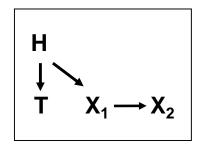
## An example of signature multiplicity due to hidden variables

Consider a simplified pathway structure and parameterization shown in the figure below. It involves 3 genes (H,  $X_1$ ,  $X_2$ ) and a phenotypic response variable T. In the distribution with all variables observed, there is only one Markov boundary of T, which is {H}. Now consider that gene H is not observed in the data (i.e., it is hidden). Because H is not observed and genes  $X_1$  and  $X_2$  contain exactly the same information about T, two Markov boundaries { $X_1$ } and { $X_2$ } can be identified in this distribution. Notice that all these Markov boundaries have reproducible but suboptimal (relative to the original distribution with H observed) predictivity of the response variable T.



$P(T \mid H)$	H = 0	H = 1
T = 0	0.9	0.2
T = 1	0.1	0.8

$P(X_1 \mid H)$	H = 0	H = 1
$X_1 = 0$	0.9	0.1
$X_{I} = 1$	0.1	0.9

$\mathbf{P}(X_2 \mid X_l)$	$X_1 = 0$	$X_{1} = 1$
$X_2 = 0$	1.0	0.0
$X_2 = 1$	0.0	1.0

**Figure:** Example pathway structure with 3 gene variables  $(H, X_1, X_2)$  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  $\{0,1\}$ .