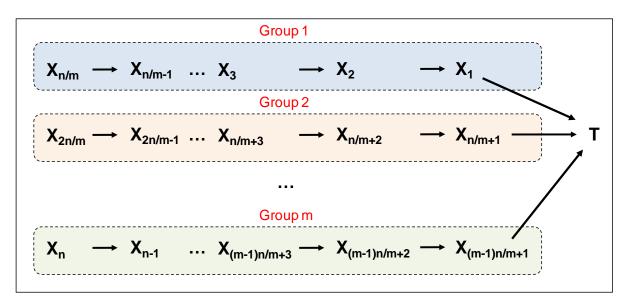
## The number of maximally predictive and non-redundant signatures is worst-case exponential to the number of variables

Consider a simplified pathway structure and parameterization shown in the figure below. It involves n genes  $(X_1, X_2, ..., X_n)$  and a phenotypic response variable T. Genes  $X_i$  (i = 1, ..., n) can be divided into m groups such that any two genes in a group contain exactly the same information about T. Since there are n/m genes in each group, the total number of Markov boundaries is  $(n/m)^m$ . Now assume that m = kn, where k < 1. Then the total number of Markov boundaries is  $(1/k)^{kn}$ . Since 1/k > 1 and kn = O(n), it follows that the number of Markov boundaries grows exponentially with the number of variables in this example.



$P(T   X_I,$	$(X_1 = 0,$	$(X_1 = 0,$		$(X_1 = 1,$
$X_{\mathrm{n/m+1}},\ldots$	$X_{n/m+1}=0,\ldots$	$X_{n/m+1}=0,\ldots$		$X_{n/m+1}=1,\ldots$
$X_{(m-1)n/m+1}$ )	$X_{(m-1)n/m+1} = 0$	$X_{(m-1)n/m+1} = 1$	•••	$X_{(m-1)n/m+1} = 1$
T = 0	0.2	0.8		0.2
T=1	0.8	0.2		0.8

For any pair of genes  $X_i$  and  $X_k$  belonging to the same group i:

$P(X_j   X_k)$	$X_k = 0$	$X_{\rm k} = 1$
$X_j = 0$	1.0	0.0
$X_{i} = 1$	0.0	1.0

**Figure:** Example pathway structure with n gene variables  $(X_1, X_2, ..., X_n)$  and phenotypic response variable T. The structure is represented by a Bayesian network. The network parameterization is defined below the graph. All variables take values  $\{0,1\}$ .