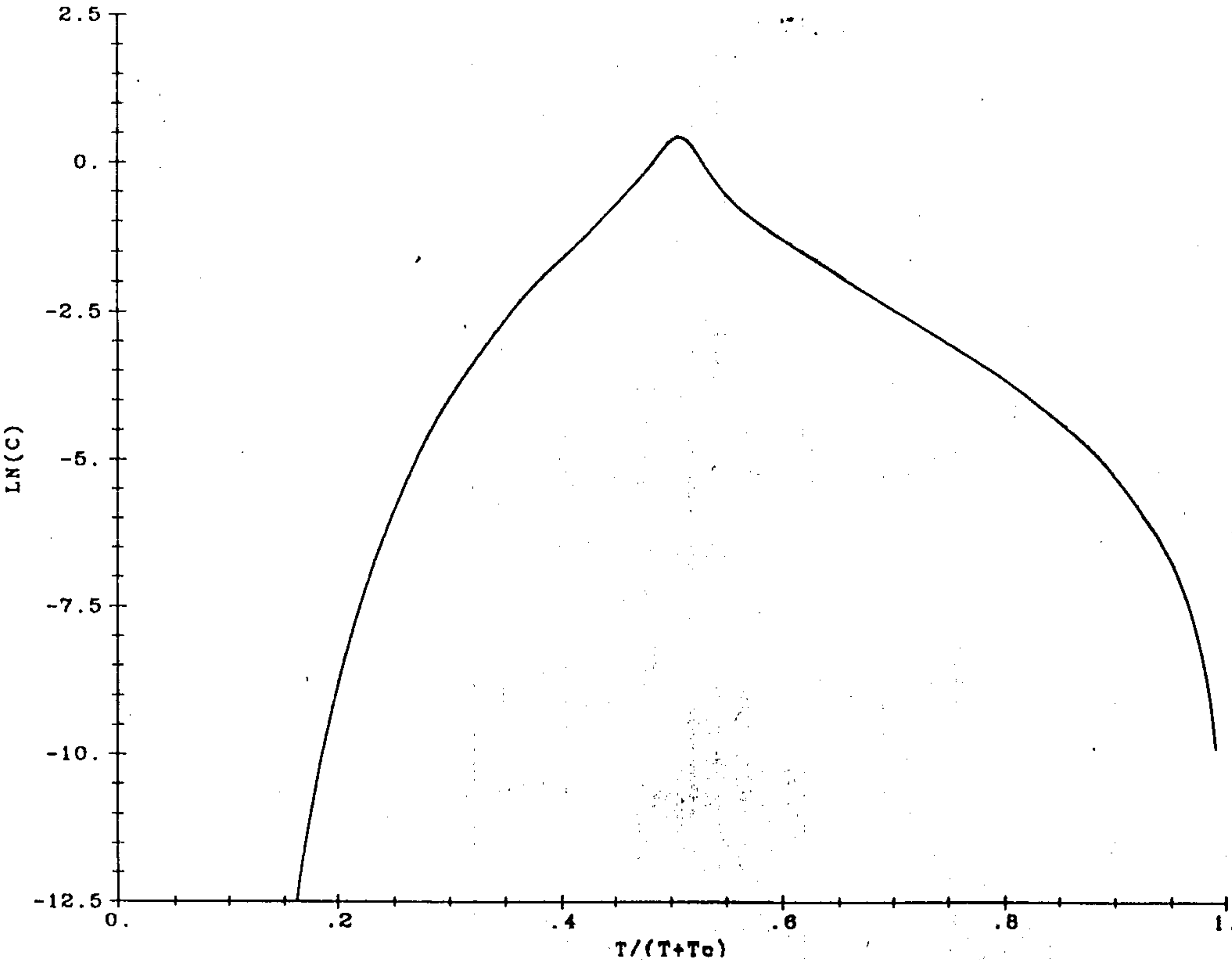


9

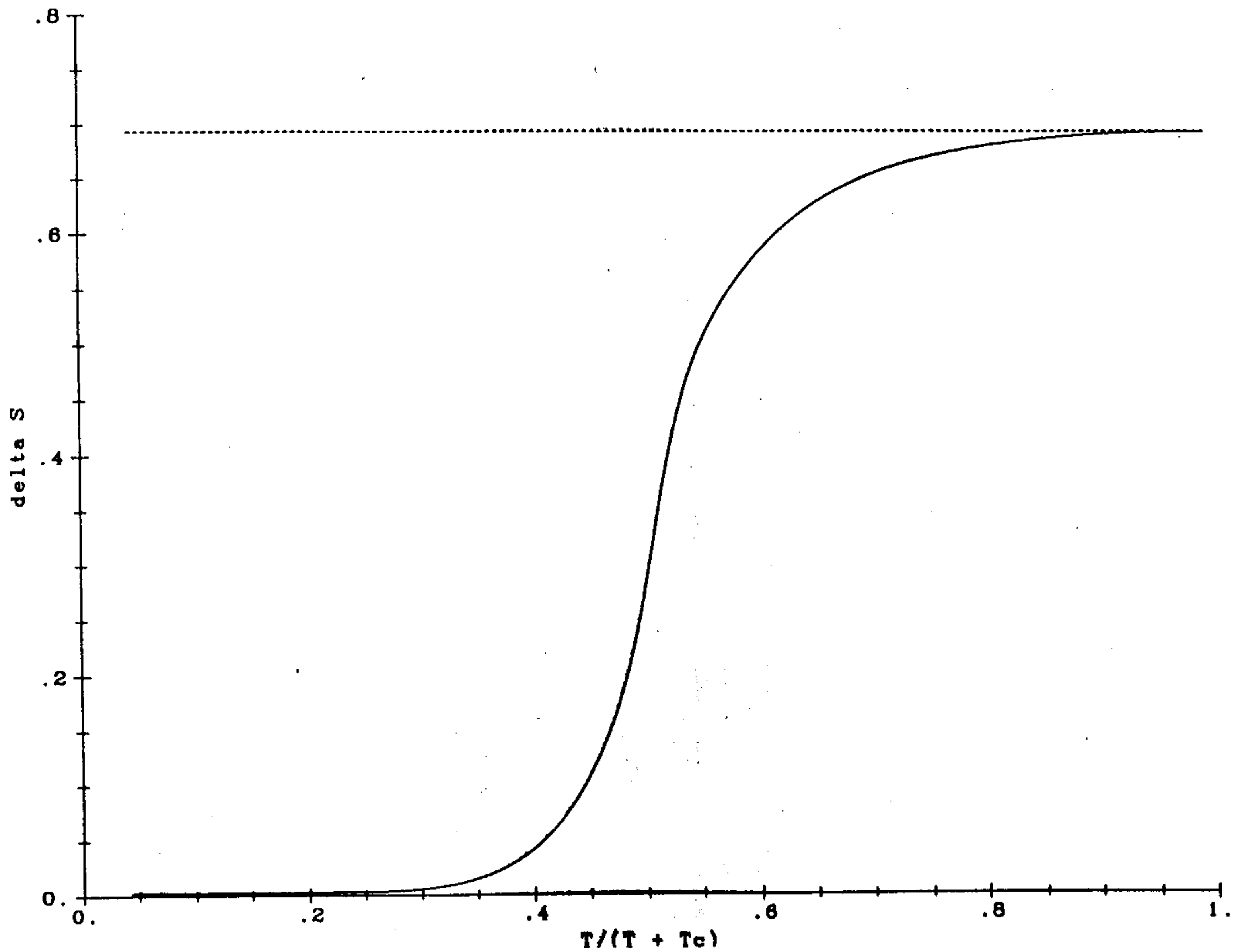


10

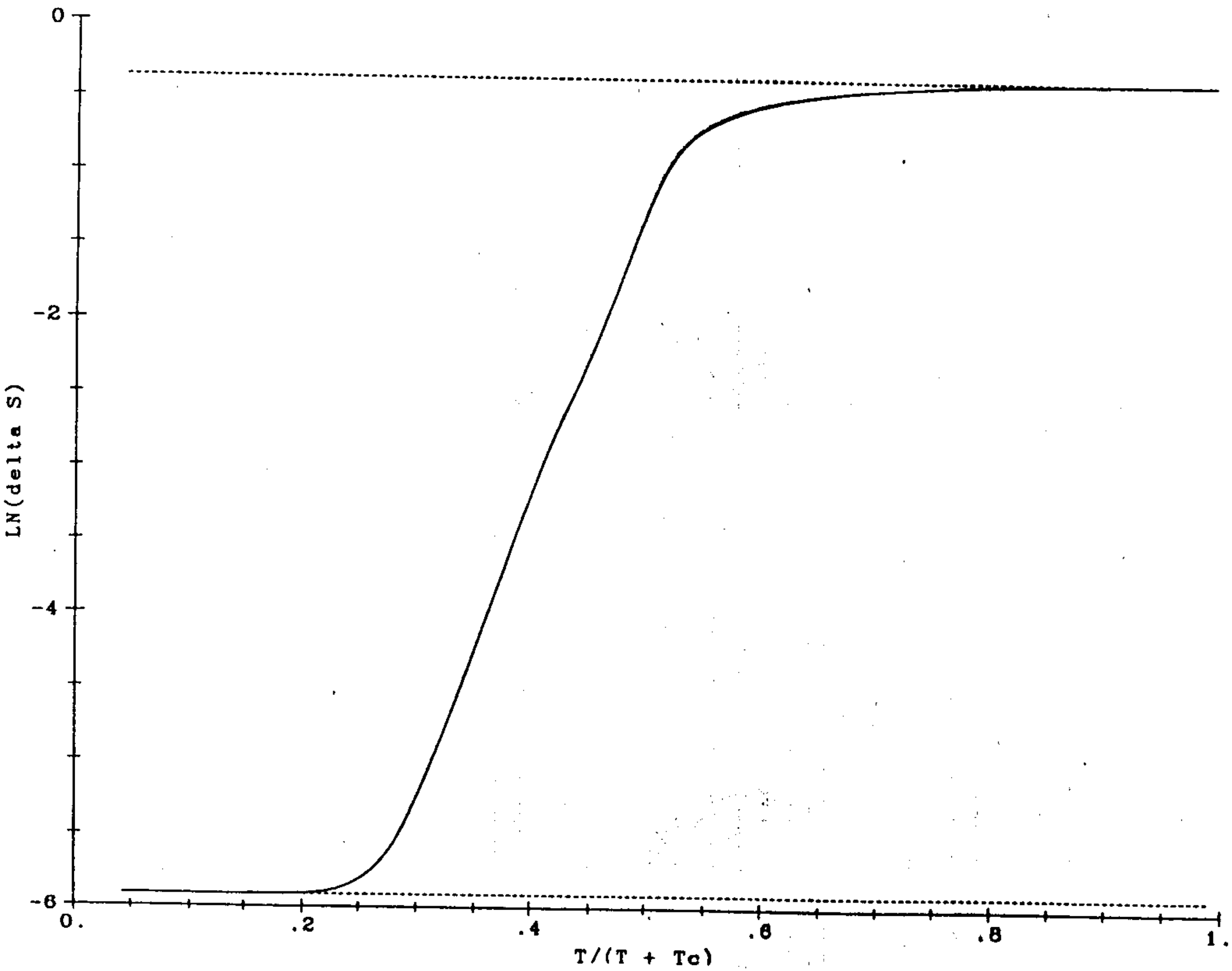
EXACT



2.5
0.
-2.5
-5.
-7.5
-10.
-12.5
LN(C)
0.
.2
.4
.6
.8
1.
T/(T+Tc)



/2



0
-2
-4
-6
LN(delta S)
0.
.2
.4
.6
.8
1.
T/(T + Tc)

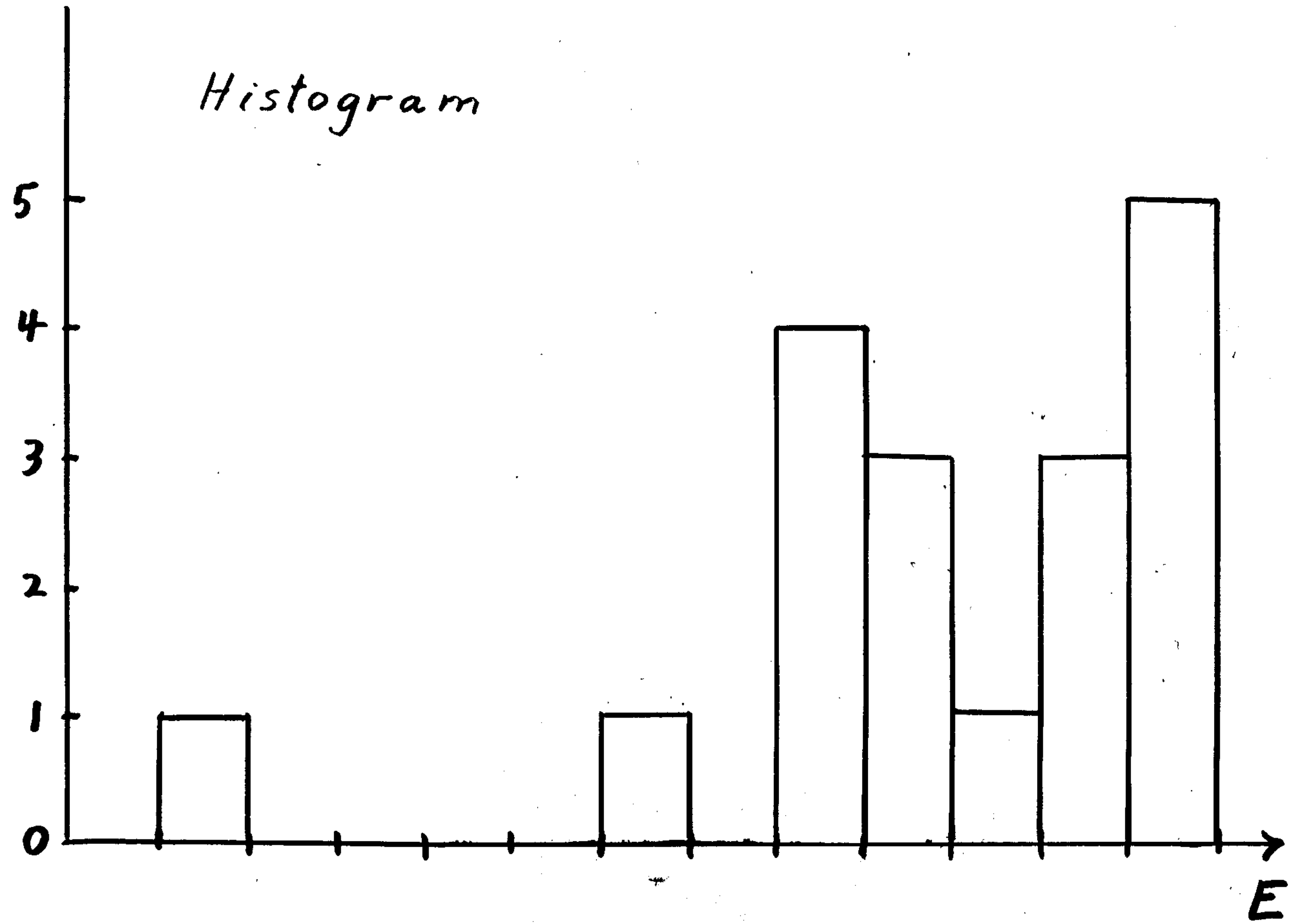
DEFINITION(S) OF PROBABILITY

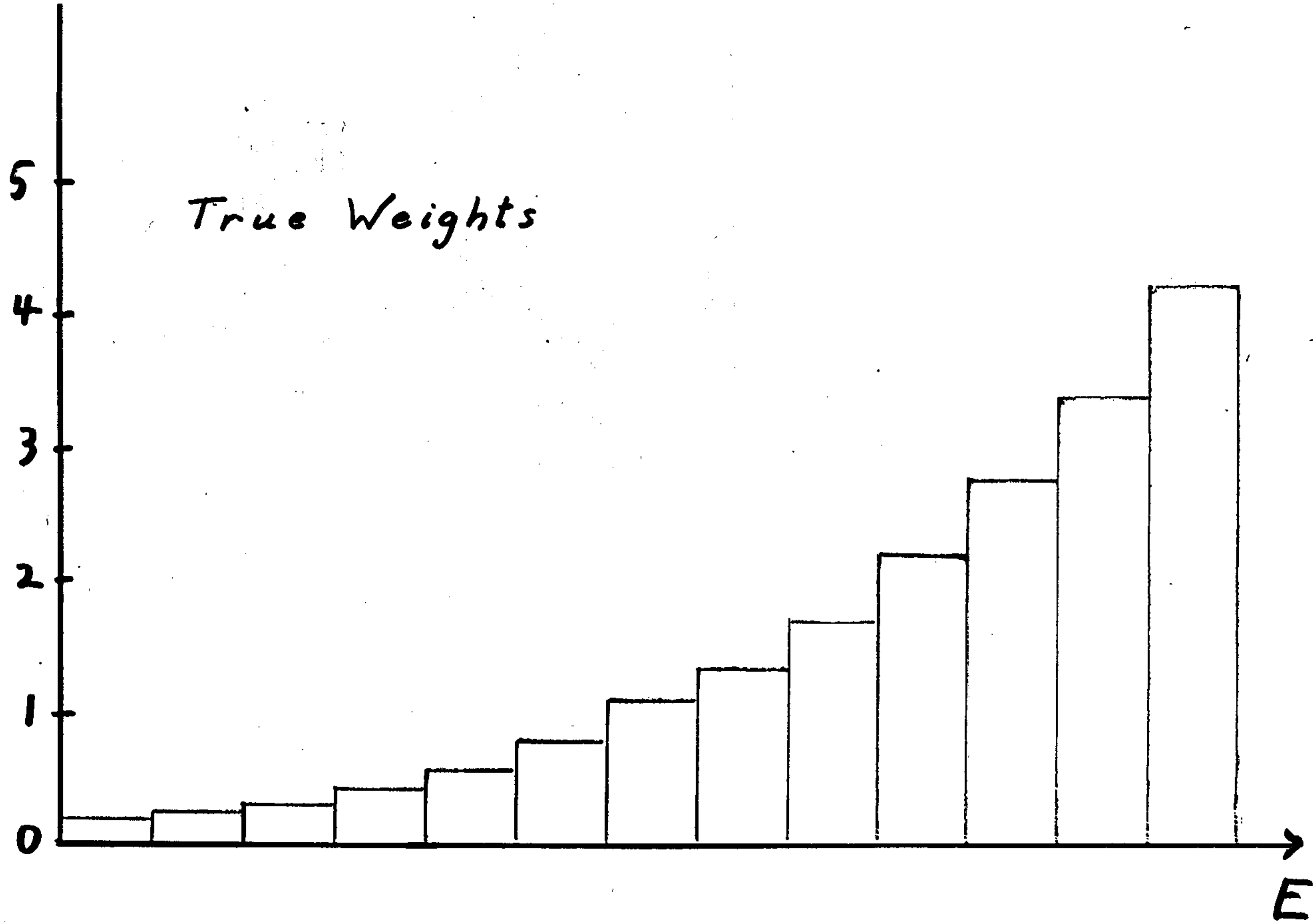
Frequentist

Ratio of "successes" to trials in the limit of an infinite number of trials

Bayesian

A description of your knowledge of the result of a trial


Histogram
5
4
3
2
1
0
E


True Weights
0
1
2
3
4
5
E

Bayes' Theorem

$$P(\theta|X) = \frac{P(X|\theta)\ P(\theta)}{P(X)}$$

Interpretation:

X - experimental results

θ - theoretical parameters

$P(\theta)$ prior knowledge

$P(\theta|X)$ is what we know about θ from both our prior knowledge and the experimental results

n independent trials

θ = probability of success

$$P(k|\theta) = \binom{n}{k} \theta^k (1-\theta)^{n-k}$$

If we observe k successes,

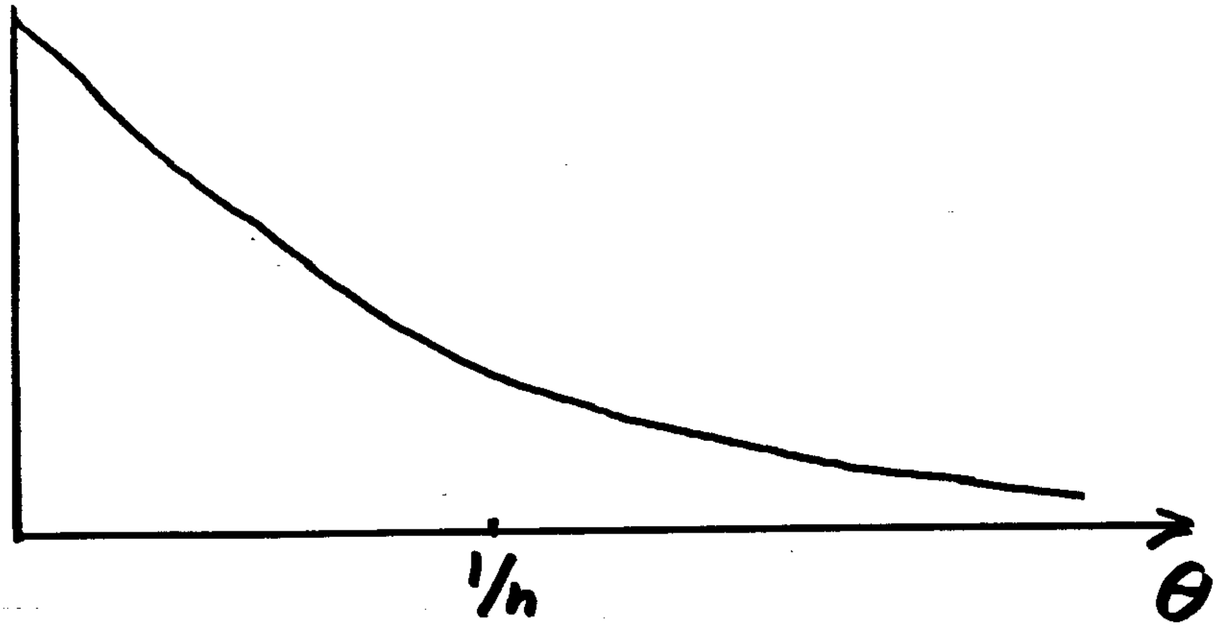
what do we know about θ?

RIOR: **Assume** $P(\theta) = 1$ for $\theta \in [0,1]$

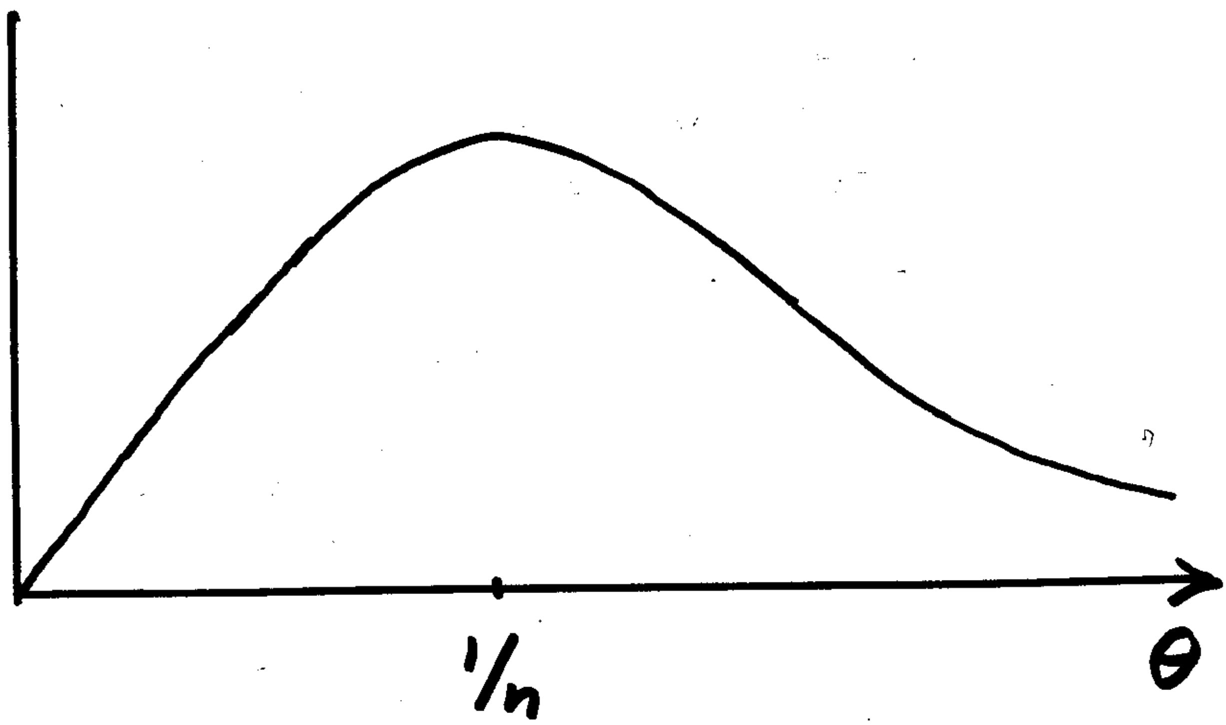
AYES: $P(\theta|k) \sim P(k|\theta)\, P(\theta)$

$$P(\theta|k) \sim \theta^k (1-\theta)^{n-k}$$

$P(\theta \mid k=0)$



$P(\theta \mid k=1)$



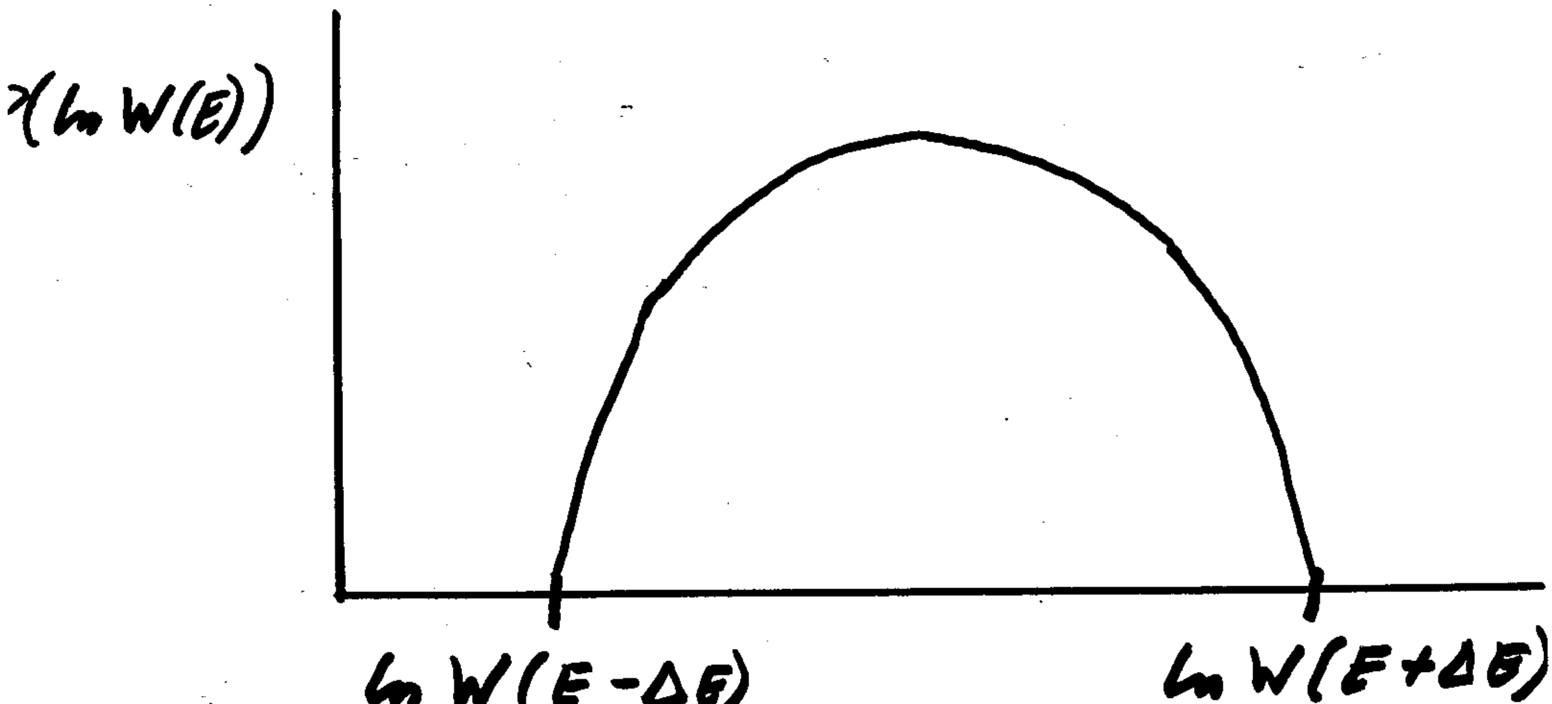
"Smoothness" of $W(E)$

$$W(E-\Delta E) < W(E) < W(E+\Delta E)$$

In critical region

$$\ln W(E) \sim \frac{1}{2}\left[\ln W(E-\Delta E) + \ln W(E+\Delta E)\right]$$

Can express this as a "prior" factor



Produces estimates for $W(E)$ that are qualitatively correct

Transition Matrix Monte Carlo

Shing-Te Li
Brian Diggs
J. Kadane
C. Genovese

"Broad histogram method"

P.M.C. de Oliveira

T.J.P. Penna

H.J. Herrmann

Brazilian Journal of Physics

<u>26</u>, 677 (1996)

Transition Matrix $\underline{T=\infty}$

$n_{\delta E}$ = number of spins that will change the energy by δE when $\sigma_i \to -\sigma_i$

$$T_{E,\delta E} \equiv \langle n_{\delta E} \rangle / N$$

$N = L^d$

gives the probability that the next spin flip will change the energy from E to $E + \delta E$

$$\sum_{\delta E} T_{E,\delta E} = 1$$

Finite Temperature

Transition Matrix

$$T^{\beta}_{E,\delta E} \begin{cases} N^{-1}\langle n_{\delta E}\rangle & [\delta E < 0] \\ N^{-1}\langle n_{\delta E}\rangle\, e^{-\beta\delta E} & [\delta E > 0] \\ N^{-1}\langle n_0\rangle + \sum\limits_{\delta E>0} N^{-1}\langle n_{\delta E}\rangle\left(1-e^{-\beta\delta E}\right) & [\delta E = 0] \end{cases}$$

$$\sum_{\delta E} T^{\beta}_{E,\delta E} = 1$$

Probability of move being rejected

$$R = \sum_{\delta E>0} \frac{\langle n_{\delta E}\rangle}{N}\left(1 - e^{-\beta\delta E}\right)$$

Density of States $\qquad W(E)$

Infinite temperature

$$\sum_{\delta E} T_{E-\delta E,\, \delta E} \; W(E-\delta E) = W(E)$$

Finite temperature

$$P_\beta(E) = \frac{1}{Z} W(E)\, e^{-\beta E}$$

$$\sum_{\delta E} T^{\beta}_{E-\delta E,\, \delta E} \; P_\beta(E-\delta E) = P_\beta(E)$$

The TTT Identity

Detailed balance: $W_1 T_{12} = W_2 T_{21}$

Transitions among three states:

$$W_1 T_{12} \; W_2 T_{23} \; W_3 T_{31} = W_1 T_{13} \; W_3 T_{32} \; W_2 T_{21}$$

$$\Rightarrow \quad T_{12} \, T_{23} \, T_{31} = T_{13} \, T_{32} \, T_{21}$$

$$T_{E-\Delta E, \Delta E} \; T_{E, \Delta E} \; T_{E+\Delta E, -2\Delta E} =$$
$$T_{E, +2\Delta E} \; T_{E+2\Delta E, -\Delta E} \; T_{E+\Delta E, -\Delta E}$$

where ΔE is the interval between energy levels

Transition Matrix

Combining data from simulations
at different temperatures
— or different ensembles —
is trivial

Used with cluster MC
histograms and transition matrix
give same accuracy

N-fold Way

For each configuration,

$$R = \sum_{\delta E > 0} \frac{n_{\delta E}}{N} \left(1 - e^{-\beta \delta E} \right)$$

is the probability of rejected moves

Rejected moves retain current state

$\Rightarrow$ weight current configuration with

$$(1-R)^{-1}$$

and make a δE spin flip with

$$\frac{n_{\delta E}}{N} (1-R)^{-1} \begin{cases} 1 & \delta E \leq 0 \\ e^{-\beta \delta E} & \delta E > 0 \end{cases}$$

Transition matrix with N-fold way

- Same accuracy as with cluster Monte Carlo

- Also works for models with frustration

Correlation time

given by second eigenvalue

$$\sum_{\delta E} T^{\beta}_{E-\delta E, \delta E} \, \phi_2^{\beta}(E-\delta E) = \lambda_2^{\beta} \, \phi_2^{\beta}(E)$$

$$\tau(\beta) = -1 / \ln \lambda \qquad [MCS]$$

Expect $\tau \sim L^z$ [MCS/S]

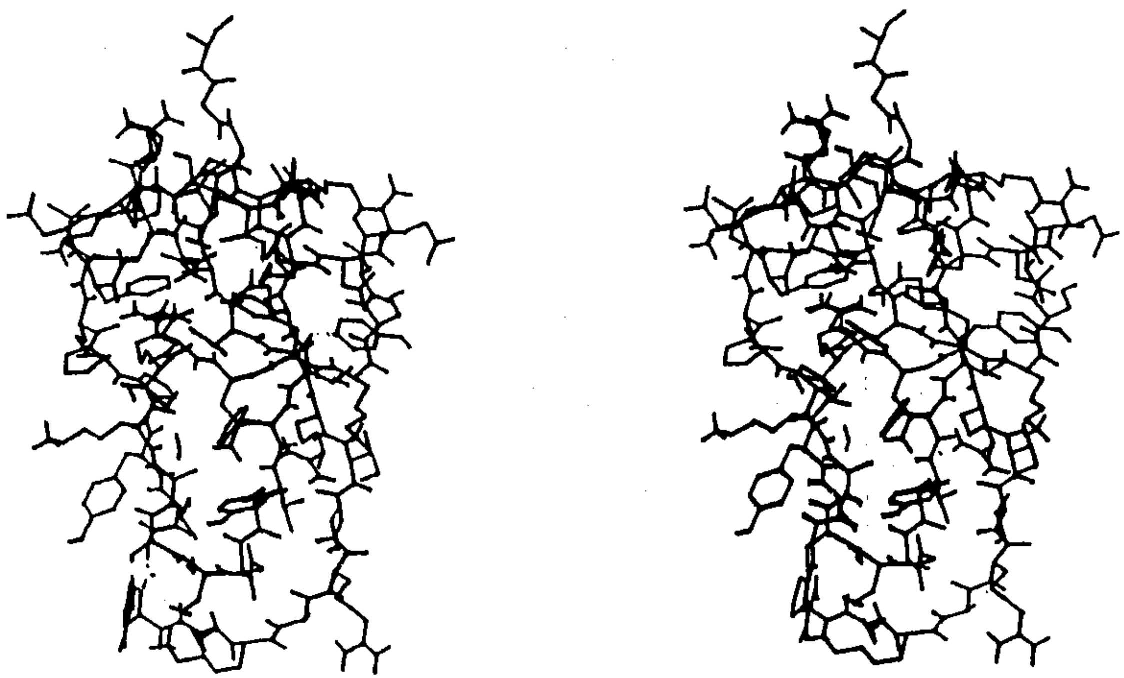
Get $\tau \sim \ln L$

Computer Simulation of Biological Molecules

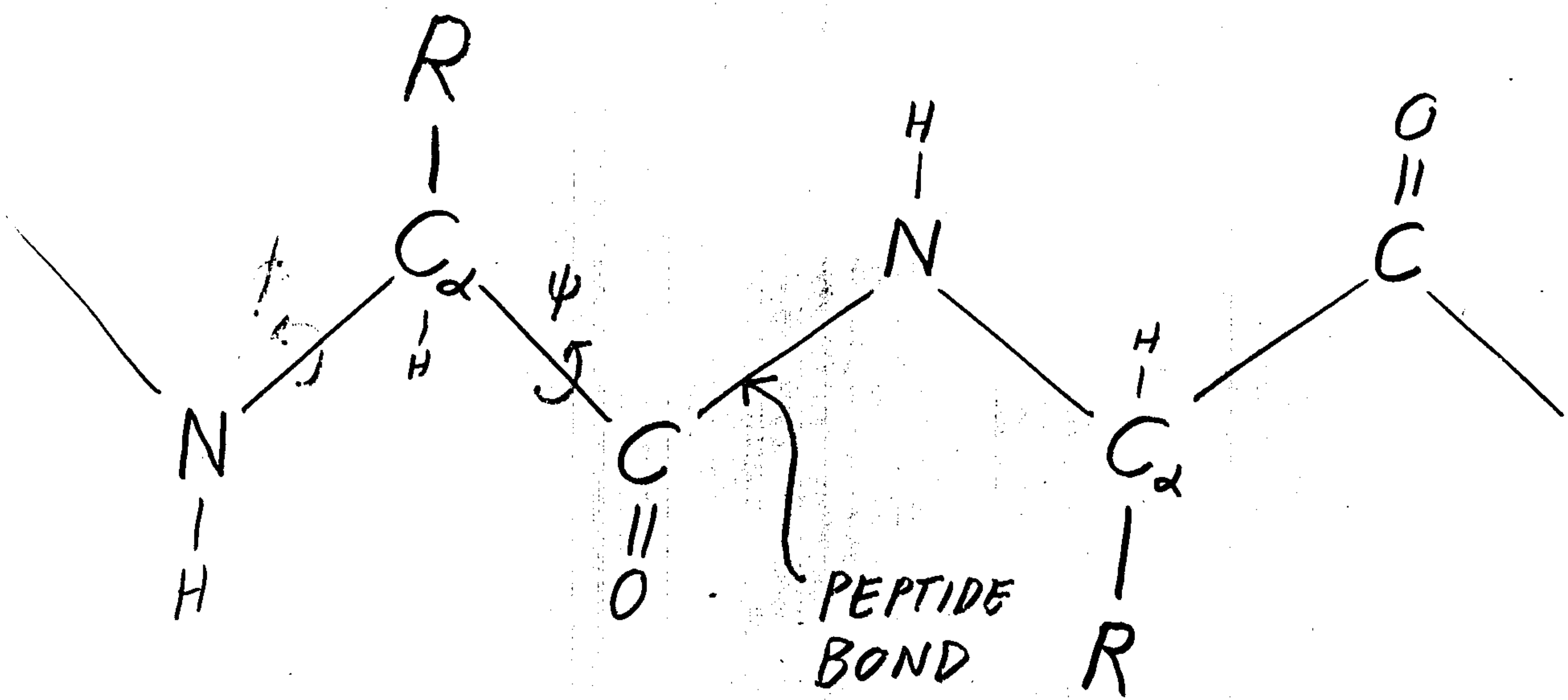
Robert H. Swendsen

Djamal Bouzida

Shankar Kumar



BPTI


R
H
O
N
C
C
ψ
H
N
C
O
PEPTIDE
BOND
C
R

Empirical potential energy function

- Bond Stretching:

$$\frac{1}{2}\sum_{bonds} K_b(b-b_{eq})^2$$

- Angle Bending:

$$\frac{1}{2}\sum_{angles} K_\theta(\theta-\theta_{eq})^2$$

- Torsion:

$$\frac{1}{2}\sum_{dihedrals} V_\varphi[1+\cos(n\varphi-\delta)]$$

- Lennard-Jones, and electric:

$$\sum_{non-bonds}[\frac{A}{r^{12}}-\frac{B}{r^6}+\frac{q_iq_j}{\varepsilon r}]$$

Monte Carlo

MC is a *stochastic* method:

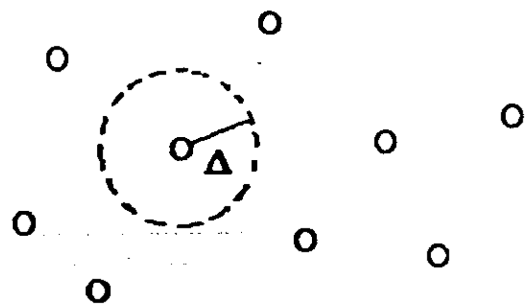
- Generate a sequence of system configurations which is distributed according to the Boltzmann distribution.
- Equilibrium properties are found by computing appropriate averages over the resulting set of configurations.
- **Metropolis Algorithm:**
  - Pick an atom, make random move.
  - Compute ΔE.
  - If $\Delta E < 0$, the move is accepted.
  - If $\Delta E > 0$, the move is accepted with probability $\exp(-\beta \Delta E)$.
- Ideal acceptance ratio is about 50%.

Classical Paper:

Metropolis et. al., Jour. Chem. Phys., Vol. 21 (6), 1087 (1953)

Simulation of liquids

How does one simulate a liquid?



Atoms are moved randomly inside spheres of equal radii.

<u>System is:</u>

- homogeneous.
- isotropic.

Differences in simulating liquids and molecules

- **Inhomogeneity**
  - Each atom of the molecule sees a different environment.
  - Wide range of variation in the atomic fluctuations.
- **Anisotropy**
  - Highly anisotropic potentials.
  - Local effective potentials change during simulation.

$d=1$ SHO

$$E = \frac{1}{2} k x^2$$

Monte Carlo move Δx

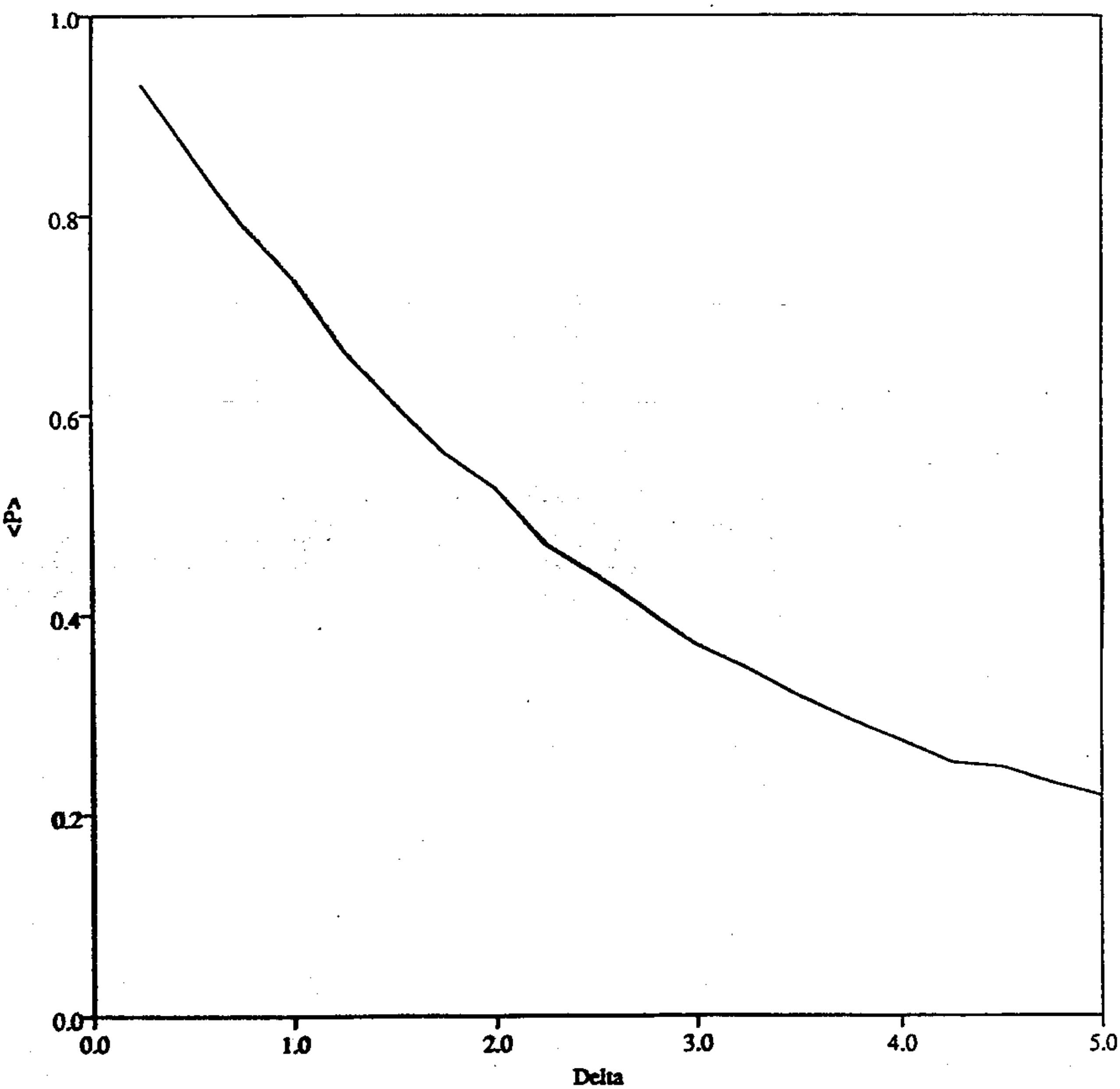
$$\delta \geqslant \Delta x \geqslant -\delta$$

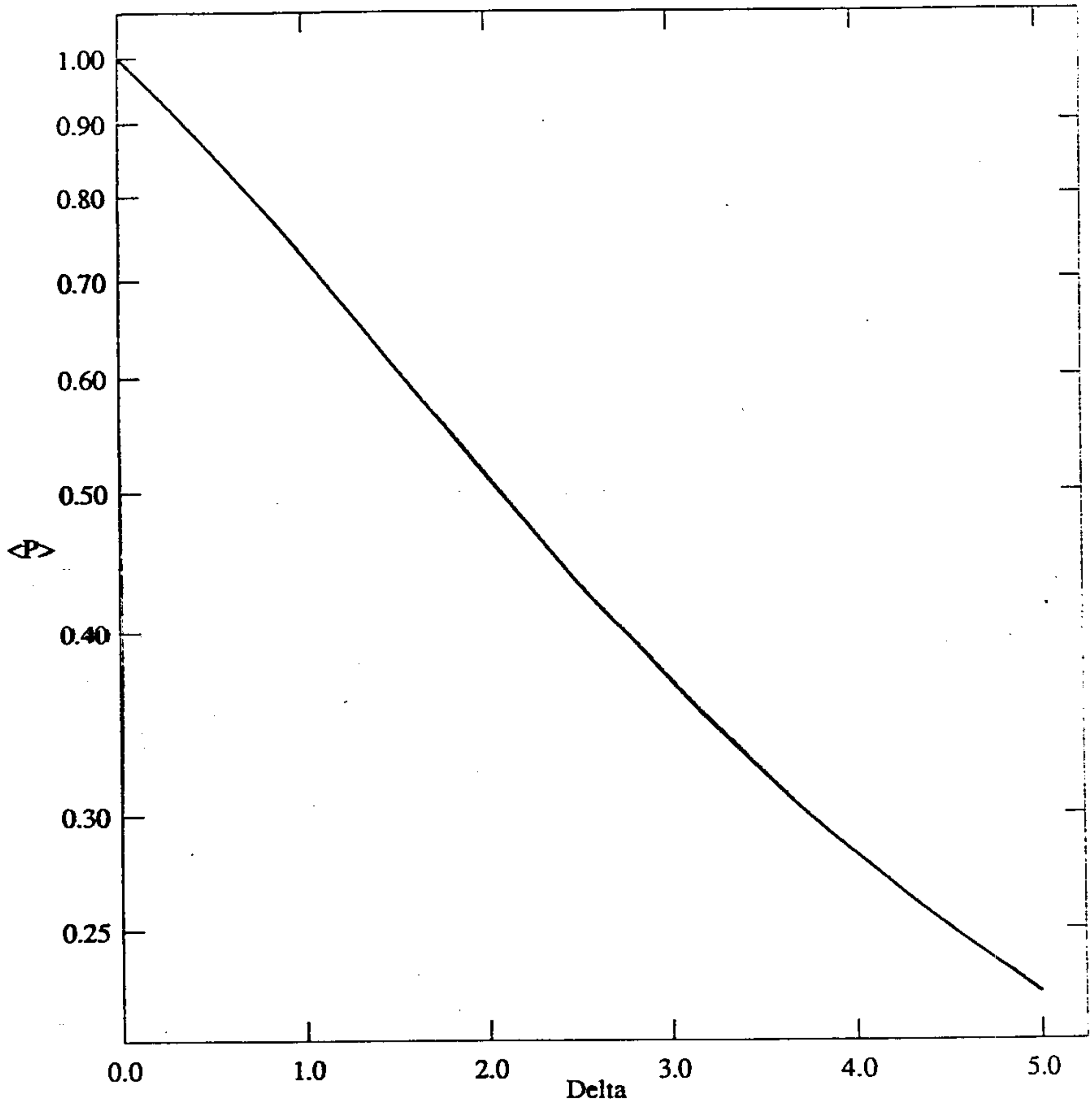
δ = optimal step size

Scaling relation:

$$\frac{1}{2} \beta k \delta^2 = F^2$$

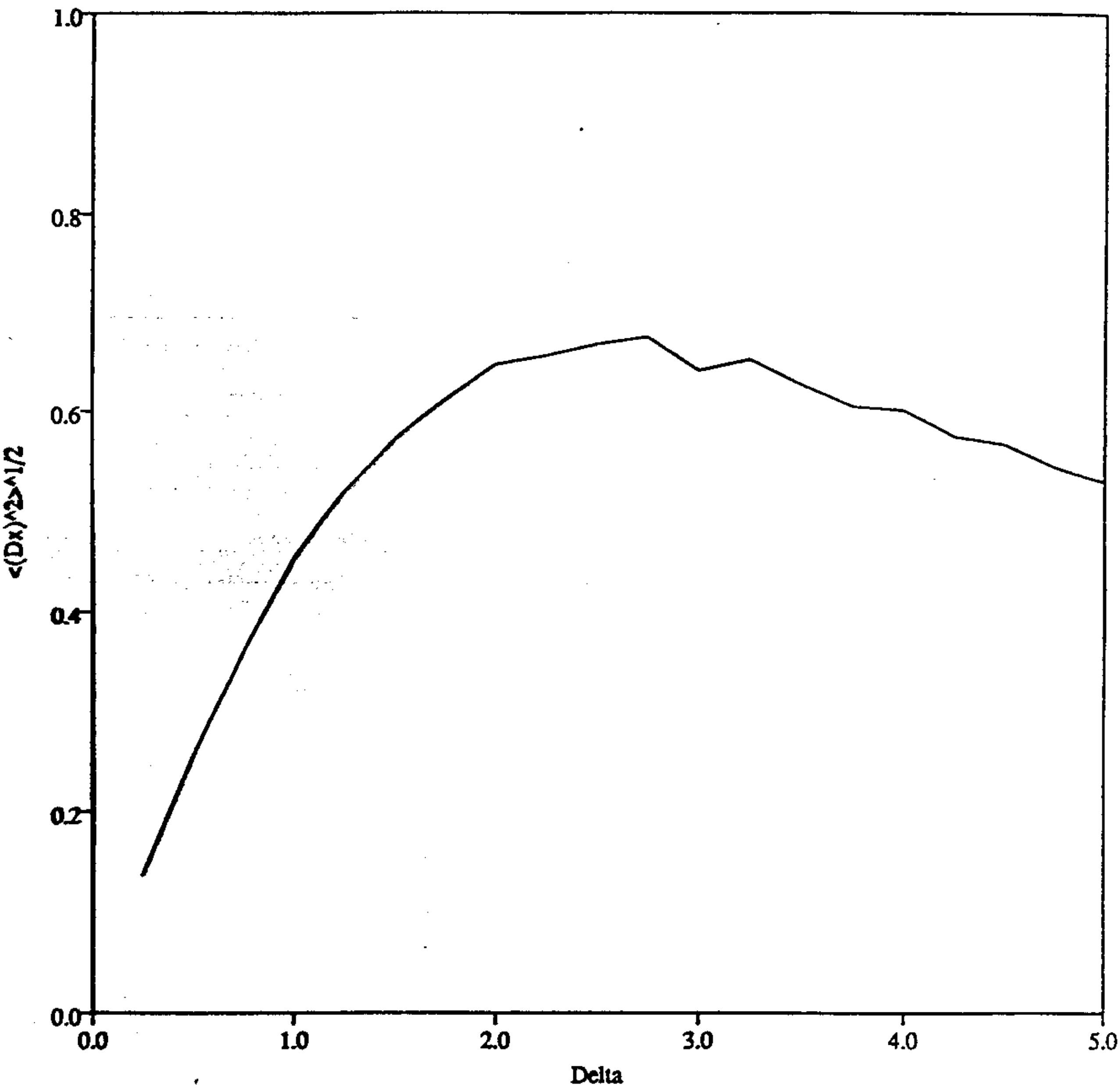
$V(x) = x^2 \quad T = 1.0 \qquad MC$



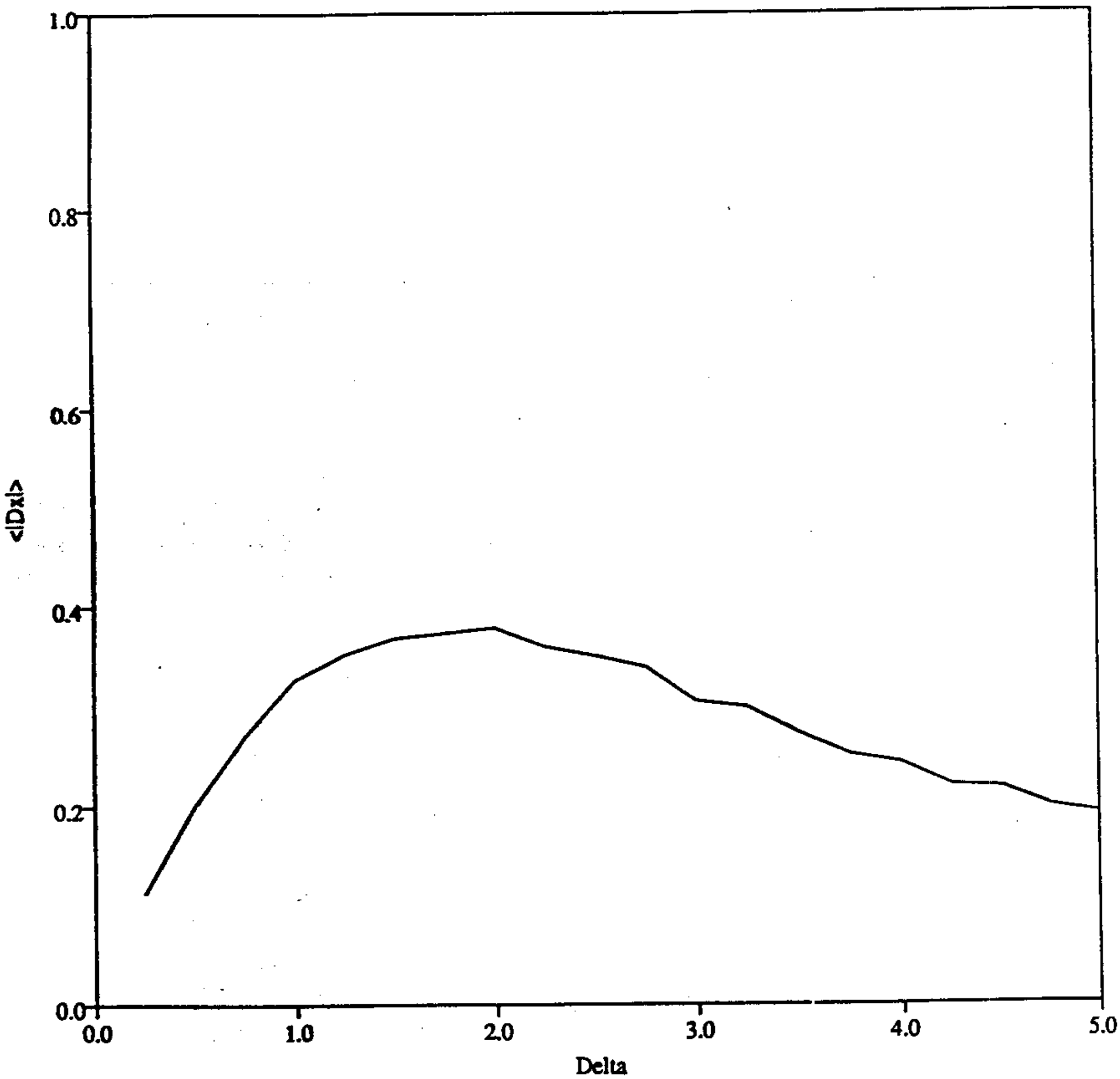


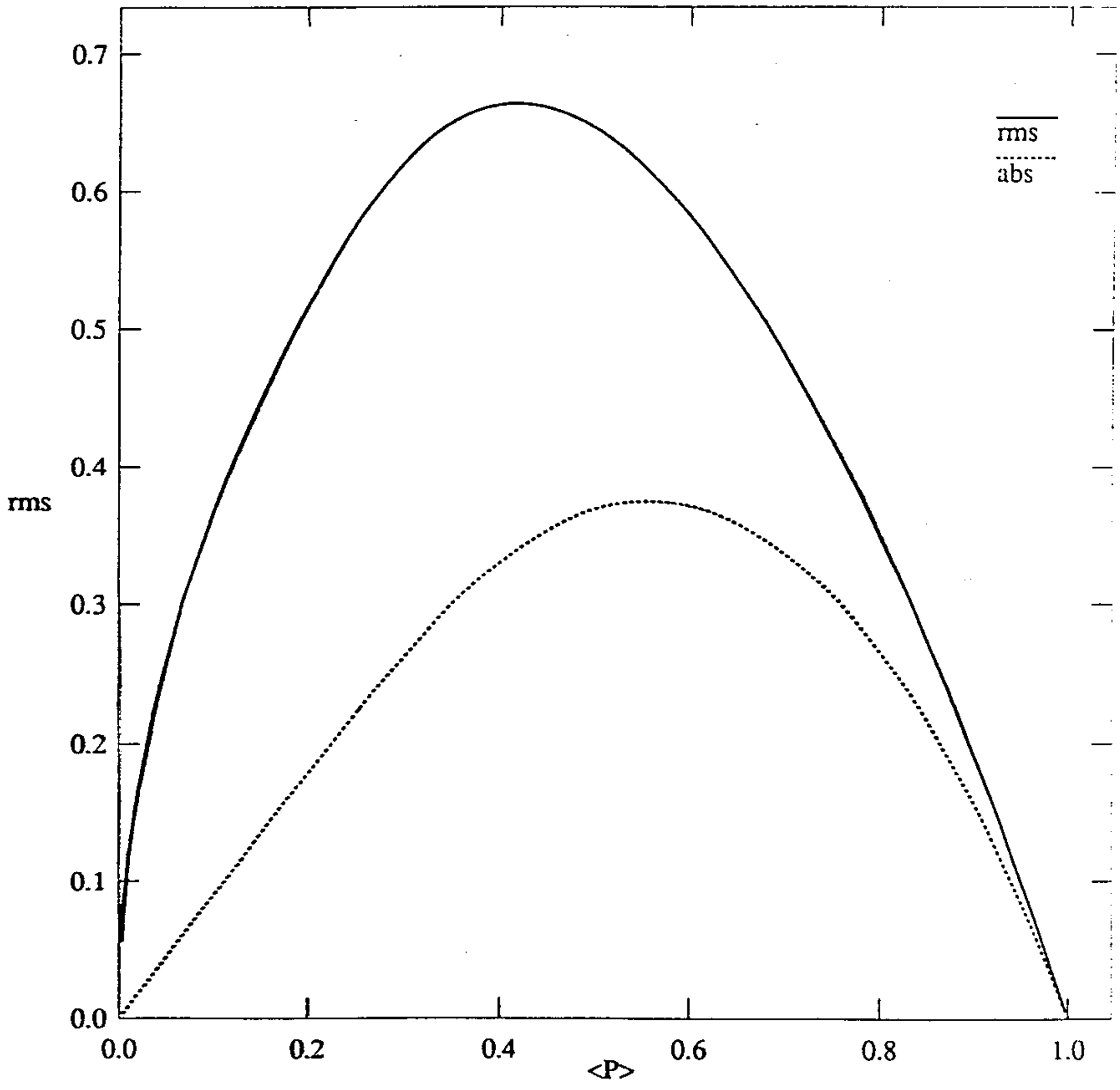
1.00
0.90
0.80
0.70
0.60
0.50
<P>
0.40
0.30
0.25
0.0
1.0
2.0
3.0
4.0
5.0
Delta

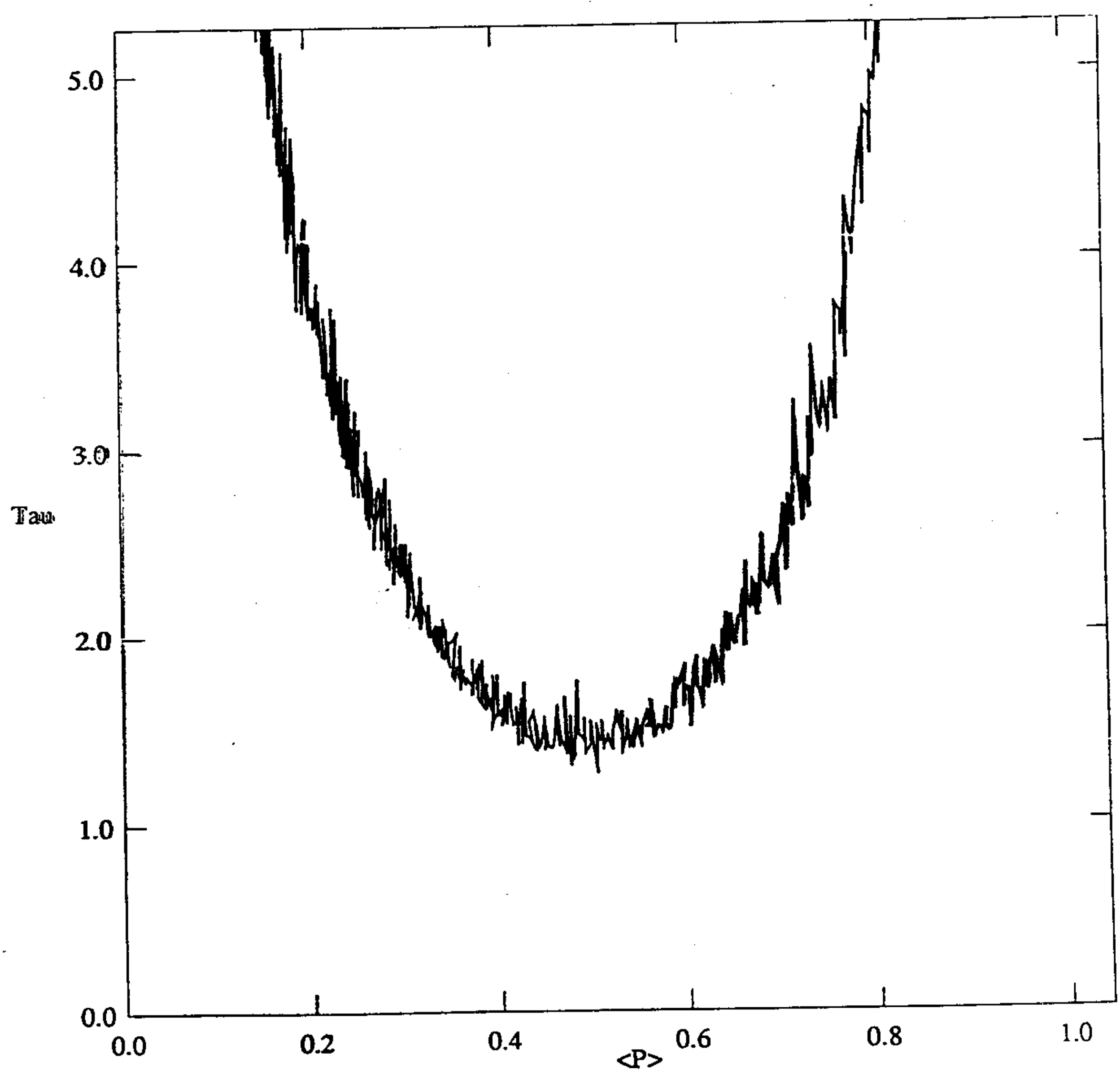
$V(x) = x^2$ $T = 1.0$ MC



$V(x) = x^2$ $T = 1.0$ MC




rms
abs
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
rms
0.0
0.2
0.4
0.6
0.8
1.0
<P>



5.0
4.0
3.0
Tau
2.0
1.0
0.0
0.0
0.2
0.4
0.6
0.8
1.0
<P>

Acceptance Ratio Method

$$P \approx \exp[-\Delta/\Delta_0]$$

Ideal ratio $\longleftrightarrow$ ideal step size

$$P_i = \exp[-\Delta_i/\Delta_0]$$

$$\Rightarrow \quad \Delta_{new} = \Delta_{old} \ln P_i / \ln P$$

Actually use:

$$\Delta_{new} = \Delta_{old} \frac{\ln(a P_i + b)}{\ln(a P + b)}$$

Dynamically Optimized Monte Carlo

[DOMC

$$E = \frac{1}{2} k x^2$$

$$\Delta E = \frac{1}{2} k (x + \Delta x)^2 - \frac{1}{2} k x^2$$

$$\Delta E = k x \Delta x + \frac{1}{2} k (\Delta x)^2$$

$[\ldots] \equiv$ average over all <u>attempted</u> moves

$$[\Delta x] = 0$$

$$[\Delta E] = \frac{1}{2} k [(\Delta x)^2]$$

$$\frac{1}{2} \beta k \delta^2 = F^2$$

$$\delta = F \left(\frac{[(\Delta x)^2]}{\beta [\Delta E]} \right)^{\frac{1}{2}}$$

DOMC for $d > 1$

$$E = \frac{1}{2} \sum_{i,j} k_{ij} x_i x_j$$

MC moves $\{\zeta_i\}$ in an ellipsoid

$$\zeta_i = \sum_{j=1} D_{ij} \xi_j$$

$\{\xi_i\}$ is a random vector from the unit sphere.

Scaling relation:

$$F^2 = \frac{1}{2} \beta \, \bar{\bar{D}}^t \cdot \bar{\bar{k}} \cdot \bar{\bar{D}}$$

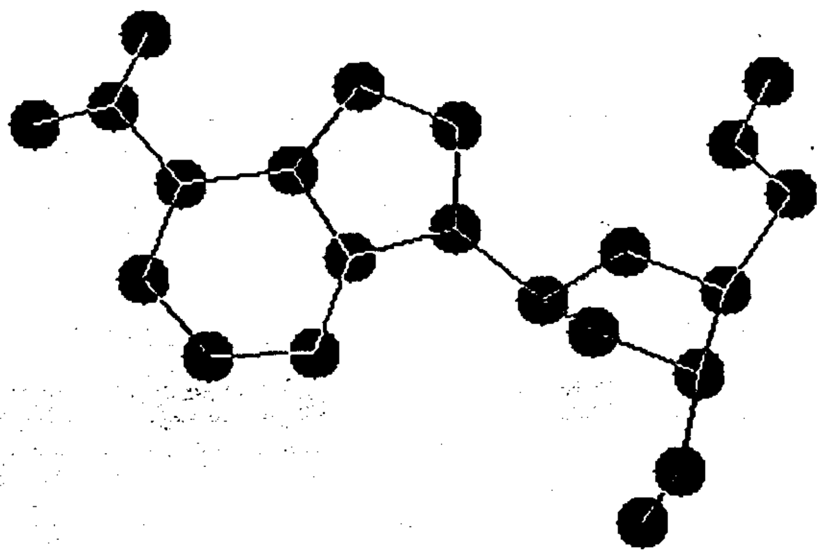
$$[\Delta E \, \zeta_\ell \zeta_m] = \frac{1}{2} \sum_{ij} k_{ij} [\zeta_i \zeta_j \zeta_\ell \zeta_m]$$

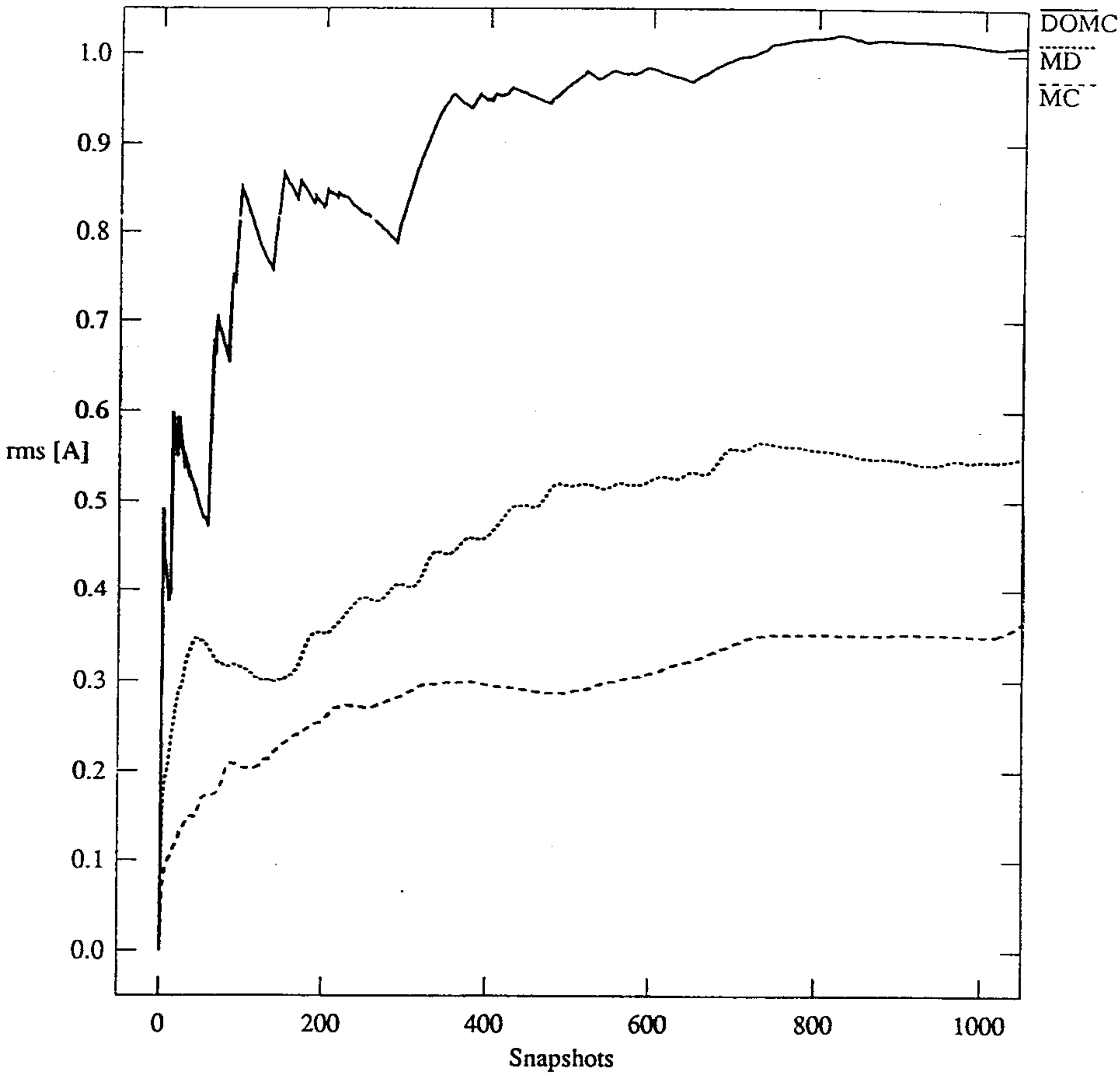
Solve for $\{k_{ij}\}$

λ_ℓ = eigenvalue of $\{k_{ij}\}$

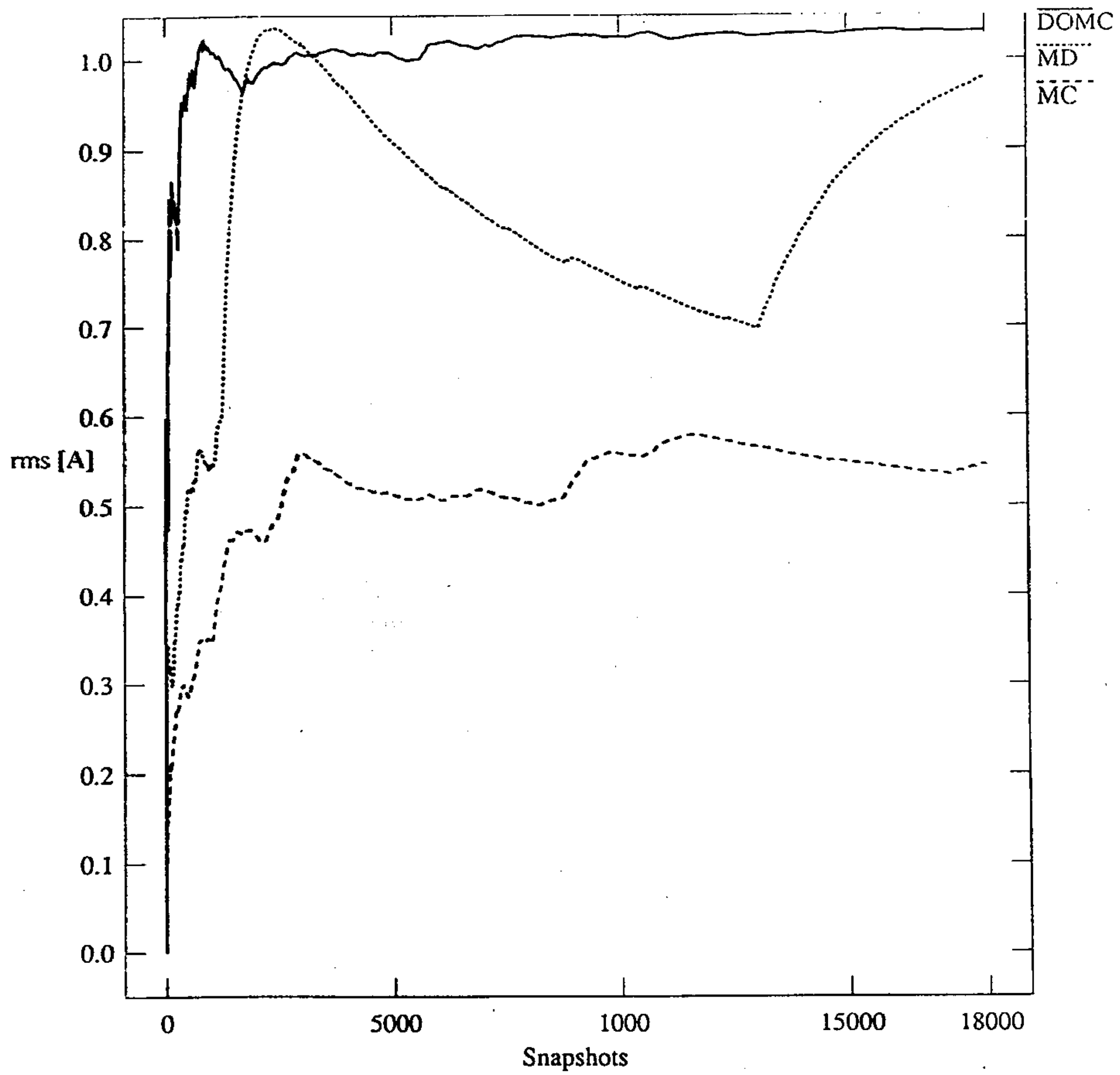
$V_{i\ell}$ = eigenvector of "

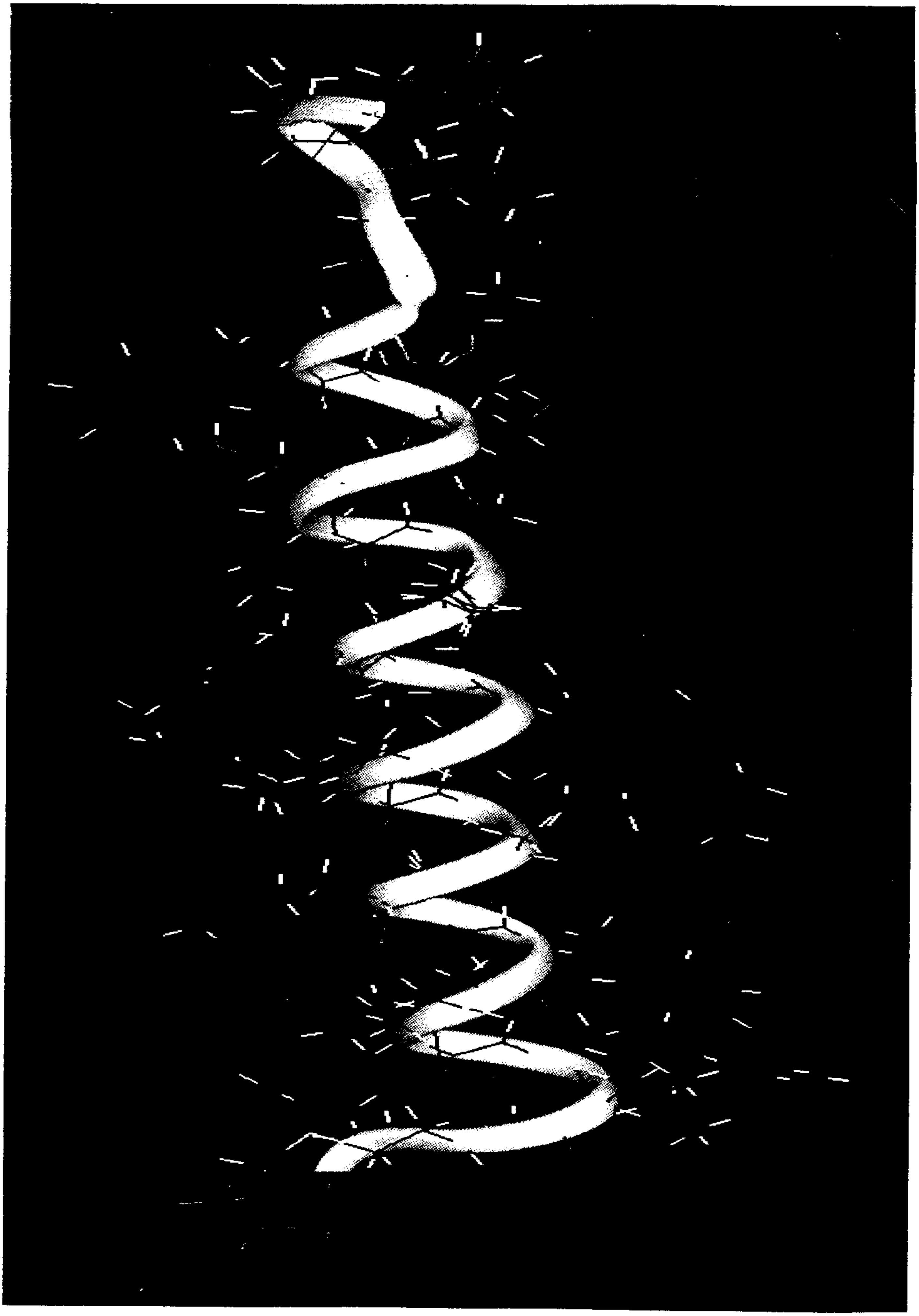
$$D_{i\ell} = F \left(\frac{2}{\beta \lambda_\ell} \right)^{\frac{1}{2}} V_{i\ell}$$





DOMC
MD
MC
rms [A]
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
200
400
600
800
1000
Snapshots


DOMC
MD
MC
rms [A]
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
5000
1000
15000
18000
Snapshots



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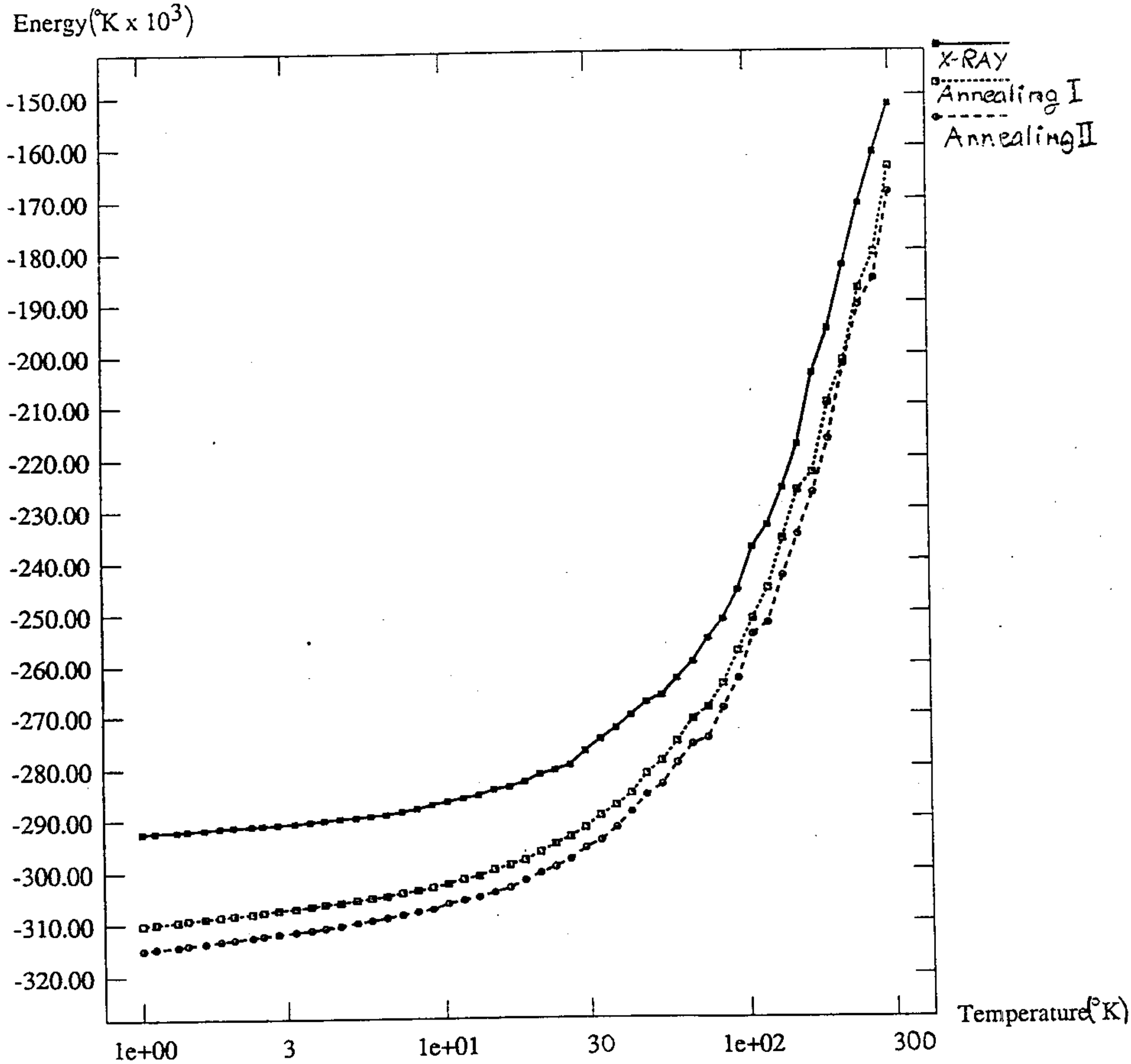
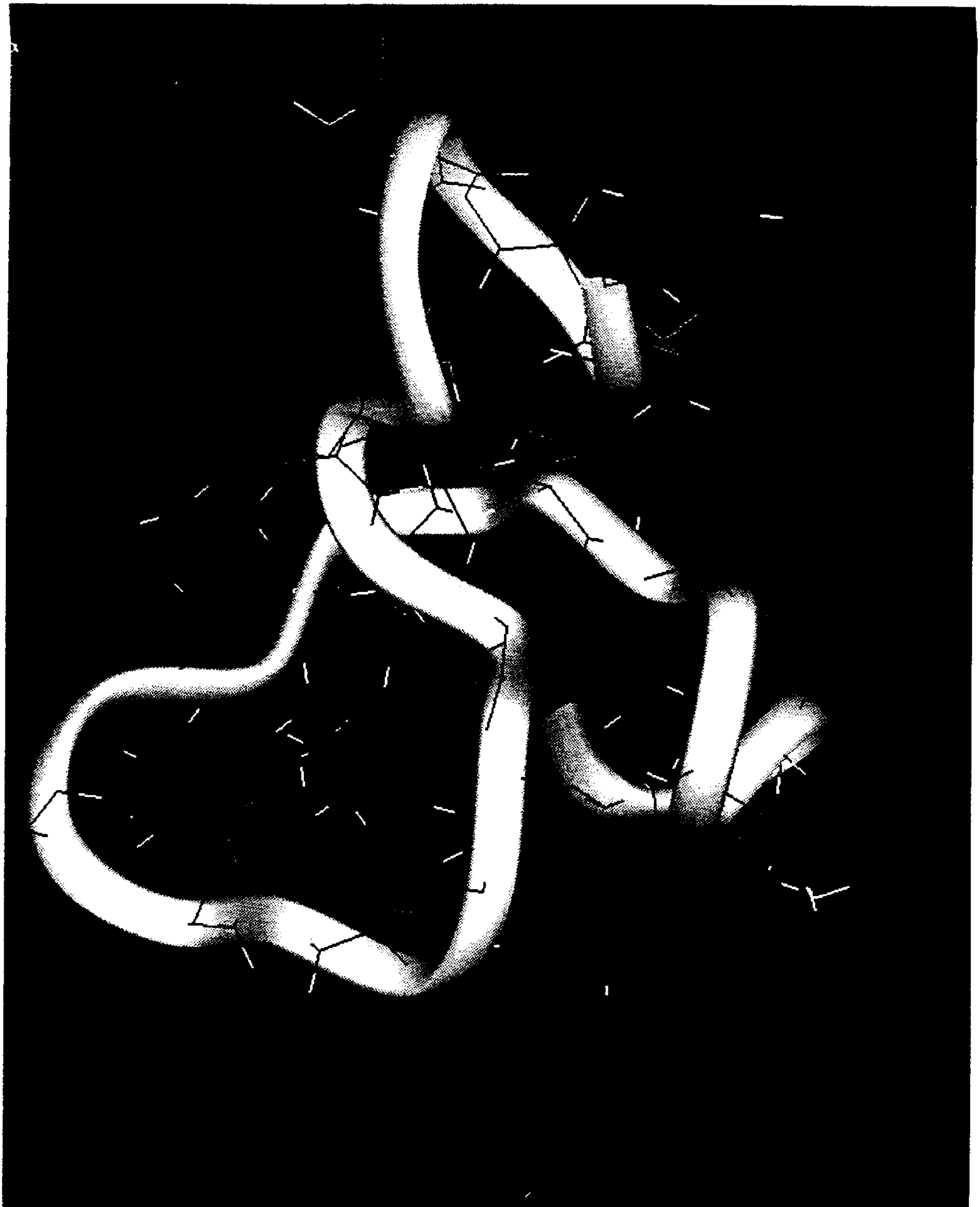


Energy(°K x 10^3)
-150.00
-160.00
-170.00
-180.00
-190.00
-200.00
-210.00
-220.00
-230.00
-240.00
-250.00
-260.00
-270.00
-280.00
-290.00
-300.00
-310.00
-320.00
X-RAY
Annealing I
Annealing II
Temperature(°K)
1e+00
3
1e+01
30
1e+02
300



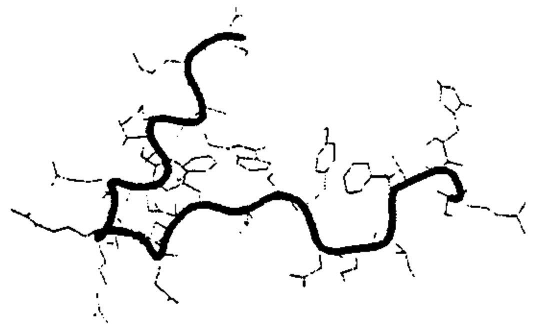


Figure 24: structure of glucagon after annealing

molecule. In the remaining cases the structure analysis program detected no helical regions. Figures 25 and 27 show the results of one of these runs.

Energetically, the helical structure lies about 20 kcal/mol below the energy of the partially folded structures. The random coils had an even higher energy, about 30 kcal/mol above the helical structure.

Even though the program did not reproduce the X-ray structure the results found agree rather well with experimental measurements by Panijpan and Gratzer [27] and Gratzer et al. [28]. From NMR studies, measurements of the temperature dependence of optical rotary dispersion and thermal difference measurements they conclude that that in dilute solution, glucagon is largely a random chain which contains about one turn of α-helix. They predict that the surmised α-helical segment is formed by residues 21 or 22 to 26 near the C-terminal. This is the region in which the simulated molecule showed the largest probability of forming an α-helical structure. The experiments also support a hypothesis brought forth by the authors of [28] that the molecule at room temperature is at the high end of a transition between a helix and a random coil state. The experiments show that the apparent helix content of glucagon in dilute solution increases as the temperature is lowered. The authors make a prediction that glucagon should fold into the helical form