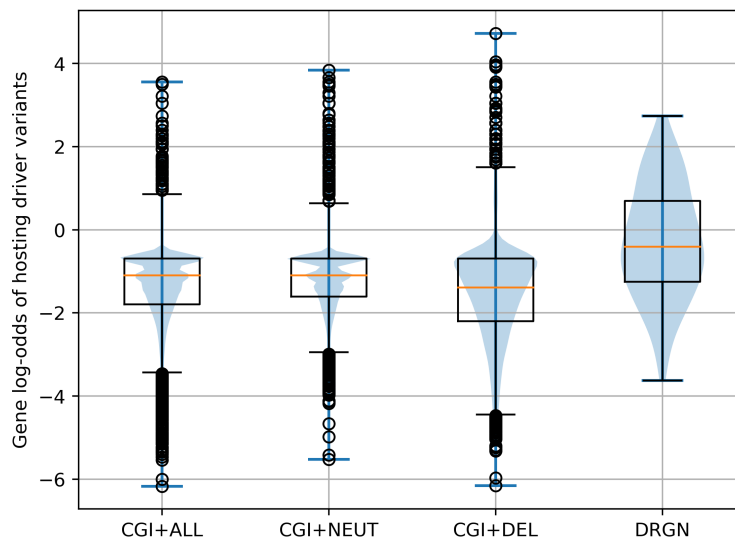


## Supplementary Material

### Figures

Figure S1: Plots showing the distributions of the per-gene log-odds of containing driver vs passenger variants over the four datasets. We can see that DRGN has the most balanced distribution. The Wilcoxon ranksums p-value of the differences between the first three distributions and the DRGN are respectively  $6.7 \times 10^{-24}$ ,  $2.8 \times 10^{-19}$ ,  $9.0 \times 10^{-25}$  and the corresponding Cohen's  $d$  effect sizes are  $-1.3$ ,  $-1.4$ ,  $-0.9$  standard deviations.



### Tables

Table S1: Table showing the percentages of the missing predictions for each cancer driver predictor on each dataset. All the predictors except FATHMM have a negligible number of missing predictions.

Method	EXPR+ALL	EXPR+DEL	EXPR+NEUT	DRGN
ParsSNP	0.0	0.0	0.0	0.0
CanDrA v+	1.0	0.3	1.5	0.0
Chasm 3.1	0.2	0.1	0.3	0.0
CHASMplus	0.6	0.2	0.9	0.0
FATHMM	17.7	21.4	15.2	25.3
TransFIC	1.4	0.4	2.2	0.0

## S1 Entropy computations

Entropy is computed as:

$$H(X) = - \sum_{i=1}^n p(X = x_i) \log_2 p(X = x_i)$$

The per-gene entropy for gene  $g$  is computed as:

$$H(X) = - \sum_{i \in g} p(X = x_i) \log_2 p(X = x_i)$$

The conditional entropy is computed as:

$$H(X|G) = - \sum_{j=1}^m \sum_{i=1}^n p(X = x_i, G = g_j) \log_2 \frac{p(G = g_j)}{p(X = x_i, G = g_j)}$$

where  $x_i$  is the class of variant  $i$  and  $g_j$  is the driver status of gene  $j$ .