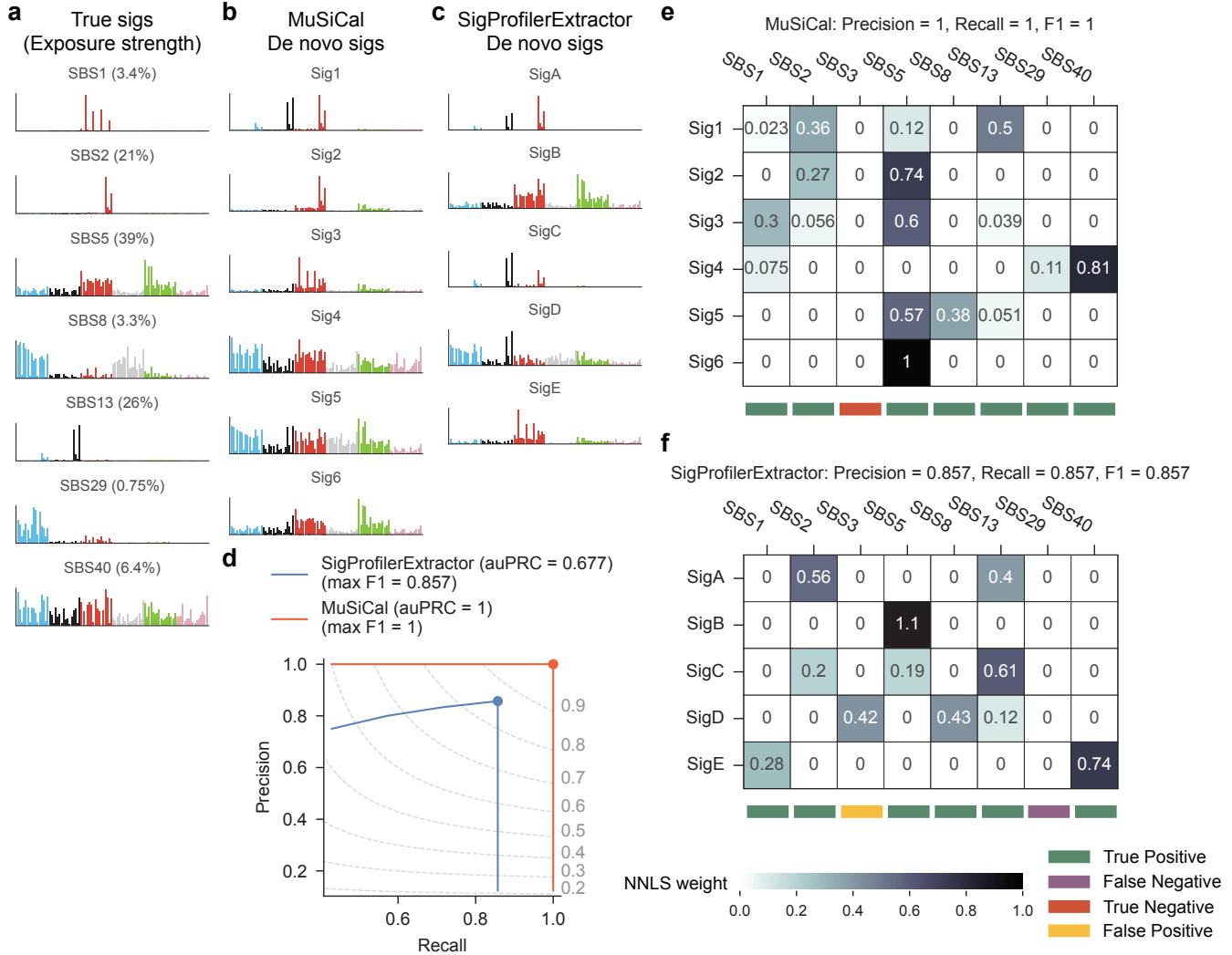


Supplementary Data

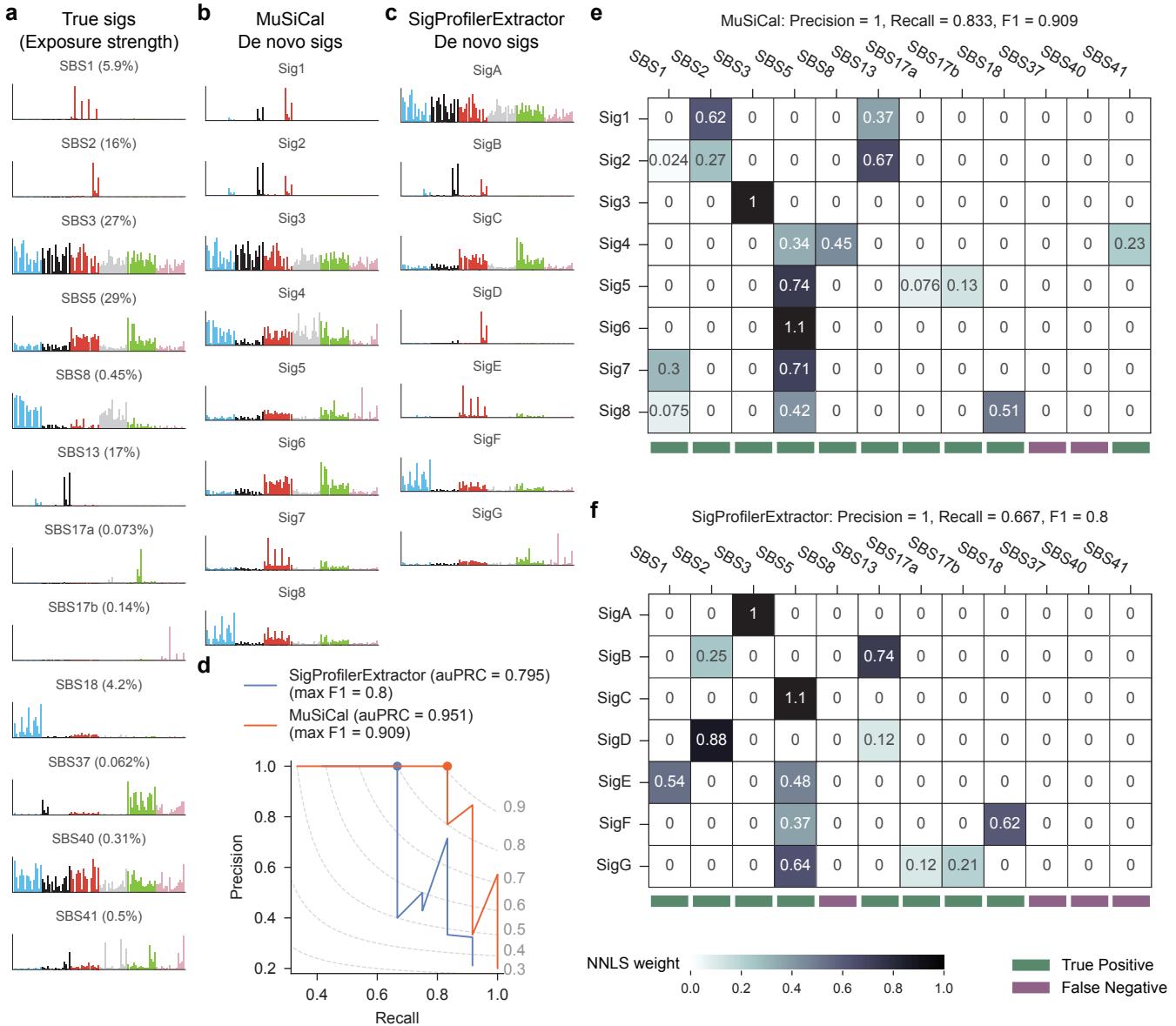
In the Supplementary Data below, we show simulated examples as in Fig. 3a, but for the other 24 tumor types. Specifically, the true signatures were plotted in panel (a), where the percentages below signature names denote exposure strengths of corresponding signatures. *De novo* signatures extracted by MuSiCal were plotted in panel (b). *De novo* signatures extracted by SigProfilerExtractor were plotted in panel (c). The precision-recall curves (PRCs) for both methods were plotted in panel (d), with area under PRC (auPRC) annotated. The matching result corresponding to the largest achieved F1 score was shown in panels (e) and (f) for MuSiCal and SigProfilerExtractor, respectively. Tumor types were ordered as in Fig. 3b.

Bladder-TCC

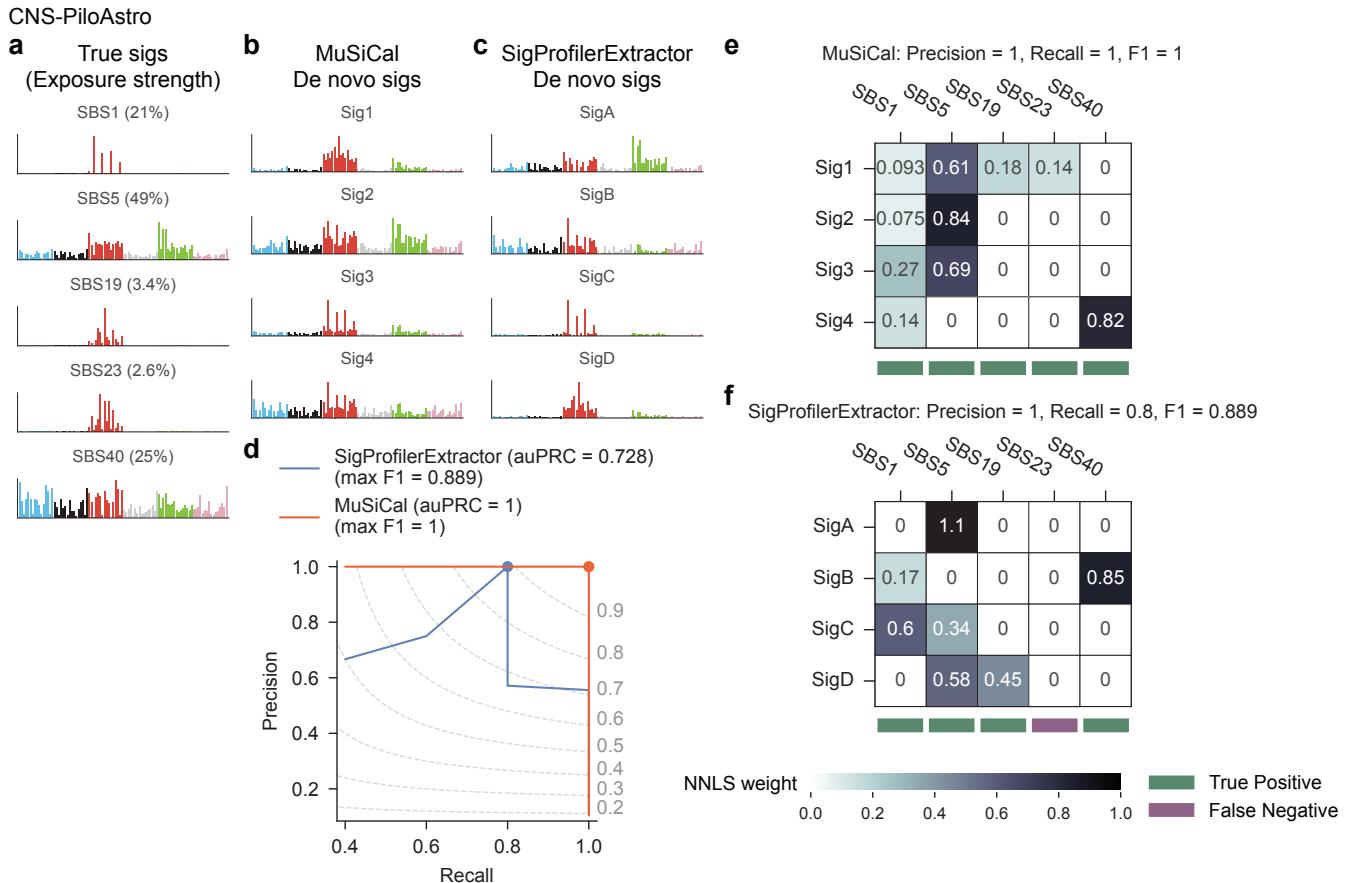


Supplementary Data Fig. 1 Same as Fig. 3a, but for Bladder-TCC.

Breast-AdenoCA

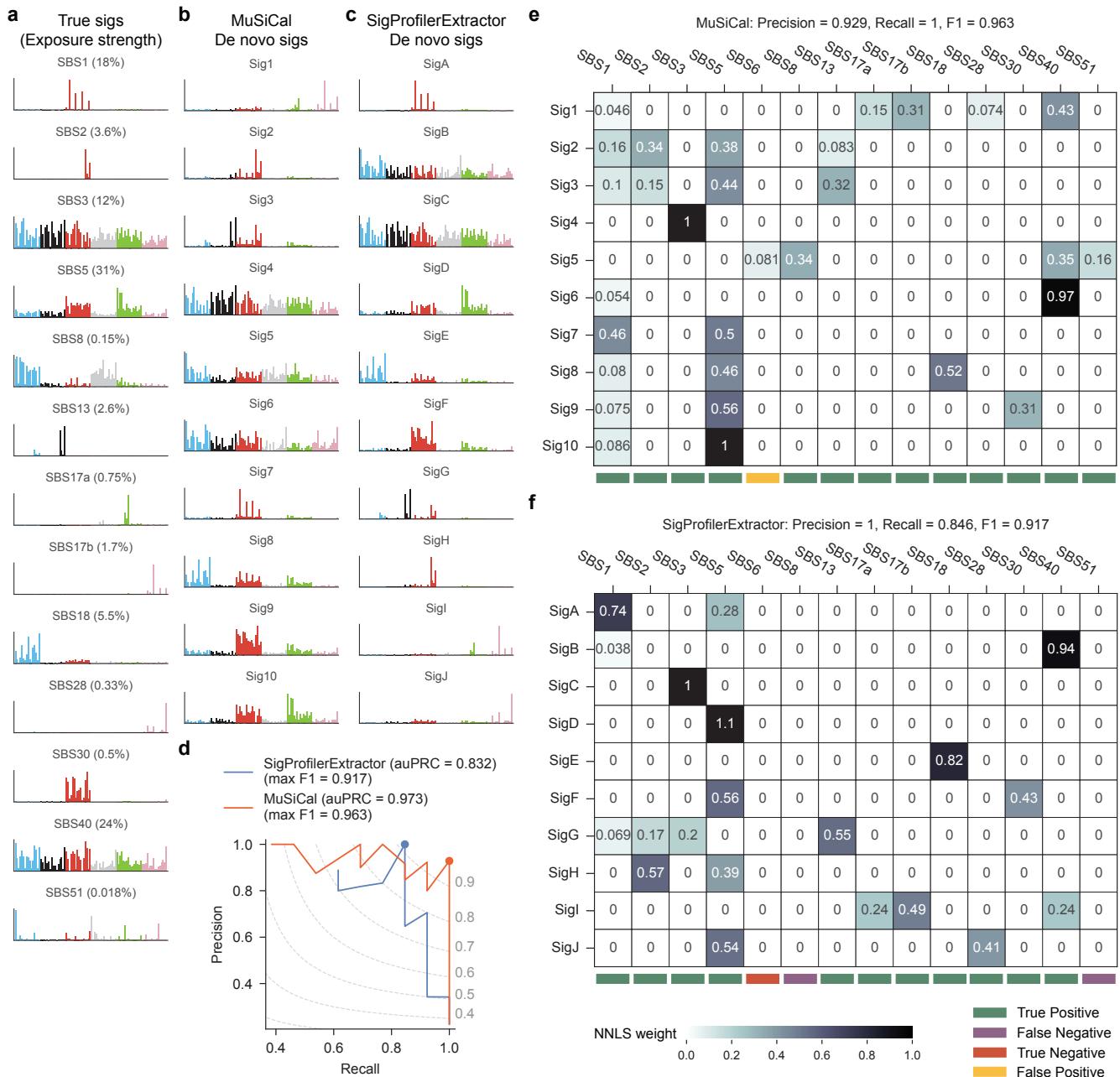


Supplementary Data Fig. 2 Same as Fig. 3a, but for Breast-AdenoCA.



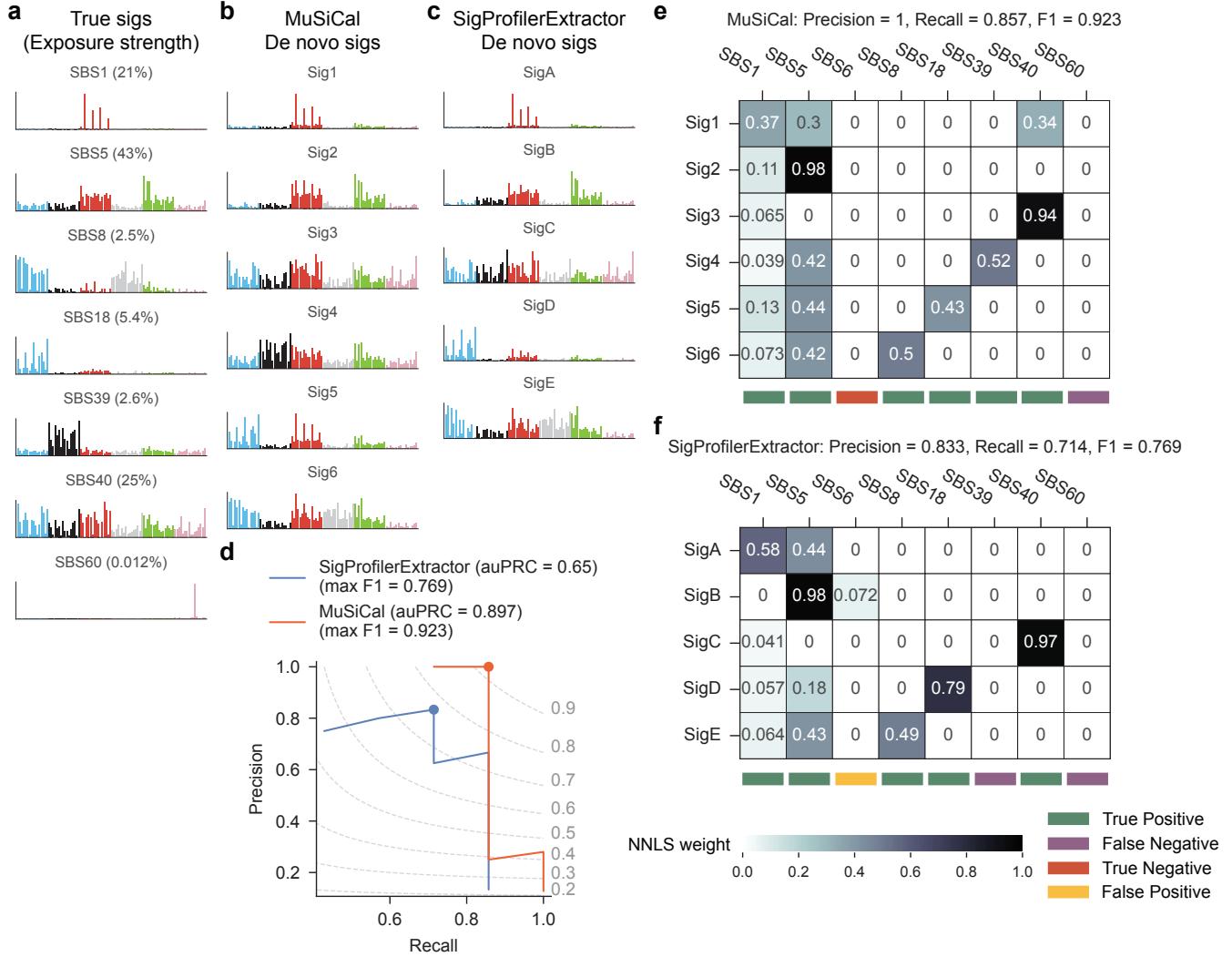
Supplementary Data Fig. 3 Same as Fig. 3a, but for CNS-PiloAstro.

Panc-AdenoCA



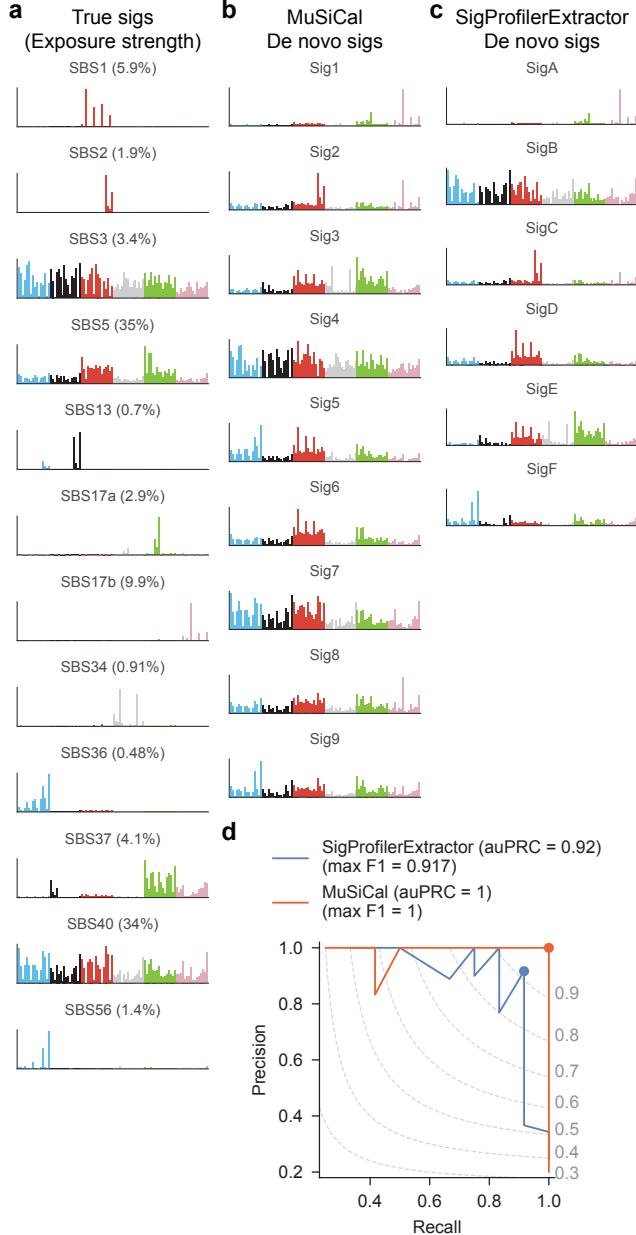
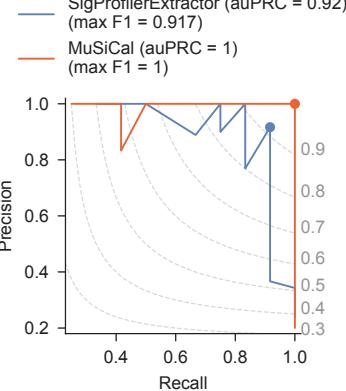
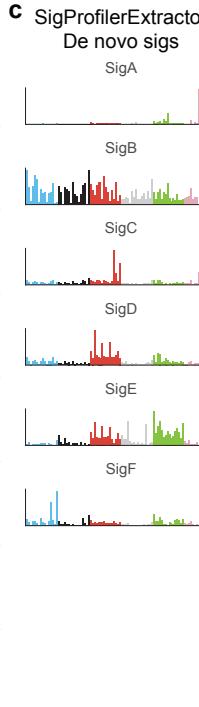
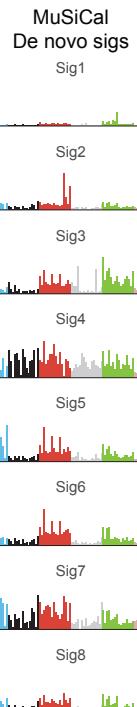
Supplementary Data Fig. 4 Same as Fig. 3a, but for Panc-AdenoCA.

CNS-Medullo



Supplementary Data Fig. 5 Same as Fig. 3a, but for CNS-Medullo.

Lymph-BNHL

**d****b****c**

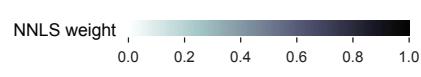
MuSiCal: Precision = 1, Recall = 1, F1 = 1

	SBS ₁	SBS ₂	SBS ₃	SBS ₅	SBS ₆	SBS ₁₃	SBS _{17a}	SBS _{17b}	SBS ₃₄	SBS ₃₆	SBS ₃₇	SBS ₄₀	SBS ₅₆
Sig1	0	0	0	0.52	0	0	0.13	0.34	0	0	0	0	0
Sig2	0.03	0.13	0	0.19	0	0	0	0.11	0	0	0	0.54	0
Sig3	0.074	0	0	0.57	0	0	0	0	0.1	0	0.28	0	0
Sig4	0.07	0	0.92	0	0	0	0	0	0	0	0	0	0
Sig5	0.13	0	0	0.42	0	0	0	0	0.023	0.18	0	0.24	0
Sig6	0.14	0	0	0.54	0	0	0	0	0	0	0	0.33	0
Sig7	0.041	0	0	0	0	0	0	0	0	0	0	0.97	0
Sig8	0.063	0	0	0.35	0	0	0	0.073	0	0	0	0.5	0
Sig9	0.046	0	0	0	0	0.029	0	0	0	0	0.18	0.66	0.094

f

SigProfilerExtractor: Precision = 0.917, Recall = 0.917, F1 = 0.917

	SBS ₁	SBS ₂	SBS ₃	SBS ₅	SBS ₆	SBS ₁₃	SBS _{17a}	SBS _{17b}	SBS ₃₄	SBS ₃₆	SBS ₃₇	SBS ₄₀	SBS ₅₆
SigA	0	0	0	0.43	0	0	0.16	0.44	0	0	0	0	0
SigB	0	0	0	1	0	0	0	0	0	0	0	0	0
SigC	0.026	0.2	0	0	0	0	0	0.063	0	0	0	0.71	0
SigD	0.21	0	0	0.75	0	0	0	0	0	0	0	0	0
SigE	0	0	0	0.4	0.13	0	0	0	0.11	0	0.4	0	0
SigF	0	0	0	0	0.046	0.057	0	0	0	0	0.24	0.43	0.24

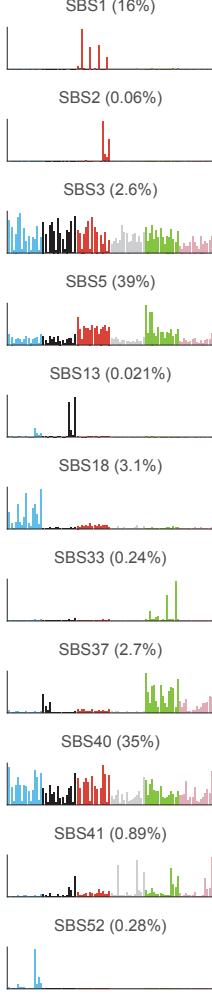


True Positive
False Negative
True Negative
False Positive

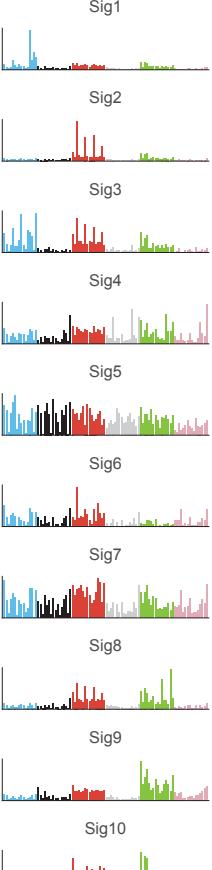
Supplementary Data Fig. 6 Same as Fig. 3a, but for Lymph-BNHL.

Prost-AdenoCA

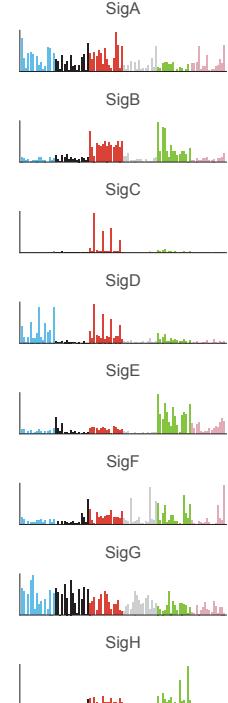
a True sigs
(Exposure strength)



b MuSiCal
De novo sigs



c SigProfilerExtractor
De novo sigs



e

MuSiCal: Precision = 1, Recall = 0.818, F1 = 0.9

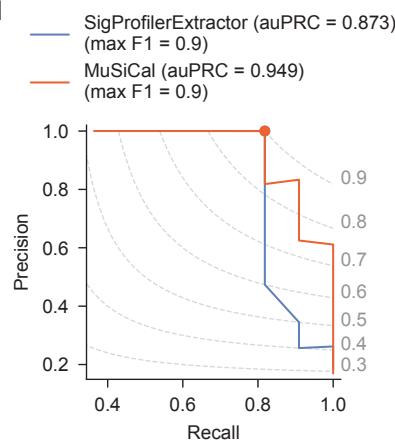
	SBS ₁	SBS ₂	SBS ₃	SBS ₅	SBS ₁₃	SBS ₁₈	SBS ₃₃	SBS ₃₇	SBS ₄₀	SBS ₄₁	SBS ₅₂
Sig1	0.037	0	0	0.61	0	0	0	0	0	0	0.28
Sig2	0.37	0	0	0.62	0	0	0	0	0	0	0
Sig3	0.11	0	0	0.51	0	0.4	0	0	0	0	0
Sig4	-0.048	0	0	0	0	0	0	0	0.57	0.35	0
Sig5	-0.032	0	0.96	0	0	0	0	0	0	0	0
Sig6	-0.14	0	0	0	0	0	0	0	0.91	0	0
Sig7	-0.053	0	0	0	0	0	0	0	0.92	0	0
Sig8	-0.12	0	0	0.68	0	0	0.18	0	0	0	0
Sig9	0	0	0	0.63	0	0	0	0.37	0	0	0
Sig10	0	0	0	1	0	0	0	0	0	0	0

f

SigProfilerExtractor: Precision = 1, Recall = 0.818, F1 = 0.9

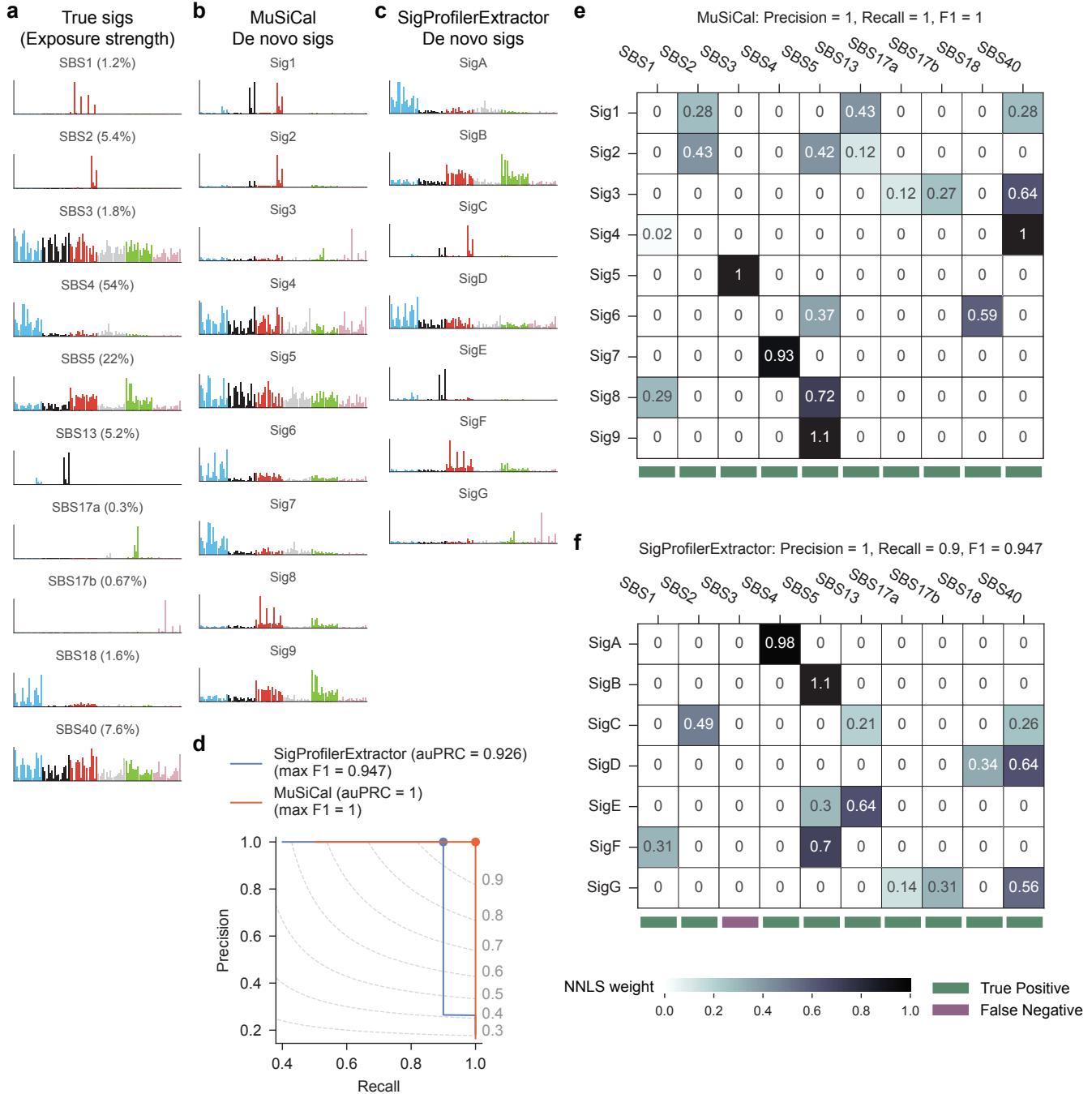
	SBS ₁	SBS ₂	SBS ₃	SBS ₅	SBS ₁₃	SBS ₁₈	SBS ₃₃	SBS ₃₇	SBS ₄₀	SBS ₄₁	SBS ₅₂
SigA	-0.039	0	0	0	0	0	0	0	0	1	0
SigB	0	0	0	1.1	0	0	0	0	0	0	0
SigC	0.66	0	0	0.34	0	0	0	0	0	0	0
SigD	0.19	0	0	0.32	0	0.53	0	0	0	0	0
SigE	0	0	0	0.28	0	0	0	0.73	0	0	0
SigF	0	0	0	0.41	0	0	0	0	0	0.6	0
SigG	-0.021	0	1	0	0	0	0	0	0	0	0
SigH	-0.086	0	0	0.52	0	0	0.43	0	0	0	0
SigI	0	0	0	0.33	0	0	0	0	0	0	0.72

NNLS weight
True Positive
False Negative



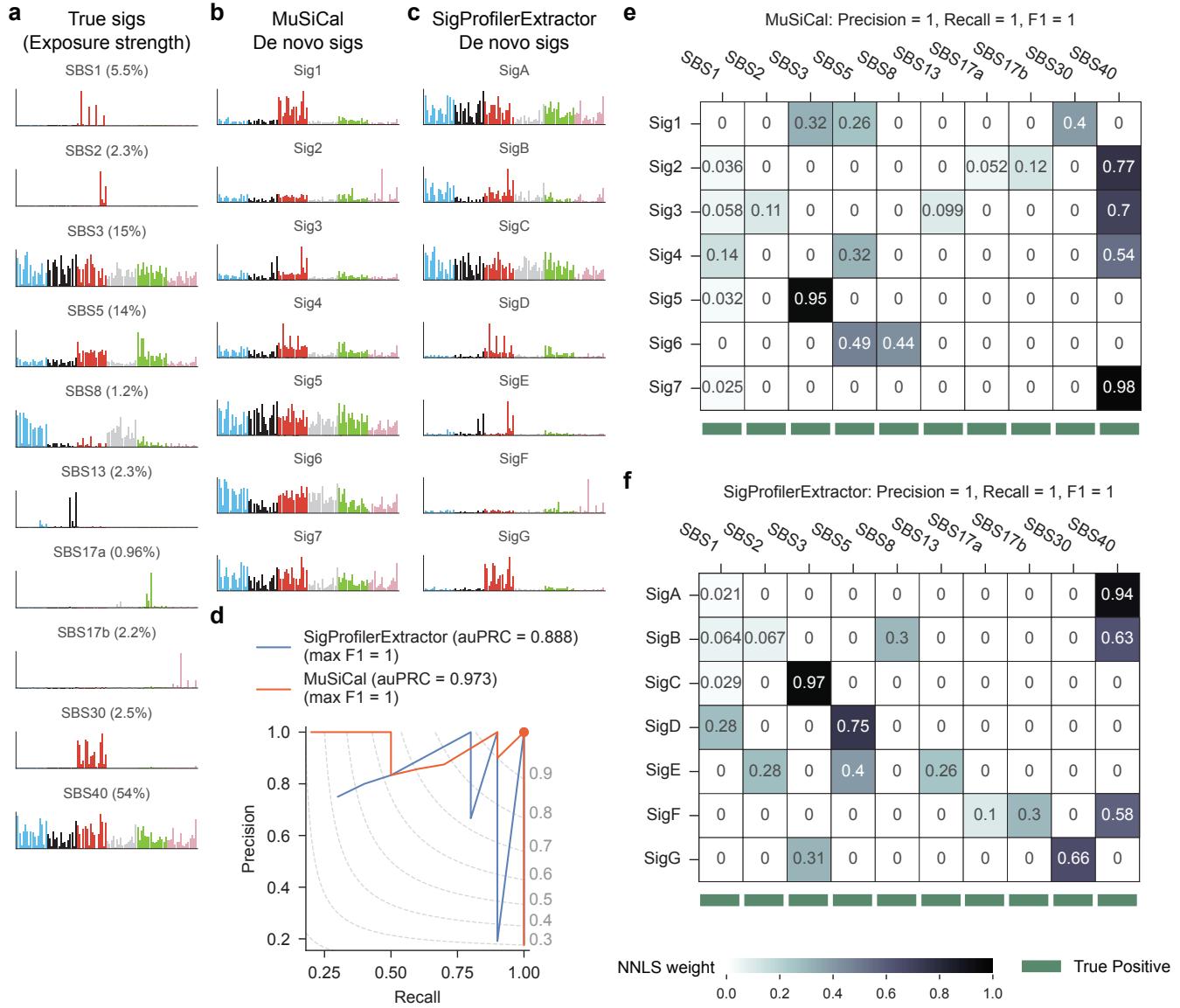
Supplementary Data Fig. 7 Same as Fig. 3a, but for Prost-AdenoCA.

Lung-AdenoCA



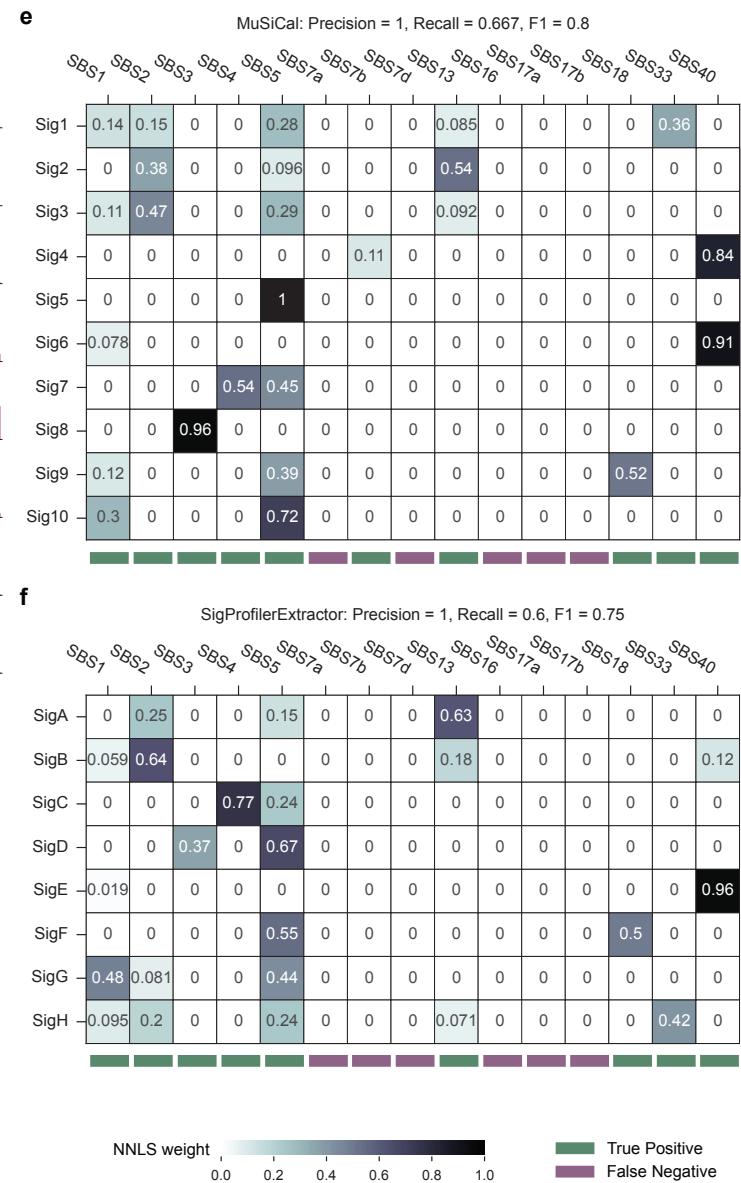
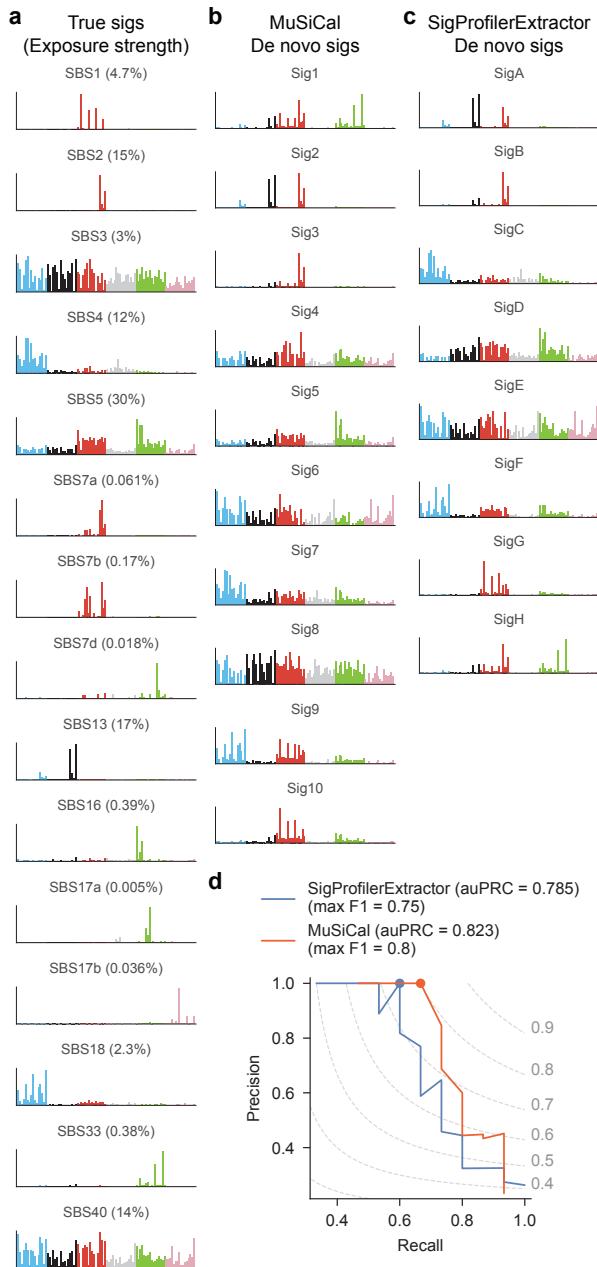
Supplementary Data Fig. 8 Same as Fig. 3a, but for Lung-AdenoCA.

Bone-Osteosarc



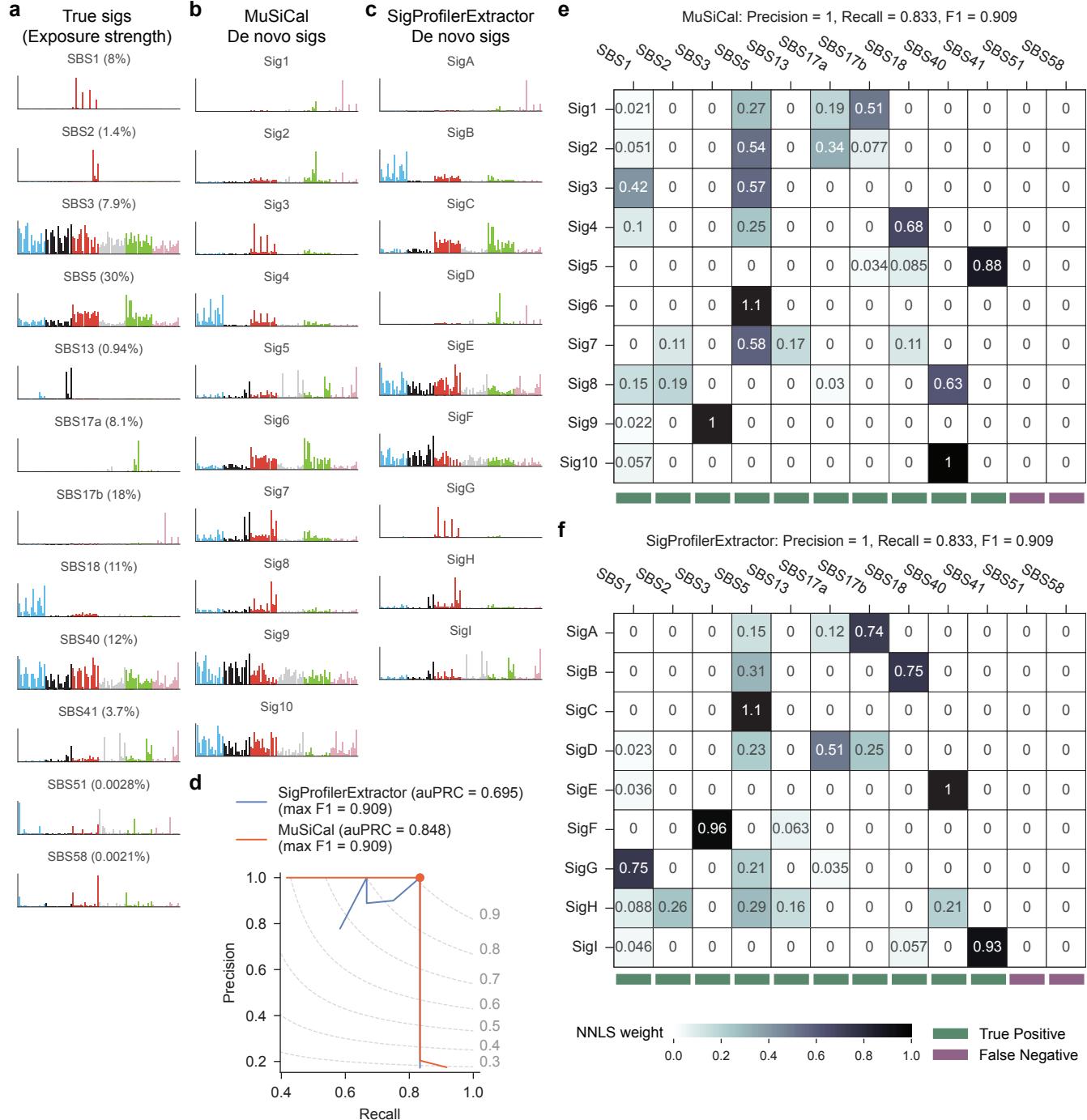
Supplementary Data Fig. 9 Same as Fig. 3a, but for Bone-Osteosarc.

Head-SCC



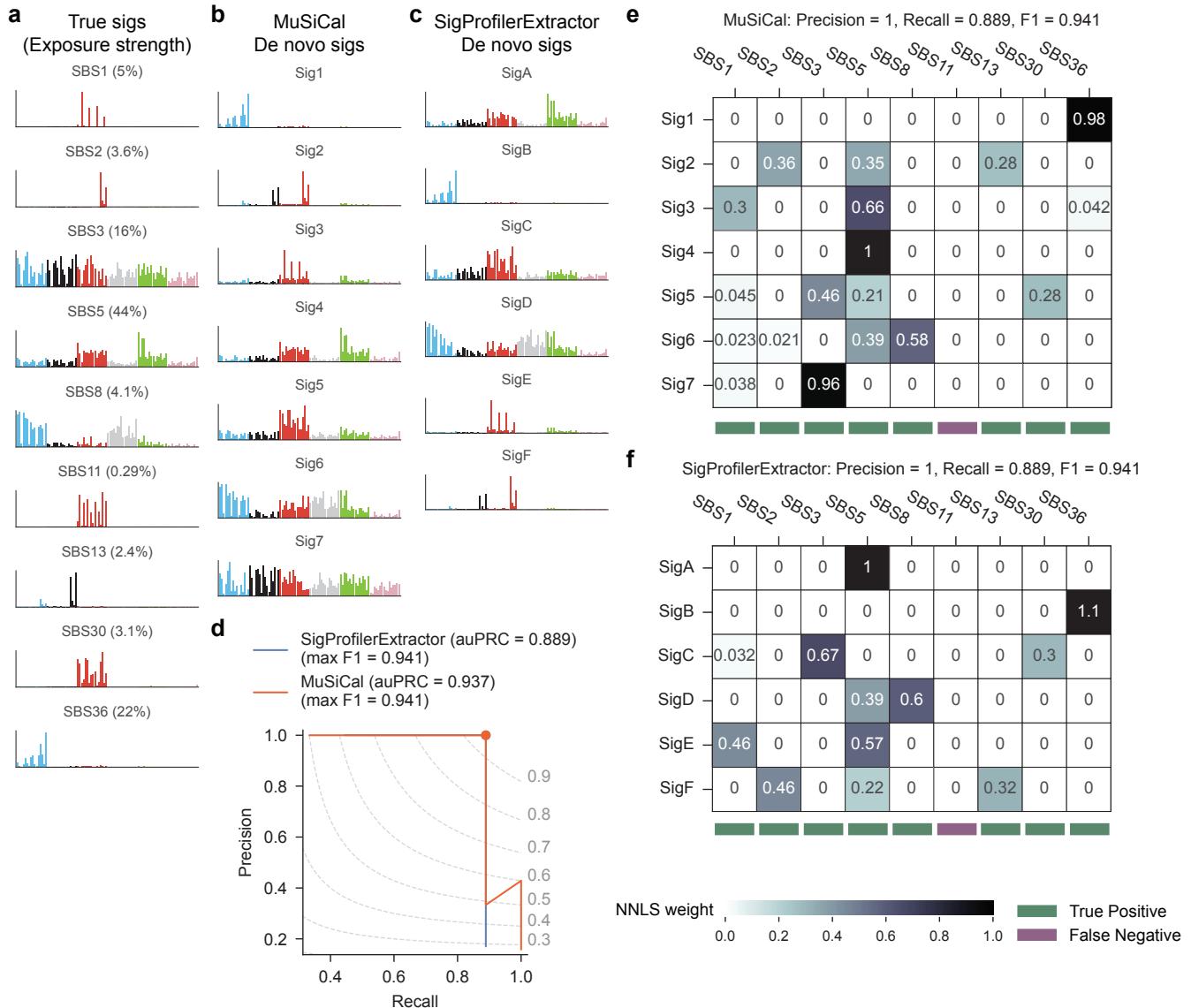
Supplementary Data Fig. 10 Same as Fig. 3a, but for Head-SCC.

Stomach-AdenoCA



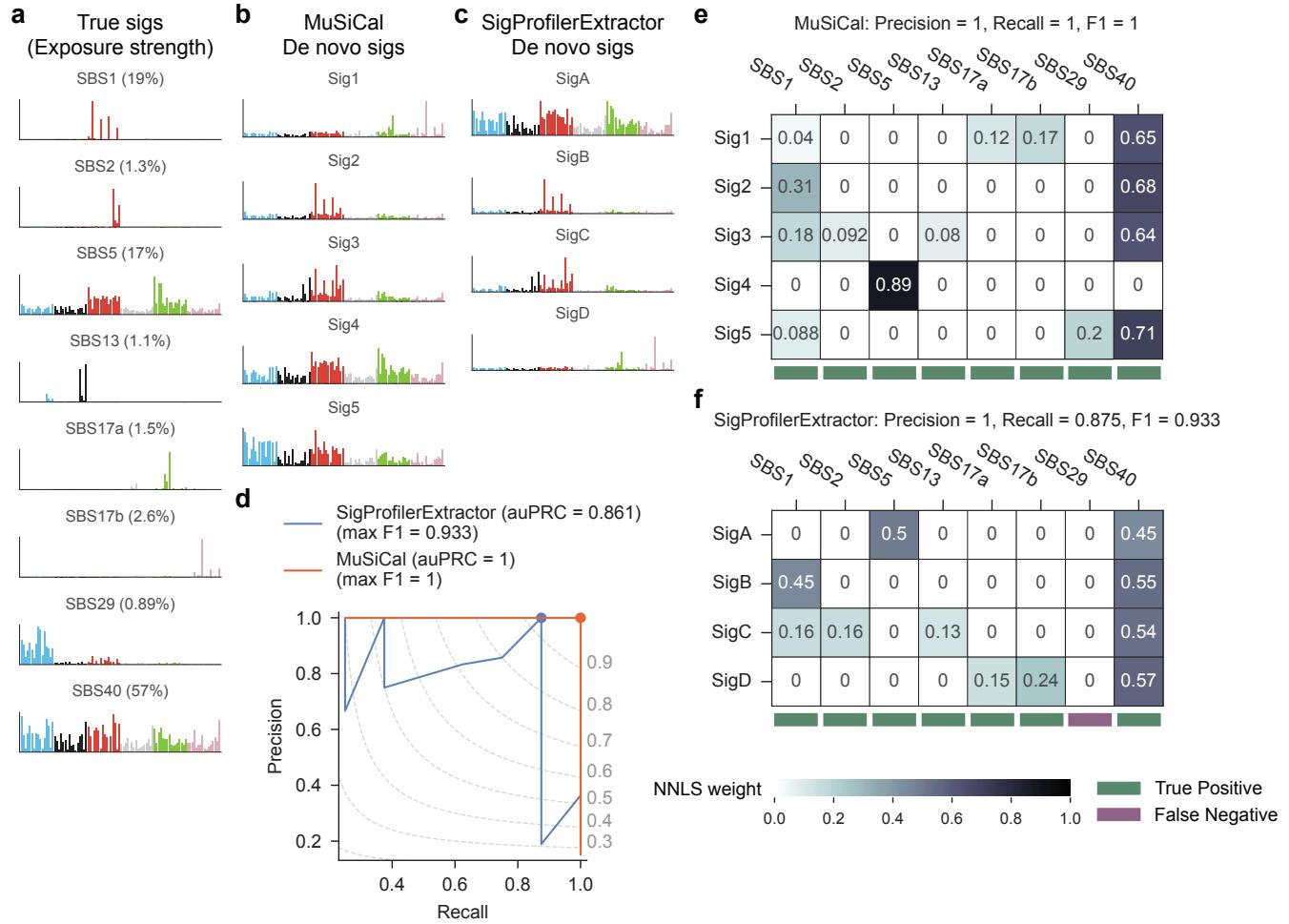
Supplementary Data Fig. 11 Same as Fig. 3a, but for Stomach-AdenoCA.

Panc-Endocrine



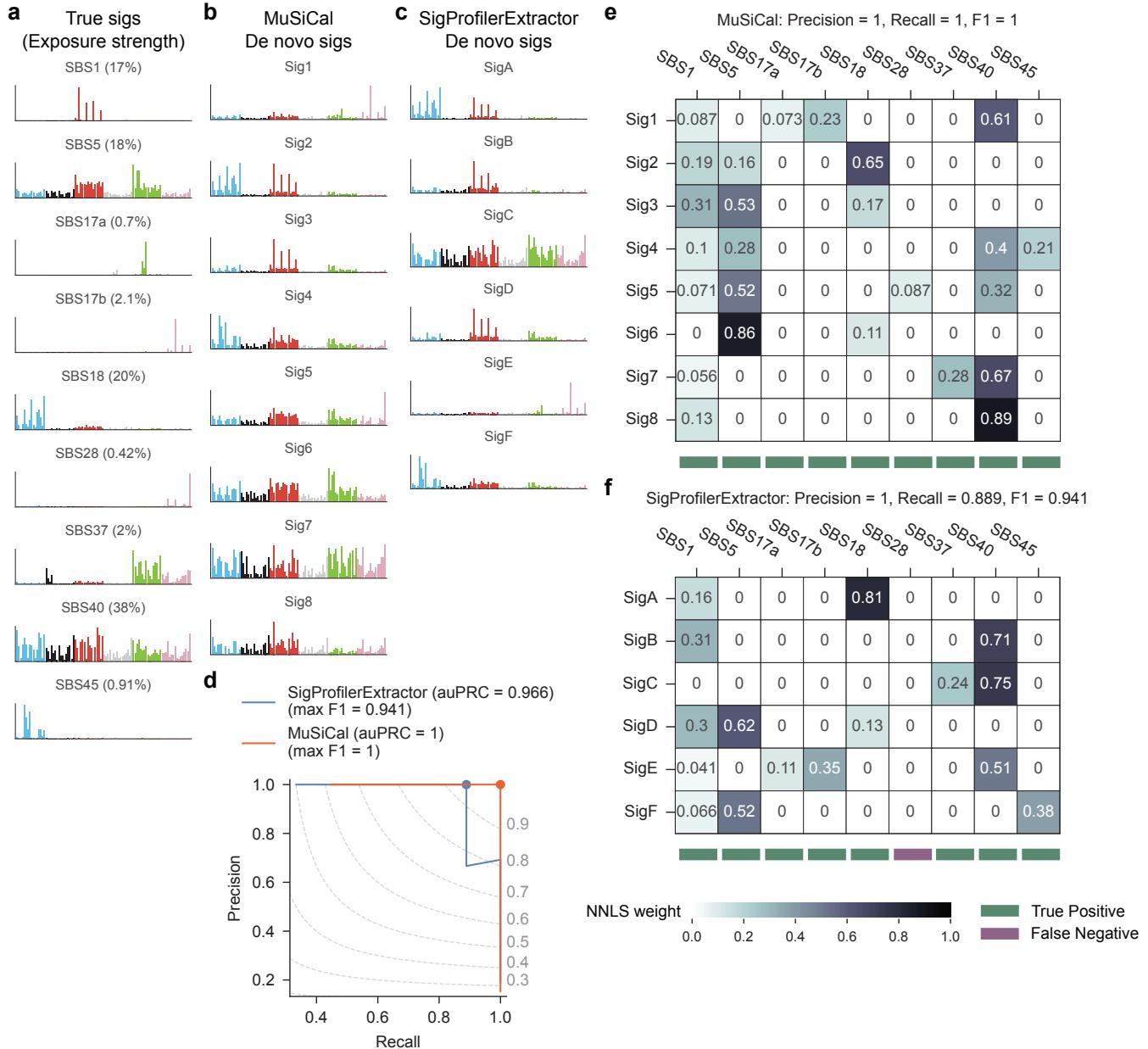
Supplementary Data Fig. 12 Same as Fig. 3a, but for Panc-Endocrine.

Kidney-ChRCC



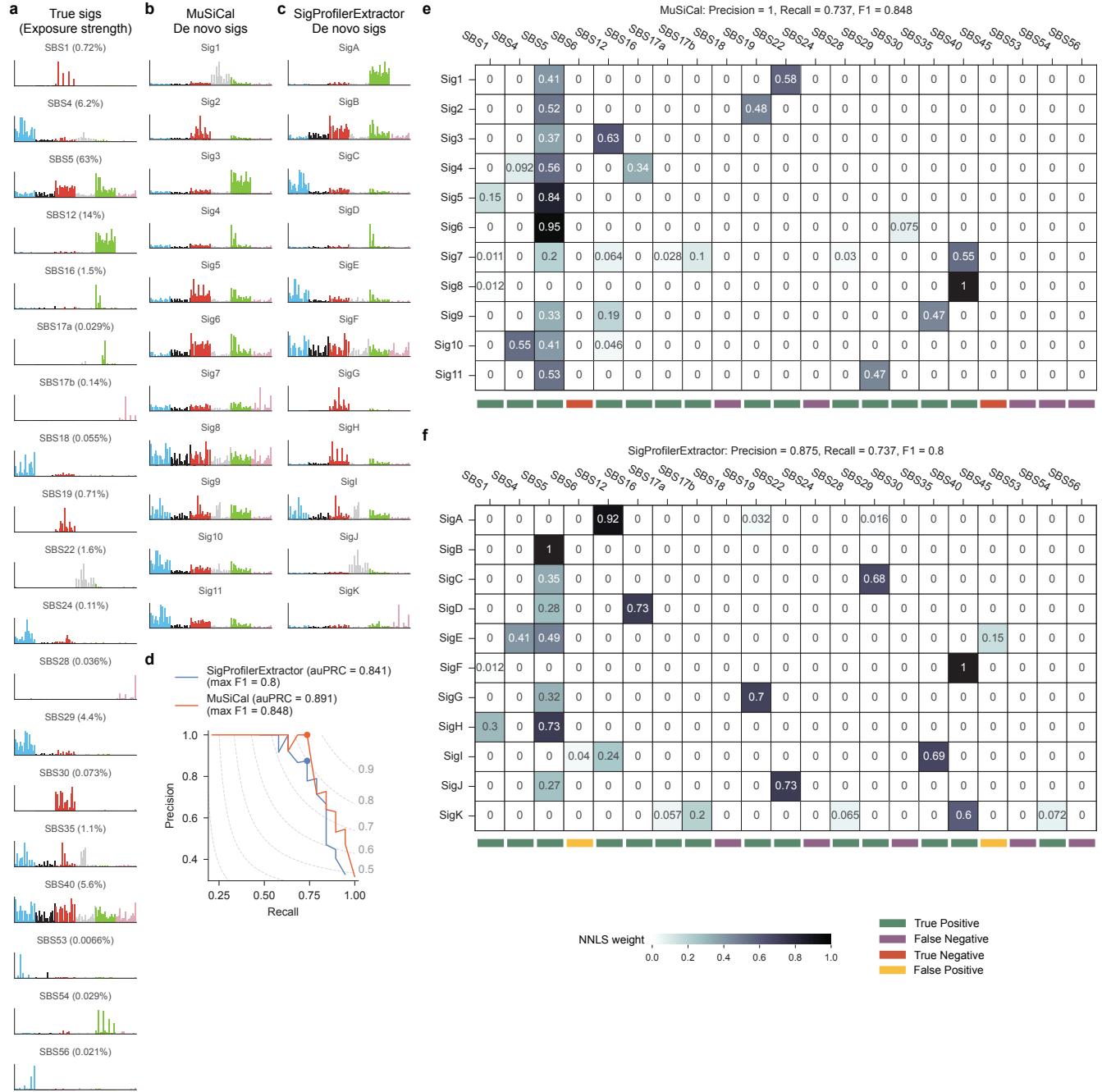
Supplementary Data Fig. 13 Same as Fig. 3a, but for Kidney-ChRCC.

ColoRect-AdenoCA



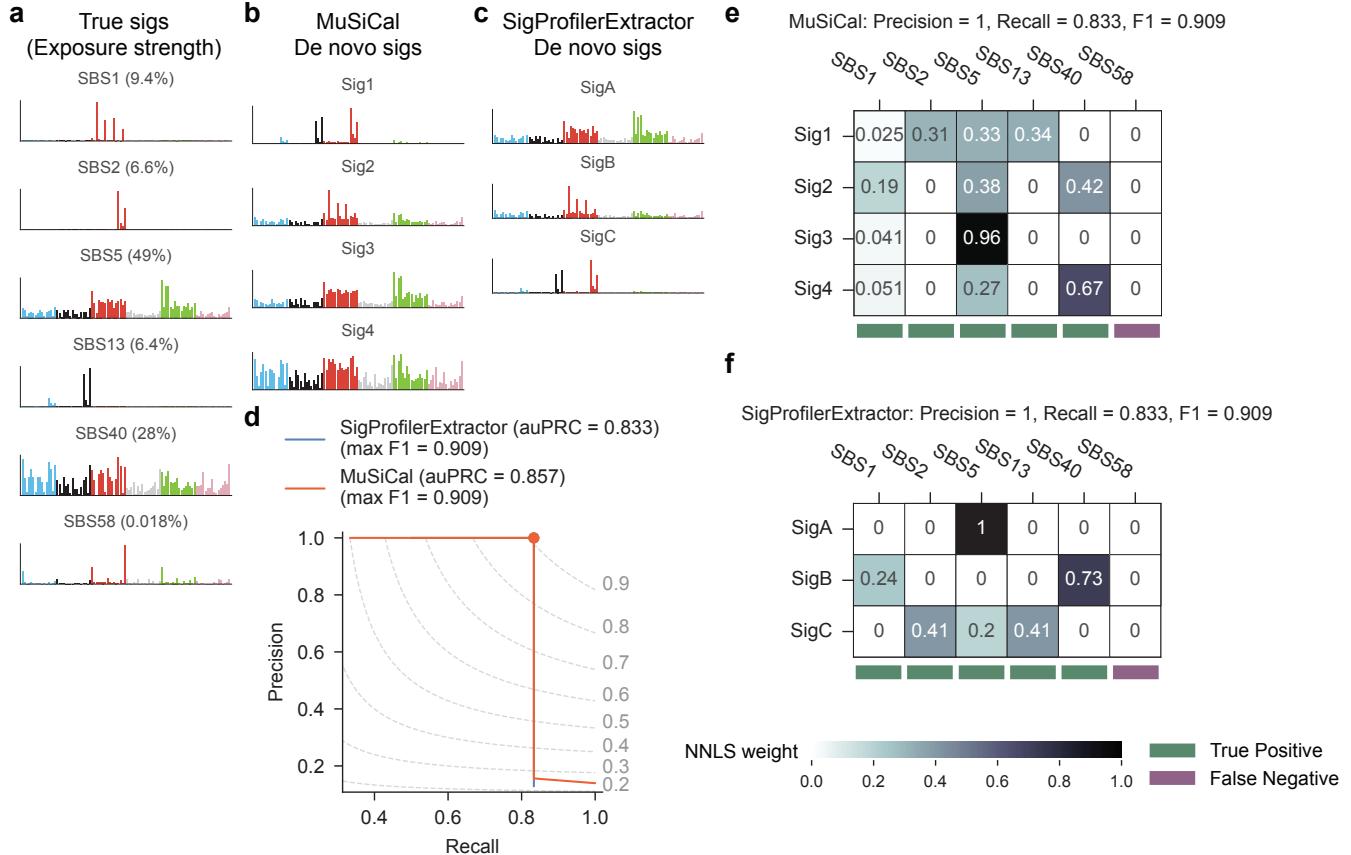
Supplementary Data Fig. 14 Same as Fig. 3a, but for ColoRect-AdenoCA.

Liver-HCC



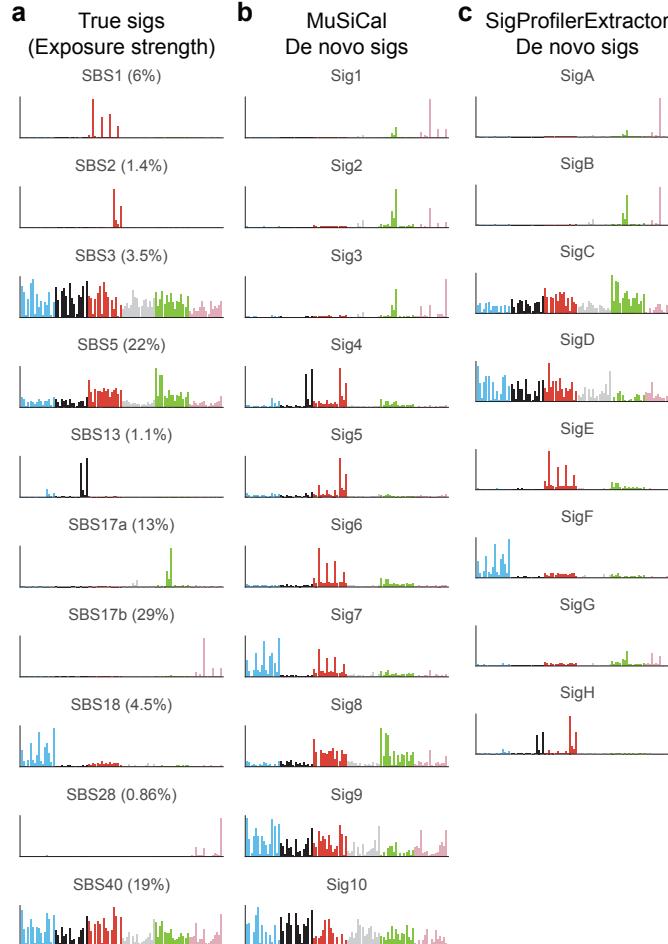
Supplementary Data Fig. 15 Same as Fig. 3a, but for Liver-HCC.

Thy-AdenoCA



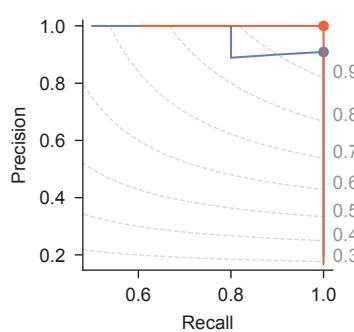
Supplementary Data Fig. 16 Same as Fig. 3a, but for Thy-AdenoCA.

Eso-AdenoCA



d

- SigProfilerExtractor (auPRC = 0.981) (max F1 = 0.952)
- MuSiCal (auPRC = 1) (max F1 = 1)

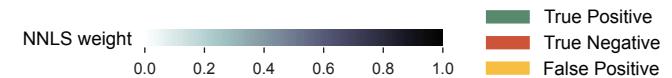


e MuSiCal: Precision = 1, Recall = 1, F1 = 1

	SBS ₁	SBS ₂	SBS ₃	SBS ₅	SBS ₁₃	SBS ₁₆	SBS _{17a}	SBS _{17b}	SBS ₁₈	SBS ₂₈	SBS ₄₀
Sig1	0	0	0	0.13	0	0	0.2	0.66	0	0	0
Sig2	0	0	0	0.36	0	0	0.45	0.18	0	0	0
Sig3	0	0	0	0.13	0	0	0.29	0	0	0.36	0.21
Sig4	-0.042	0.19	0	0.46	0.28	0	0.025	0	0	0	0
Sig5	0.15	0.3	0	0	0.032	0	0	0	0	0	0.53
Sig6	0.36	0	0	0.64	0	0	0	0	0	0	0
Sig7	0.14	0	0	0.2	0	0	0	0	0.67	0	0
Sig8	0	0	0	1.1	0	0	0	0.029	0	0	0
Sig9	-0.047	0	0	0	0	0	0	0	0	0	0.99
Sig10	0	0	1	0	0	0	0	0	0	0	0

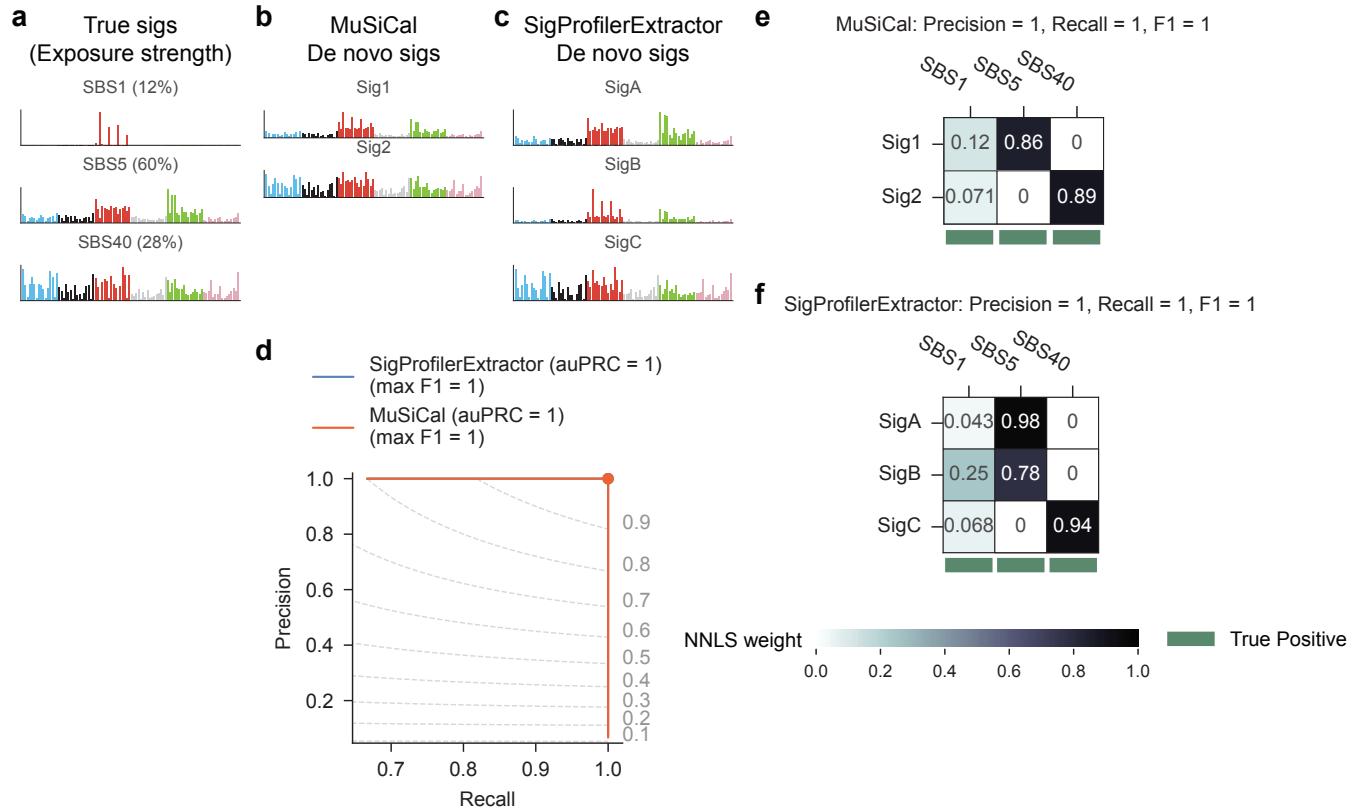
f SigProfilerExtractor: Precision = 0.909, Recall = 1, F1 = 0.952

	SBS ₁	SBS ₂	SBS ₃	SBS ₅	SBS ₁₃	SBS ₁₆	SBS _{17a}	SBS _{17b}	SBS ₁₈	SBS ₂₈	SBS ₄₀
SigA	0	0	0	0.15	0	0	0.12	0.75	0	0	0
SigB	0	0	0	0.063	0	0	0.46	0.47	0	0	0
SigC	0	0	0.34	0.68	0	0	0	0	0	0	0
SigD	0.08	0	0	0	0	0	0	0	0	0	0.88
SigE	0.45	0	0	0.62	0	0	0	0	0	0	0
SigF	0	0	0	0	0	0.052	0	0	0.93	0	0
SigG	0	0	0	0.46	0	0	0.16	0	0	0.41	0
SigH	-0.069	0.43	0.16	0	0.34	0	0	0	0	0	0



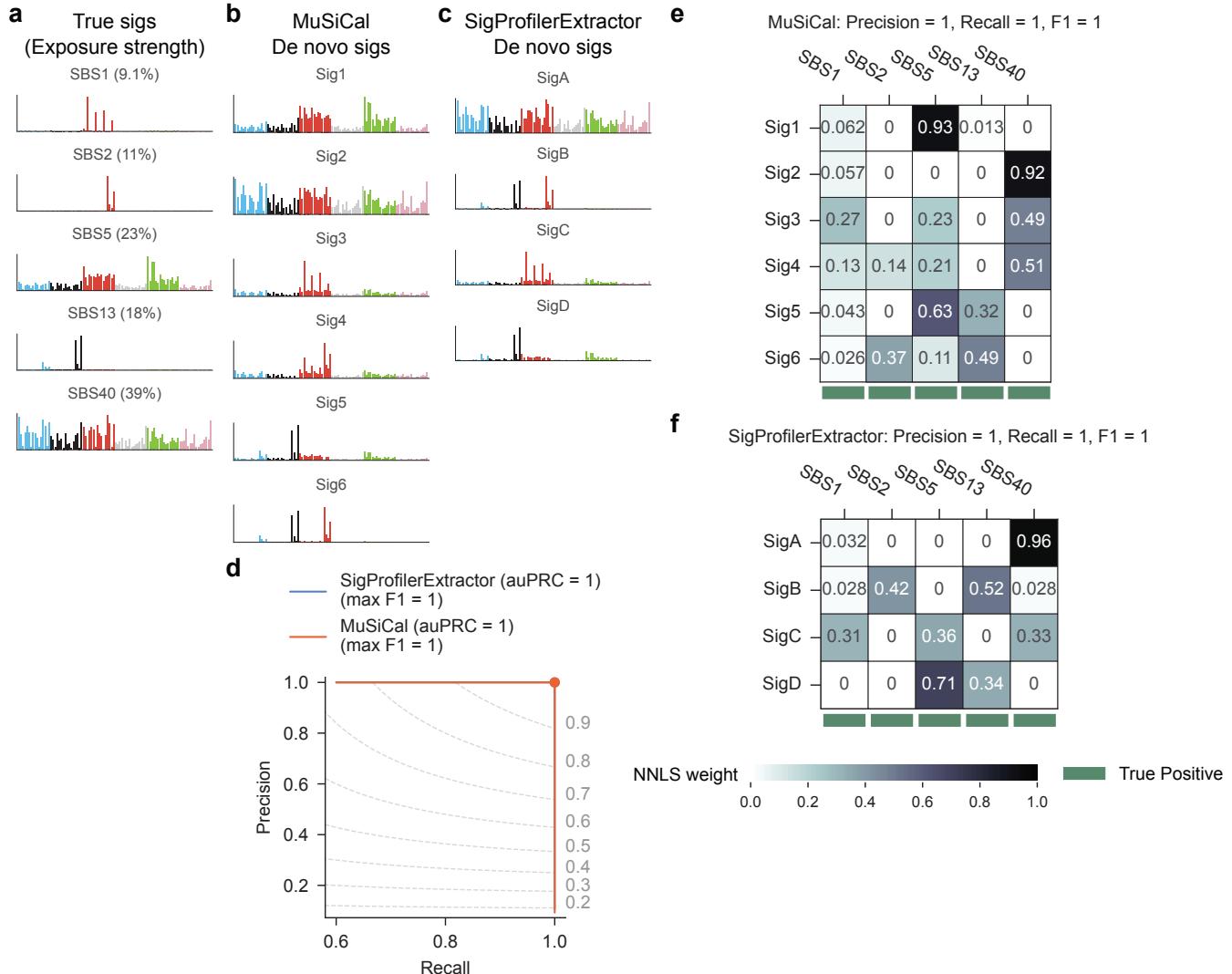
Supplementary Data Fig. 17 Same as Fig. 3a, but for Eso-AdenoCA.

Lymph-CLL



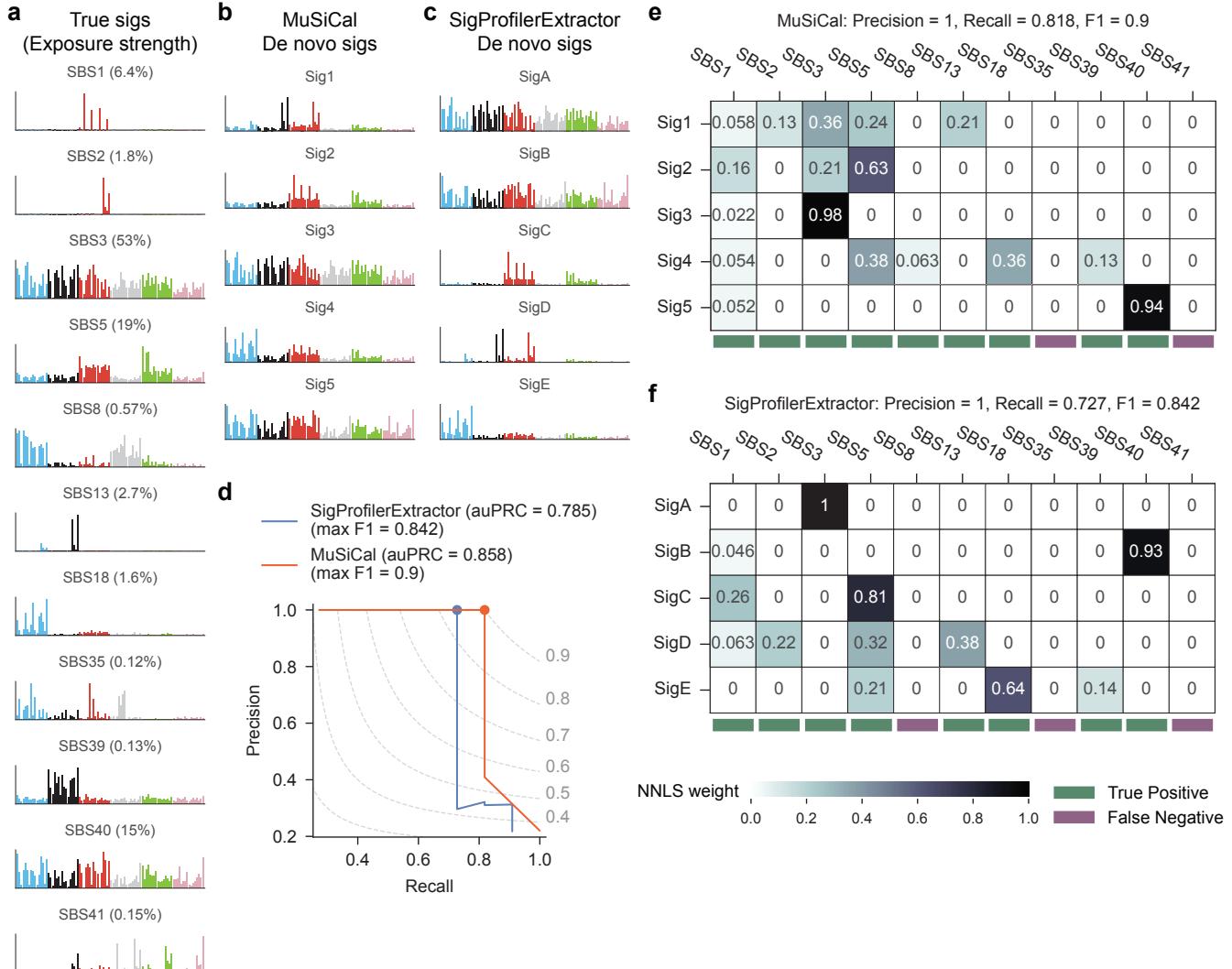
Supplementary Data Fig. 18 Same as Fig. 3a, but for Lymph-CLL.

Uterus-AdenoCA



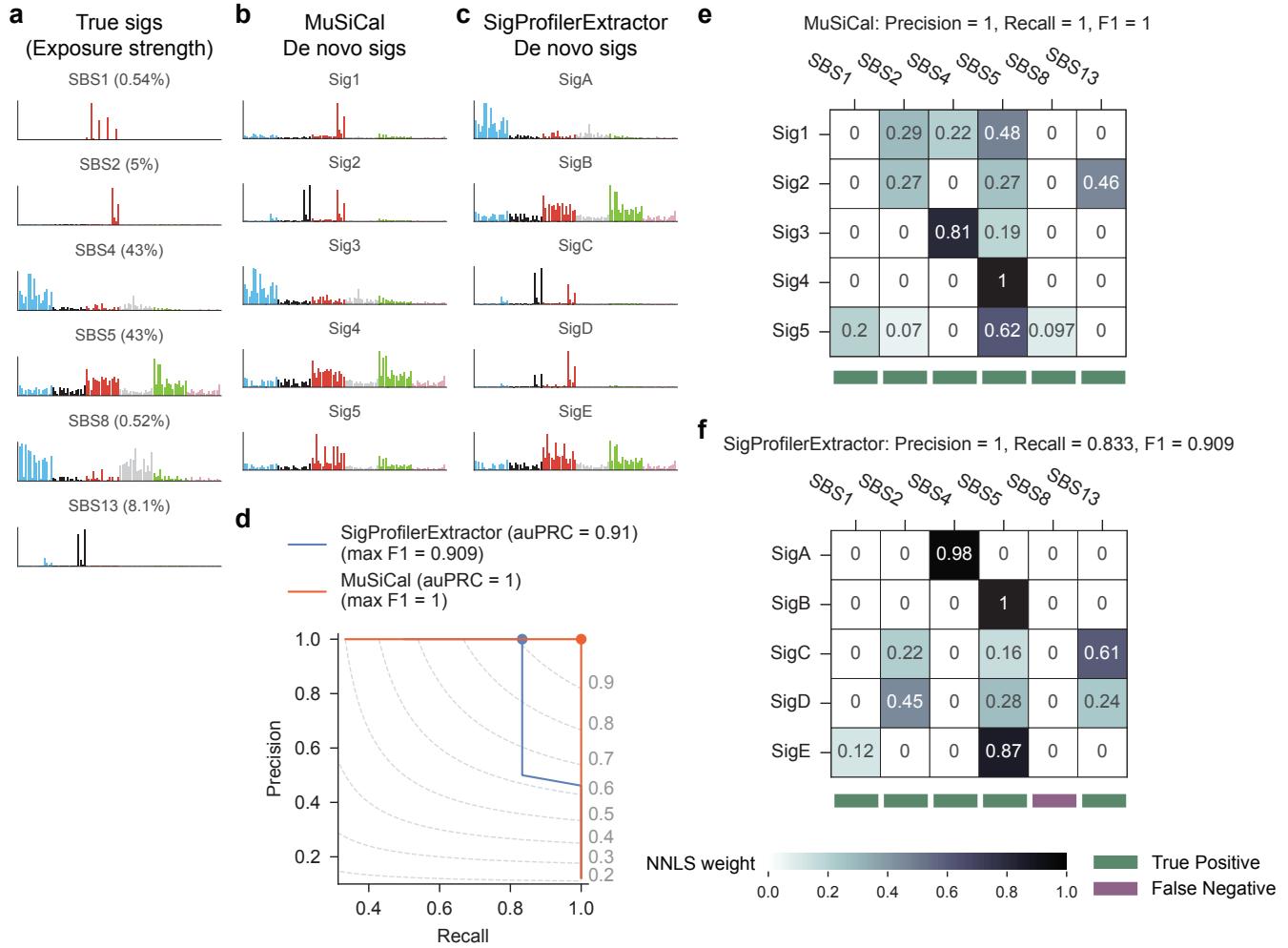
Supplementary Data Fig. 19 Same as Fig. 3a, but for Uterus-AdenoCA.

Ovary-AdenoCA



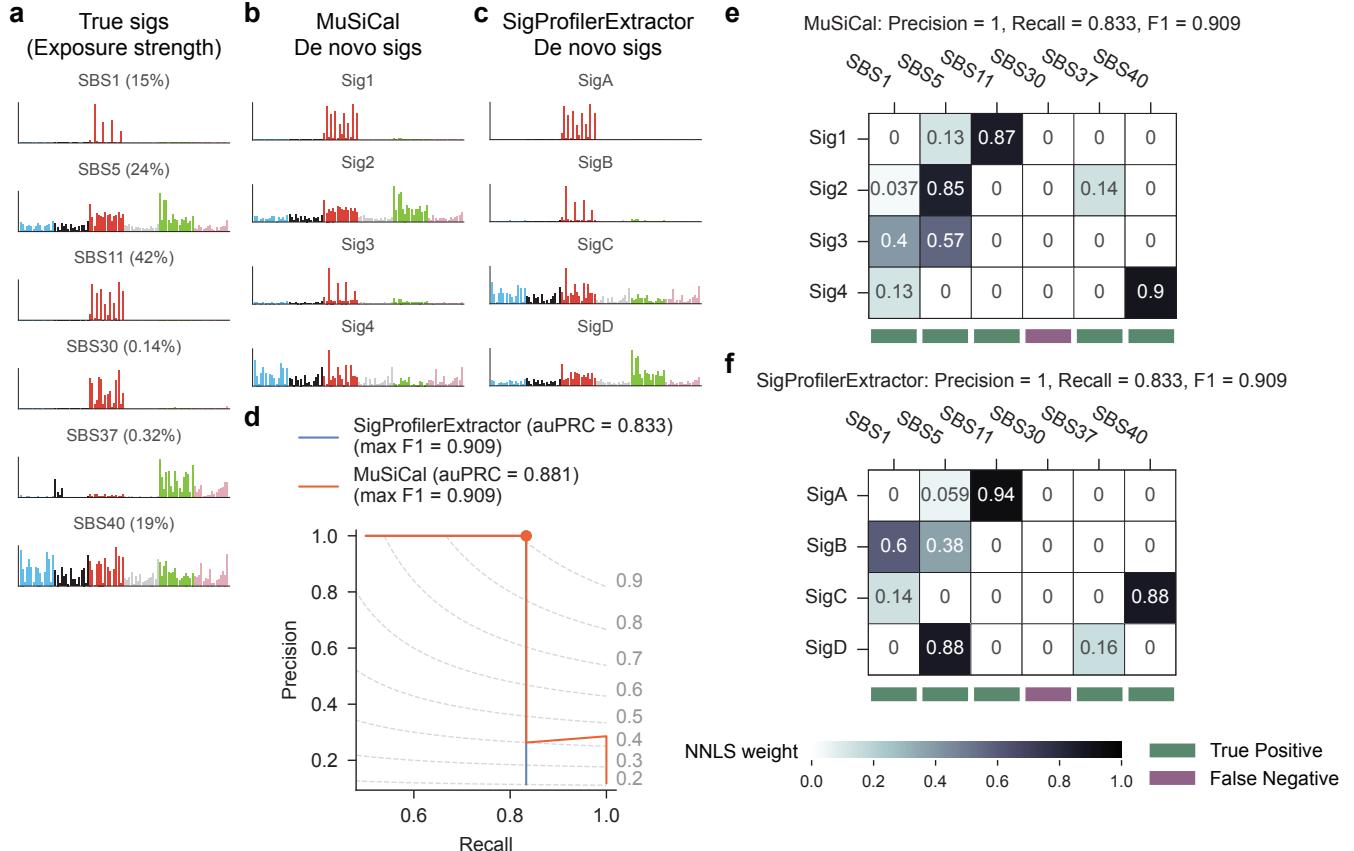
Supplementary Data Fig. 20 Same as Fig. 3a, but for Ovary-AdenoCA.

Lung-SCC



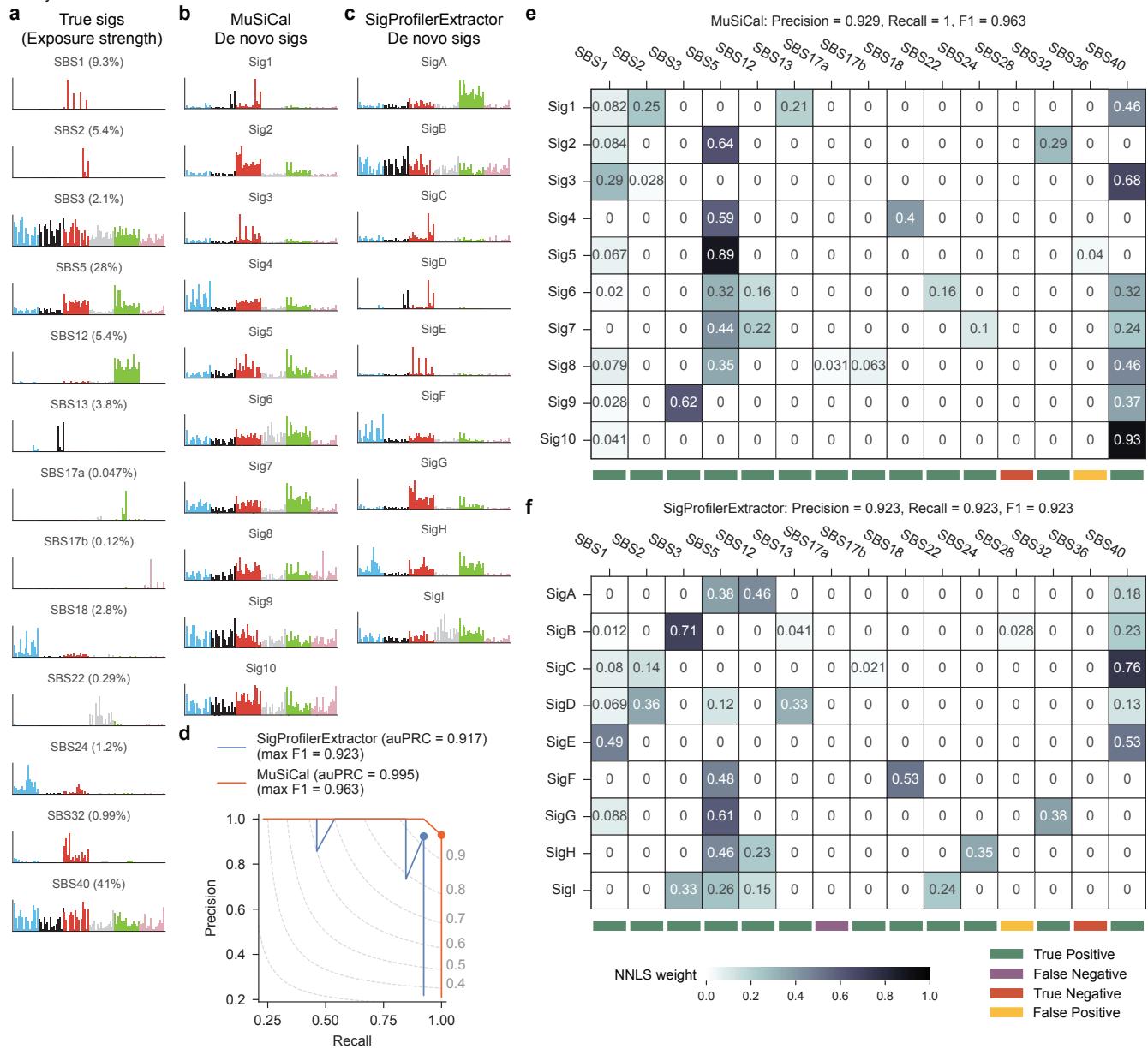
Supplementary Data Fig. 21 Same as Fig. 3a, but for Lung-SCC.

CNS-GBM



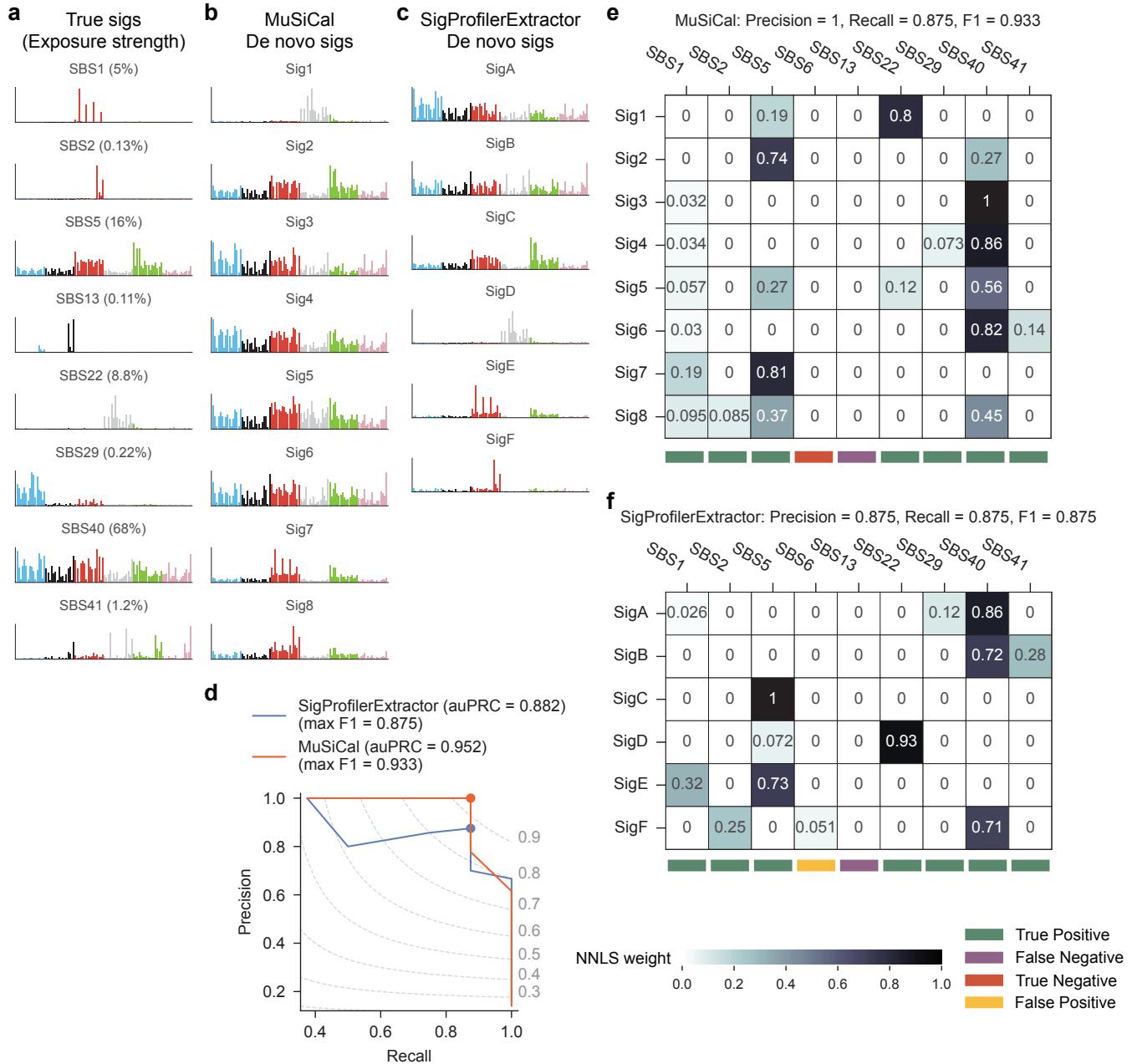
Supplementary Data Fig. 22 Same as Fig. 3a, but for CNS-GBM.

Biliary-AdenoCA



Supplementary Data Fig. 23 Same as Fig. 3a, but for Biliary-AdenoCA.

Kidney-RCC



Supplementary Data Fig. 24 Same as Fig. 3a, but for Kidney-RCC.