SUPPLEMENTAL MATERIAL

Supplemental Tables

Supplementary Table I. Human Heart History

Heart No.	Age	Sex	Prep	Diagnoses
Heart #1	54	F	Biatrial	HTN, drug abuse
Heart #2[1,2]	47	M	LRA	ICM, CAD, LVAD, ICD
Heart #3[1,2]	40	M	LRA	NICM, PM/ICD, LVAD
Heart #4[1,2]	60	F	LRA	AF, NICM, PM/ICD
Heart #5[1]	62	F	LRA	NICM, HTN, DM, PM/ICD
Heart #6	53	M	LRA	AF, NICM, HTN, LVAD,CRTD,
Heart #7	31	F	Biatrial	SCD, VF
Heart #8	50	F	Biatrial	Hyperthyroidism
Heart #9	24	F	Biatrial	Asthma, Cardiopulmonary arrest
Heart #10	60	F	Biatrial	HTN, drug abuse
Heart #11	43	M	Biatrial	AF, SND, NICM, LVAD, ICD

AF-atrial fibrillation; CAD-coronary artery disease; CRTD-cardiac resynchronization therapy defibrillator; DM-diabetes; HTN-hypertension; (PM/)ICD-(pacemaker/)implantable cardioverter-defibrillator; LRA-lateral right atrium; LVAD-left ventricular assist device; (N/)ICM- (non/)ischemic cardiomyopathy; SCD-sudden cardiac death; SND-sinus node dysfunction; VF – ventricular fibrillation.

Previous publications in which some ex-vivo hearts were included shown below:

1. Hansen BJ, Zhao J, Li N, et al. Human Atrial Fibrillation Drivers Resolved With Integrated Functional and Structural Imaging to Benefit Clinical Mapping. *JACC Clin Electrophysiol*. 2018;4(12):1501-1515. doi:10.1016/j.jacep.2018.08.024
2. Li N, Csepe TA, Hansen BJ, et al. Adenosine-Induced Atrial Fibrillation. *Circulation*. 2016;134(6):486-498. doi:10.1161/CIRCULATIONAHA.115.021165

Supplementary Table II. Statistical performance metrics

Algorithm		MEM Single-electrode					
		LD center	LD center + periphery	HD center	HD center + periphery	LD+HD center	LD+HD center + periphery
kNN	accuracy	0.84 ± 0.06	0.76 ± 0.03	0.84 ± 0.03	0.78 ± 0.09	0.87 ± 0.03	0.76 ± 0.03
	precision	0.36 ± 0.21	0.35 ± 0.11	0.63 ± 0.12	0.63 ± 0.21	0.43 ± 0.19	0.44 ± 0.10
	recall	0.22 ± 0.11	0.24 ± 0.08	0.46 ± 0.13	0.65 ± 0.24	0.25 ± 0.10	0.35 ± 0.08
	f1-score	0.27 ± 0.15	0.28 ± 0.09	**0.53 ± 0.12**	0.63 ± 0.21	0.31 ± 0.12	0.39 ± 0.09
XGBoost	accuracy	0.83 ± 0.08	0.77 ± 0.04	0.74 ± 0.06	0.72 ± 0.06	0.88 ± 0.02	0.77 ± 0.05
	precision	0.36 ± 0.22	0.33 ± 0.11	0.37 ± 0.1	0.54 ± 0.1	0.41 ± 0.13	0.48 ± 0.13
	recall	0.26 ± 0.16	0.19 ± 0.1	0.4 ± 0.17	0.75 ± 0.15	0.15 ± 0.07	0.28 ± 0.1
	f1-score	**0.28 ± 0.15**	0.23 ± 0.1	0.37 ± 0.12	0.62 ± 0.1	0.21 ± 0.09	0.35 ± 0.11
RF	accuracy	0.74 ± 0.04	0.66 ± 0.03	0.70 ± 0.07	0.68 ± 0.08	0.70 ± 0.06	0.77 ± 0.04
	precision	0.08 ± 0.06	0.24 ± 0.06	0.34 ± 0.09	0.5 ± 0.12	0.22 ± 0.07	0.52 ± 0.13
	recall	0.24 ± 0.16	0.35 ± 0.12	0.5 ± 0.09	0.77 ± 0.2	0.6 ± 0.16	0.23 ± 0.06
	f1-score	0.12 ± 0.07	0.28 ± 0.06	0.4 ± 0.09	0.6 ± 0.13	0.32 ± 0.10	0.31 ± 0.08
SVM	accuracy	0.89 ± 0.03	0.77 ± 0.06	0.80 ± 0.02	0.79 ± 0.08	0.87 ± 0.03	0.75 ± 0.04
	precision	0.15 ± 0.19	0.41 ± 0.15	0.52 ± 0.16	0.66 ± 0.17	0.41 ± 0.22	0.45 ± 0.09
	recall	0.09 ± 0.1	0.4 ± 0.13	0.27 ± 0.13	0.66 ± 0.26	0.19 ± 0.11	0.49 ± 0.11
	f1-score	0.11 ± 0.12	**0.4 ± 0.14**	0.33 ± 0.12	0.64 ± 0.19	0.26 ± 0.14	**0.47 ± 0.09**
LR	accuracy	0.928 ± 0.001	0.720 ± 0.013	0.812 ± 0.019	0.770 ± 0.018	0.826 ± 0.012	0.698 ± 0.008
	precision	0.30 ± 0.05	0.31 ± 0.02	0.52 ± 0.06	0.63 ± 0.03	0.30 ± 0.03	0.39 ± 0.01
	recall	0.07 ± 0.02	0.40 ± 0.04	0.46 ± 0.04	0.69 ± 0.04	0.46 ± 0.05	0.54 ± 0.03
	f1-score	0.11 ± 0.03	0.35 ± 0.03	0.49 ± 0.05	**0.66 ± 0.03**	**0.36 ± 0.04**	0.45 ± 0.02

Supplementary Table II continued

Algorithm		MEM Neighborhood					
		LD center	LD center + periphery	HD center	HD center + periphery	LD+HD center	LD+HD center + periphery
kNN	accuracy	0.893 ± 0.011	0.875 ± 0.014	0.892 ± 0.005	0.875 ± 0.016	0.902 ± 0.008	0.819 ± 0.011
	precision	0.26 ± 0.05	0.69 ± 0.04	0.73 ± 0.01	0.78 ± 0.03	0.55 ± 0.04	0.62 ± 0.03
	recall	0.34 ± 0.08	0.63 ± 0.05	0.70 ± 0.04	0.84 ± 0.04	0.52 ± 0.04	0.59 ± 0.03
	f1-score	**0.30 ± 0.06**	**0.66 ± 0.04**	**0.72 ± 0.02**	**0.81 ± 0.02**	**0.54 ± 0.04**	0.60 ± 0.02
XGBoost	accuracy	0.923 ± 0.008	0.866 ± 0.011	0.840 ± 0.018	0.811 ± 0.014	0.902 ± 0.005	0.821 ± 0.010
	precision	0.4 ± 0.1	0.84 ± 0.05	0.56 ± 0.04	0.64 ± 0.02	0.60 ± 0.03	0.63 ± 0.02
	recall	0.20 ± 0.06	0.37 ± 0.04	0.81 ± 0.05	0.94 ± 0.02	0.31 ± 0.05	0.56 ± 0.05
	f1-score	0.26 ± 0.07	0.51 ± 0.05	0.66 ± 0.04	0.76 ± 0.02	0.41 ± 0.05	0.59 ± 0.03

RF	accuracy	0.898 ± 0.004	0.807 ± 0.011	0.880 ± 0.015	0.837 ± 0.020	0.886 ± 0.008	0.801 ± 0.012
	precision	0.22 ± 0.04	0.50 ± 0.02	0.71 ± 0.05	0.71 ± 0.03	0.47 ± 0.04	0.57 ± 0.03
	recall	0.21 ± 0.05	0.57 ± 0.02	0.64 ± 0.03	0.84 ± 0.03	0.43 ± 0.03	0.58 ± 0.02
	f1-score	0.21 ± 0.05	0.53 ± 0.01	0.67 ± 0.03	0.77 ± 0.03	0.45 ± 0.03	0.57 ± 0.02
SVM	accuracy	0.915 ± 0.007	0.875 ± 0.014	0.868 ± 0.016	0.866 ± 0.013	0.903 ± 0.004	0.834 ± 0.009
	precision	0.24 ± 0.07	0.72 ± 0.04	0.74 ± 0.06	0.80 ± 0.02	0.61 ± 0.04	0.67 ± 0.02
	recall	0.13 ± 0.04	0.57 ± 0.07	0.49 ± 0.06	0.77 ± 0.03	0.32 ± 0.03	0.57 ± 0.03
	f1-score	0.17 ± 0.05	0.64 ± 0.05	0.59 ± 0.06	0.78 ± 0.02	0.42 ± 0.03	**0.61 ± 0.02**
LR	accuracy	0.891 ± 0.008	0.758 ± 0.009	0.825 ± 0.013	0.788 ± 0.009	0.841 ± 0.014	0.721 ± 0.012
	precision	0.14 ± 0.05	0.36 ± 0.02	0.54 ± 0.03	0.67 ± 0.02	0.34 ± 0.04	0.43 ± 0.02
	recall	0.12 ± 0.05	0.32 ± 0.03	0.64 ± 0.04	0.66 ± 0.02	0.48 ± 0.03	0.56 ± 0.04
	f1-score	0.13 ± 0.05	0.34 ± 0.03	0.59 ± 0.03	0.67 ± 0.02	0.40 ± 0.04	0.48 ± 0.03

Statistical performance metrics comparing the binary spectral classifiers including k-Nearest Neighbors (kNN), Scalable Gradient Boosting (XGBoost), Support Vector Machine (SVM), Random Forest (RF) and Logistic Regression (LR) for different datasets and feature sets. Datasets contain samples from low-density catheters (LD), samples from high-density catheters (HD), and a combination of both datasets (HD+LD). Feature sets contain features generated from the spectra of multi-electrode mapping (MEM) samples (MEM single-electrode), features from the spectra of electrode-neighborhood MEM samples (MEM electrode-neighborhood). All metrics are calculated on 10-folds of the testing set at their optimal ROC threshold computed on the training set.

Supplementary Table III. Driver contrast for each AF recordings.

Type of catheter	Number of recording	Driver Contrast	Type of catheter	Number of recording	Driver Contrast
High Density	HD_1	0.48	Low Density	LD_10	0.37
	HD_2	0.44		LD_11	0.02
	HD_3	0.28		LD_12	-0.07
	HD_4	0.19		LD_13	0.12
	HD_5	-0.01		LD_14	0.29
	HD_6	0.32		LD_15	0.41
	HD_7	0.27		LD_16	-0.13
Low Density	LD_1	0.48		LD_17	0.22
	LD_2	0.21		LD_18	0.22
	LD_3	0.35		LD_19	0.44
	LD_4	0.18		LD_20	-0.04
	LD_5	-0.02		LD_21	0.39
	LD_6	0.02		LD_22	0.62
	LD_7	0.06		LD_23	0.73
	LD_8	0.10		LD_24	-0.20
	LD_9	0.70		LD_25	0.20

Abbreviations as in **Supplementary Table II**.

Supplementary Table IV. Feature Values for MEM and NIOM Feature Sets.

	MEM single-electrode center				MEM neighborhood center			
	Driver mean	Non-driver mean	Driver SD	Non-driver SD	Driver mean	Non-driver mean	Driver SD	Non-driver SD
#peaks_0.05	5.93	10.44	5.21	6.99	6.52	10.49	4.53	5.81
#peaks_0.1	3.24	6.05	3.20	4.82	3.62	6.08	2.75	3.86
frequency 1	11.24	9.63	3.38	3.80	10.98	9.59	2.90	2.86
frequency 2	11.15	9.37	4.77	4.77	10.83	9.35	3.19	3.22
frequency 3	9.78	8.56	4.51	4.79	9.70	8.53	3.10	3.31
frequency 4	9.26	7.79	4.61	4.49	9.13	7.81	3.09	2.93
frequency 5	9.02	7.68	4.37	4.30	8.93	7.68	2.85	2.75
height 1	0.0342	0.0202	0.0265	0.0188	0.0327	0.0204	0.0189	0.0151
height 2	0.0100	0.0097	0.0079	0.0086	0.0103	0.0097	0.0058	0.0066
height 3	0.0062	0.0066	0.0036	0.0058	0.0066	0.0067	0.0034	0.0043
height 4	0.0047	0.0054	0.0028	0.0050	0.0050	0.0054	0.0027	0.0037
height 5	0.0040	0.0047	0.0023	0.0043	0.0042	0.0047	0.0022	0.0033
width 1	1.66	2.03	1.12	1.99	1.74	2.05	1.00	1.41
width 2	1.91	2.01	1.80	1.96	1.97	2.01	1.35	1.21
width 3	1.67	1.80	1.27	1.31	1.68	1.79	0.59	0.63
width 4	1.61	1.68	1.17	1.14	1.60	1.68	0.51	0.53
width 5	1.59	1.61	1.11	1.05	1.57	1.61	0.46	0.48
prominence 1	0.0339	0.0199	0.0265	0.0187	0.0324	0.0200	0.0189	0.0151
prominence 2	0.0083	0.0080	0.0078	0.0079	0.0085	0.0080	0.0057	0.0061
prominence 3	0.0041	0.0045	0.0034	0.0045	0.0044	0.0045	0.0031	0.0031
prominence 4	0.0028	0.0033	0.0024	0.0037	0.0030	0.0033	0.0021	0.0025
prominence 5	0.0022	0.0026	0.0018	0.0029	0.0023	0.0026	0.0014	0.0020
height ratio between peaks 1 and 2	4.33	2.50	4.26	2.49	4.04	2.52	3.02	1.97
height ratio between peaks 1 and 3	6.81	3.89	6.23	4.05	6.36	3.90	4.82	3.11
height ratio between peaks 1 and 4	8.56	5.14	7.14	5.25	8.09	5.14	5.63	4.16
height ratio between peaks 2 and 3	1.76	1.65	1.37	1.38	1.70	1.64	0.81	1.00
height ratio between peaks 2 and 4	2.40	2.27	2.10	2.30	2.33	2.26	1.32	1.83
height ratio between peaks 3 and 4	1.43	1.38	0.88	0.95	1.42	1.38	0.64	0.82
prominence ratio between peaks 1 and 2	333.00	13.88	15396.89	528.26	226.44	27.94	4335.01	1187.52

prominence ratio between peaks 1 and 3	44.24	19.96	415.70	365.40	43.33	19.86	200.95	153.11
prominence ratio between peaks 1 and 4	111.49	38.88	2074.35	655.12	101.14	45.56	806.49	505.88
prominence ratio between peaks 2 and 3	7.05	6.59	49.20	141.48	7.78	6.03	32.84	50.69
prominence ratio between peaks 2 and 4	31.08	17.72	739.78	414.54	28.24	21.31	296.73	318.20
prominence ratio between peaks 3 and 4	10.57	8.57	239.17	190.74	9.68	9.73	83.49	114.69
PSDR	5.52	5.35	0.66	0.75	5.49	5.34	0.55	0.59

Supplementary Table IV continued.

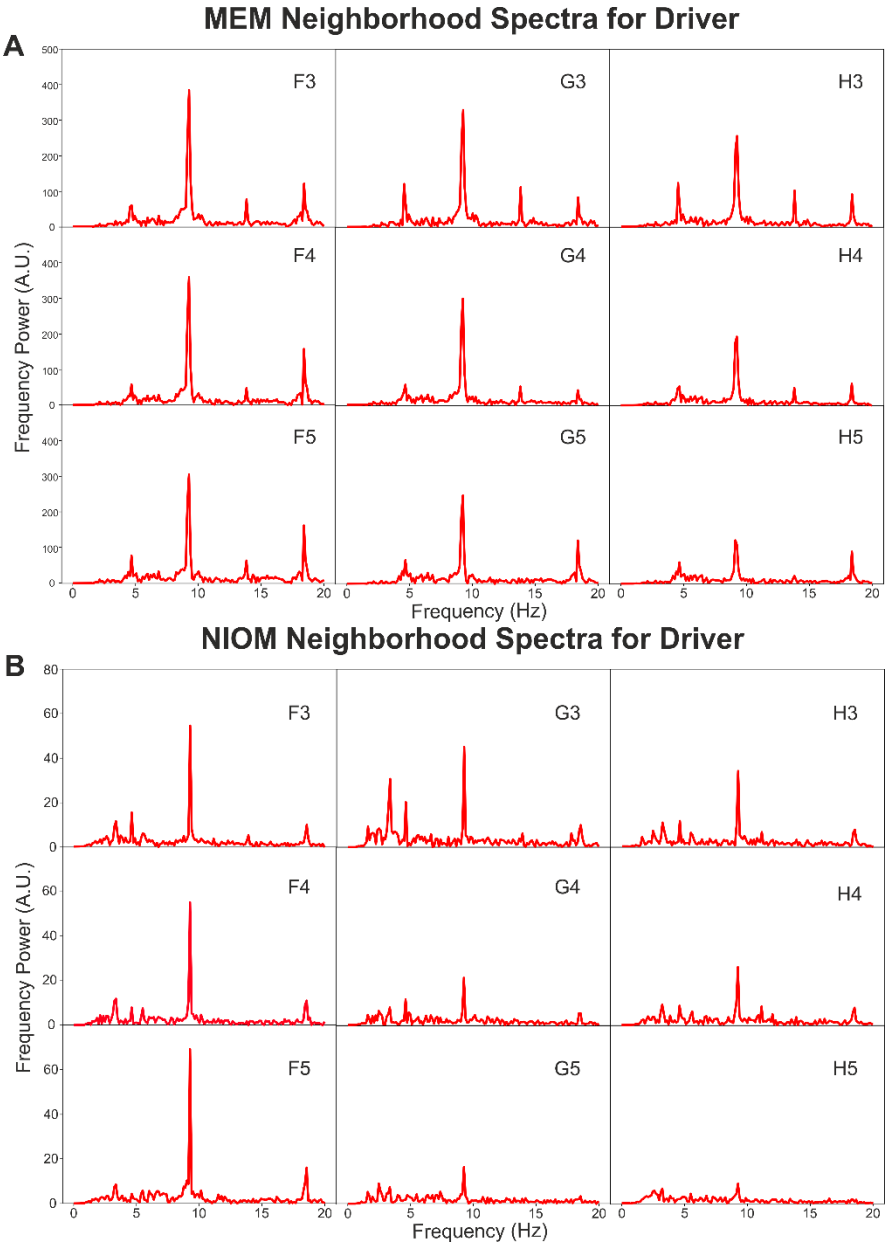
	MEM single-electrode center+periphery				MEM neighborhood center+periphery			
	Driver mean	Non-driver mean	Driver SD	Non-driver SD	Driver mean	Non-driver mean	Driver SD	Non-driver SD
#peaks_0.05	6.52	10.49	4.53	5.81	7.63	10.80	4.97	5.86
#peaks_0.1	3.62	6.08	2.75	3.86	4.25	6.29	3.13	3.90
frequency 1	10.98	9.59	2.90	2.86	10.58	9.49	2.93	2.84
frequency 2	10.83	9.35	3.19	3.22	10.50	9.21	3.32	3.17
frequency 3	9.70	8.53	3.10	3.31	9.25	8.48	3.20	3.31
frequency 4	9.13	7.81	3.09	2.93	8.69	7.74	3.10	2.90
frequency 5	8.93	7.68	2.85	2.75	8.50	7.61	2.87	2.73
height 1	0.0327	0.0204	0.0189	0.0151	0.0296	0.0193	0.0185	0.0144
height 2	0.0103	0.0097	0.0058	0.0066	0.0106	0.0096	0.0064	0.0065
height 3	0.0066	0.0067	0.0034	0.0043	0.0068	0.0066	0.0037	0.0043
height 4	0.0050	0.0054	0.0027	0.0037	0.0053	0.0054	0.0030	0.0038
height 5	0.0042	0.0047	0.0022	0.0033	0.0044	0.0047	0.0025	0.0033
width 1	1.74	2.05	1.00	1.41	1.84	2.07	1.09	1.45
width 2	1.97	2.01	1.35	1.21	2.00	2.01	1.34	1.20
width 3	1.68	1.79	0.59	0.63	1.72	1.79	0.60	0.63
width 4	1.60	1.68	0.51	0.53	1.62	1.68	0.50	0.53
width 5	1.57	1.61	0.46	0.48	1.59	1.61	0.46	0.48
prominence 1	0.0324	0.0200	0.0189	0.0151	0.0293	0.0190	0.0184	0.0143
prominence 2	0.0085	0.0080	0.0057	0.0061	0.0088	0.0078	0.0062	0.0060
prominence 3	0.0044	0.0045	0.0031	0.0031	0.0046	0.0045	0.0031	0.0032
prominence 4	0.0030	0.0033	0.0021	0.0025	0.0032	0.0033	0.0022	0.0025
prominence 5	0.0023	0.0026	0.0014	0.0020	0.0025	0.0026	0.0016	0.0021
height ratio between peaks 1 and 2	4.04	2.52	3.02	1.97	3.52	2.43	2.70	1.90

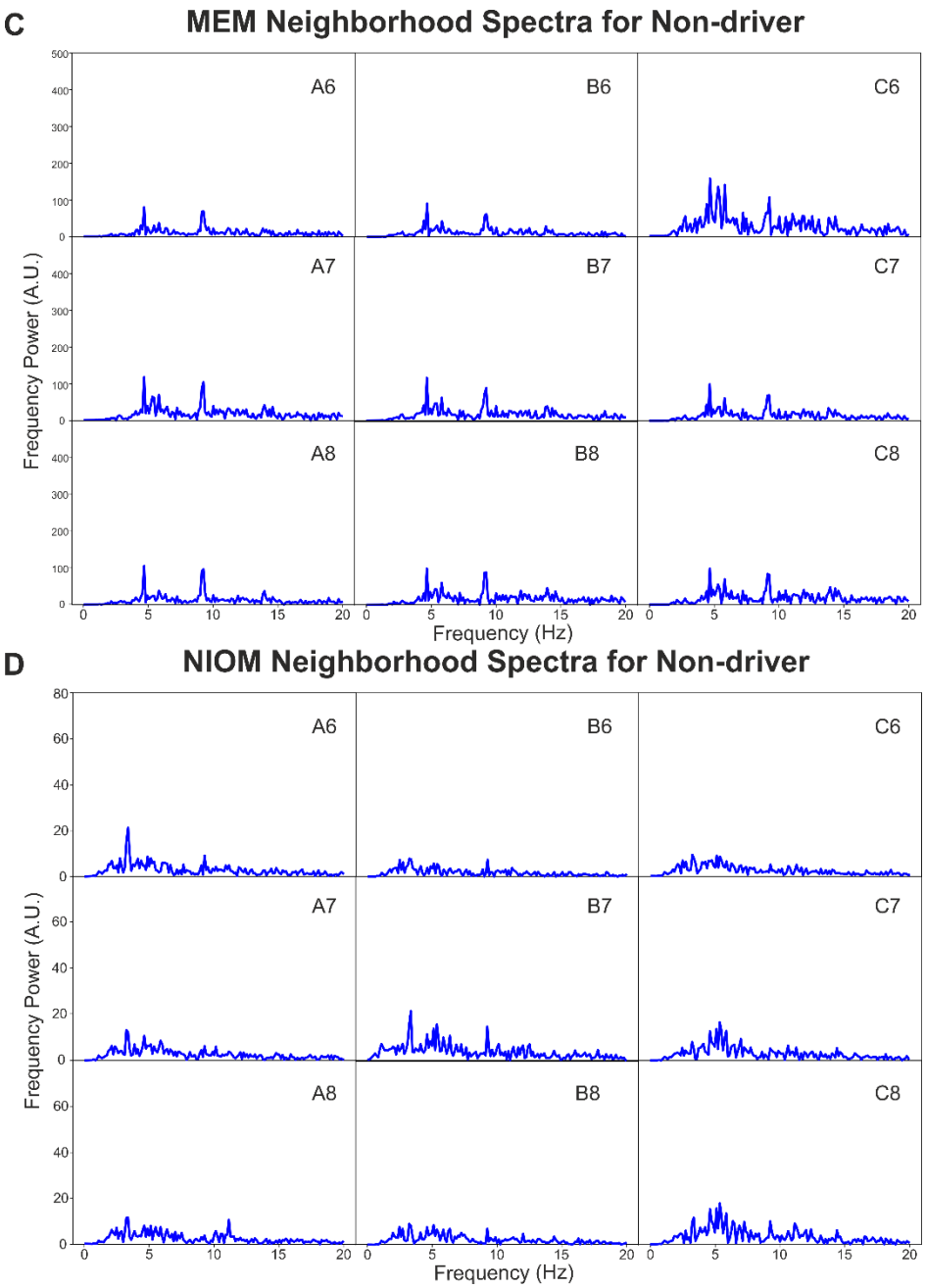
height ratio between peaks 1 and 3	6.36	3.90	4.82	3.11	5.54	3.75	4.35	2.97
height ratio between peaks 1 and 4	8.09	5.14	5.63	4.16	7.07	4.97	5.23	4.05
height ratio between peaks 2 and 3	1.70	1.64	0.81	1.00	1.71	1.63	1.02	0.97
height ratio between peaks 2 and 4	2.33	2.26	1.32	1.83	2.34	2.25	1.66	1.82
height ratio between peaks 3 and 4	1.42	1.38	0.64	0.82	1.40	1.38	0.69	0.83
prominence ratio between peaks 1 and 2	226.44	27.94	4335.01	1187.52	160.56	15.81	3731.31	272.85
prominence ratio between peaks 1 and 3	43.33	19.86	200.95	153.11	32.38	19.38	159.57	158.94
prominence ratio between peaks 1 and 4	101.14	45.56	806.49	505.88	72.94	45.13	605.12	527.81
prominence ratio between peaks 2 and 3	7.78	6.03	32.84	50.69	6.68	6.08	28.74	53.74
prominence ratio between peaks 2 and 4	28.24	21.31	296.73	318.20	21.40	22.27	218.17	340.12
prominence ratio between peaks 3 and 4	9.68	9.73	83.49	114.69	7.97	10.26	65.73	122.31
PSDR	5.49	5.34	0.55	0.59	5.45	5.33	0.58	0.59

PSDR = peak to standard deviation ratio, SD = standard deviation.

Supplemental Figure and Figure Legend

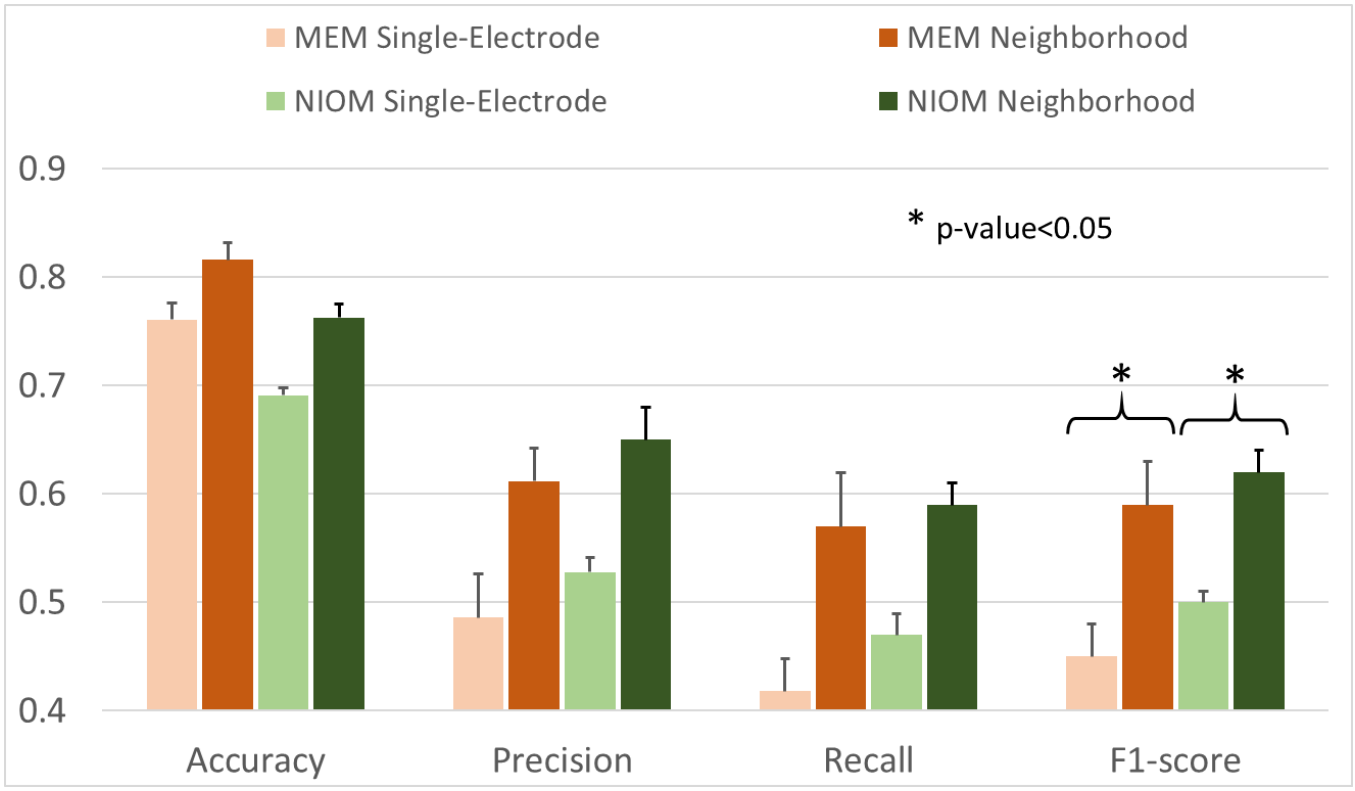
Supplementary Figure I. Example of Single-Electrode and Neighborhood Spectra





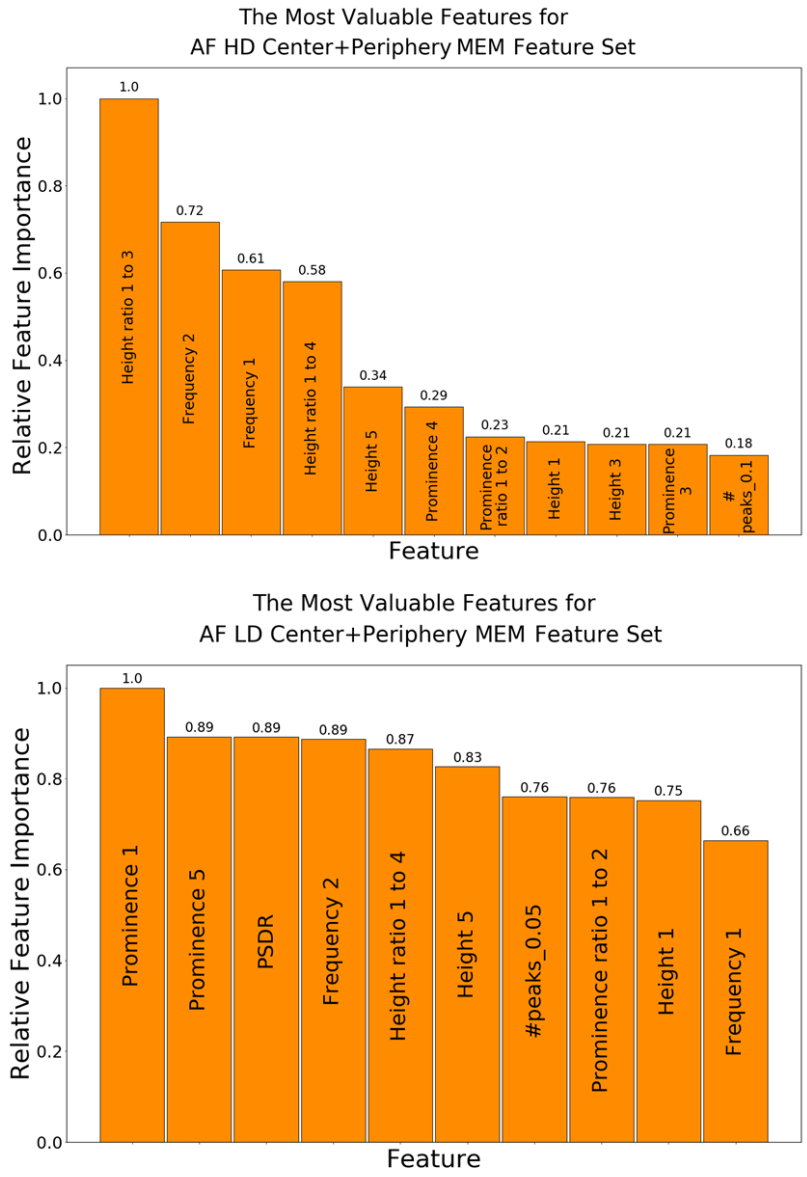
Red color denotes Fourier spectra from driver electrodes, blue color denotes Fourier spectra from non-driver electrodes. A.U. = arbitrary units, MEM = multi-electrode mapping, NIOM = near-infrared optical mapping

Supplementary Figure II. Comparison between Performance on Single-Electrode Vs Neighborhood Feature Sets.



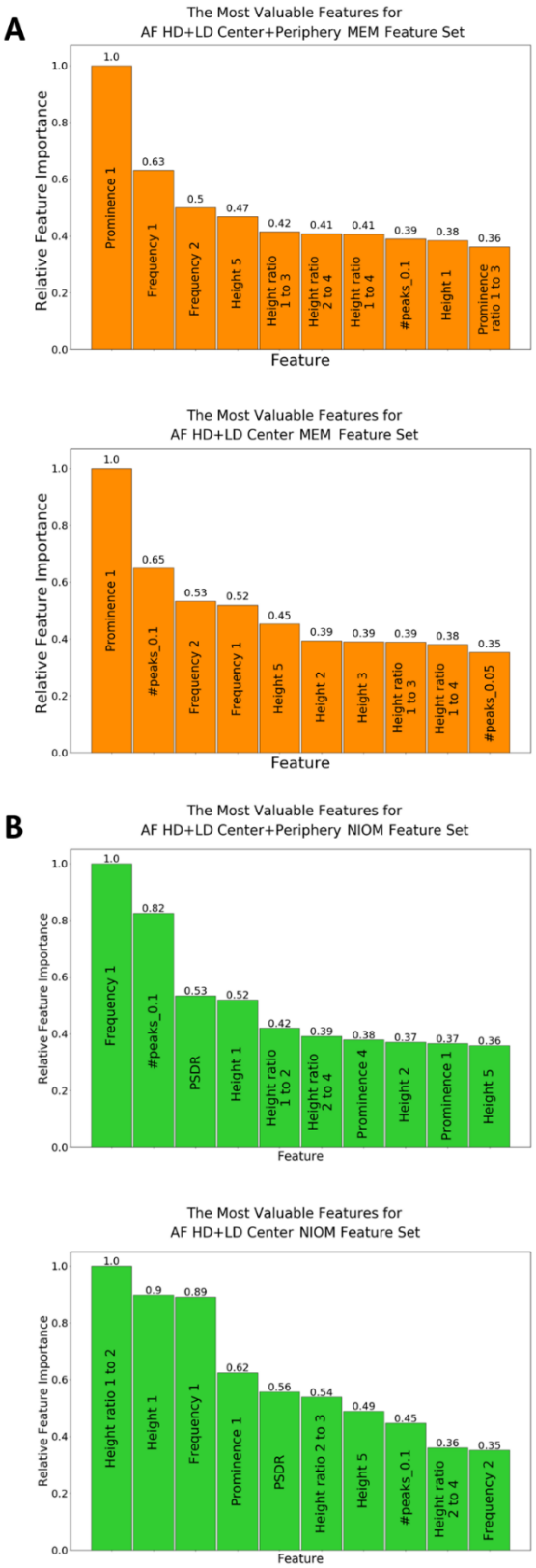
Abbreviations as in **Supplementary Figure I.**

Supplementary Figure III. The Most Valuable Features for HD and LD datasets.



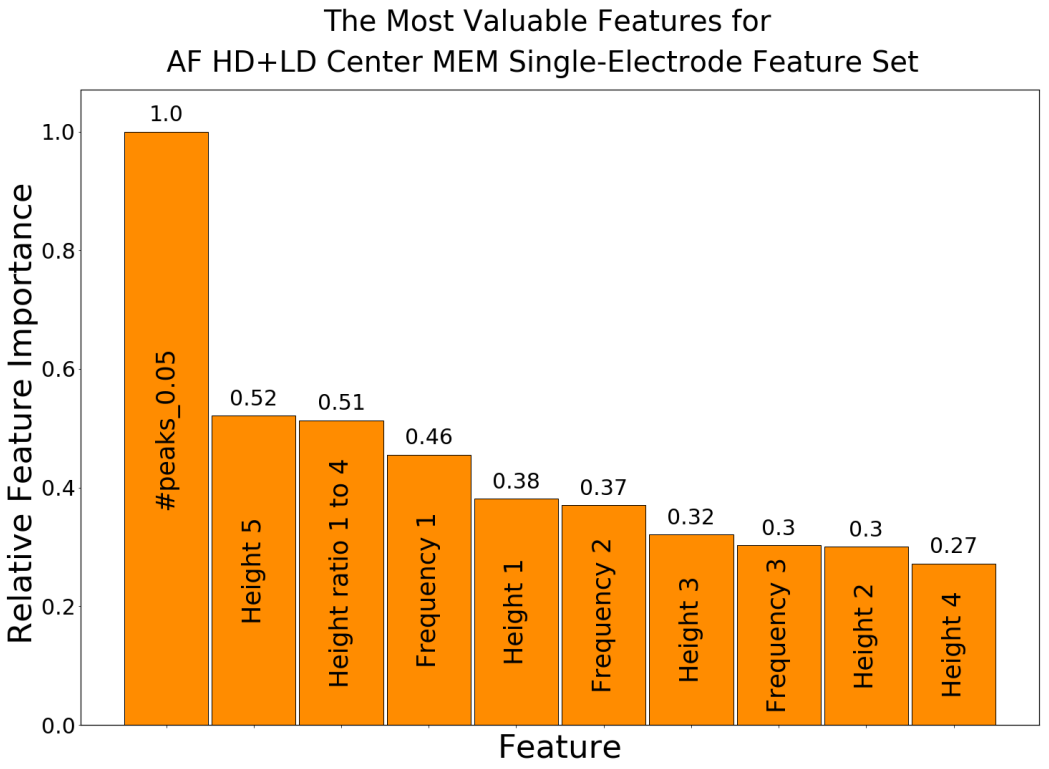
Names and relative feature importance of top valuable features for neighbor-electrodes MEM feature set for the samples from high-density catheter (AF HD, top Panel) and from low-density catheter (AF LD, bottom Panel). Abbreviations as in **Supplementary Figure I**. PSDR – Peak to Standard Deviation Ratio.

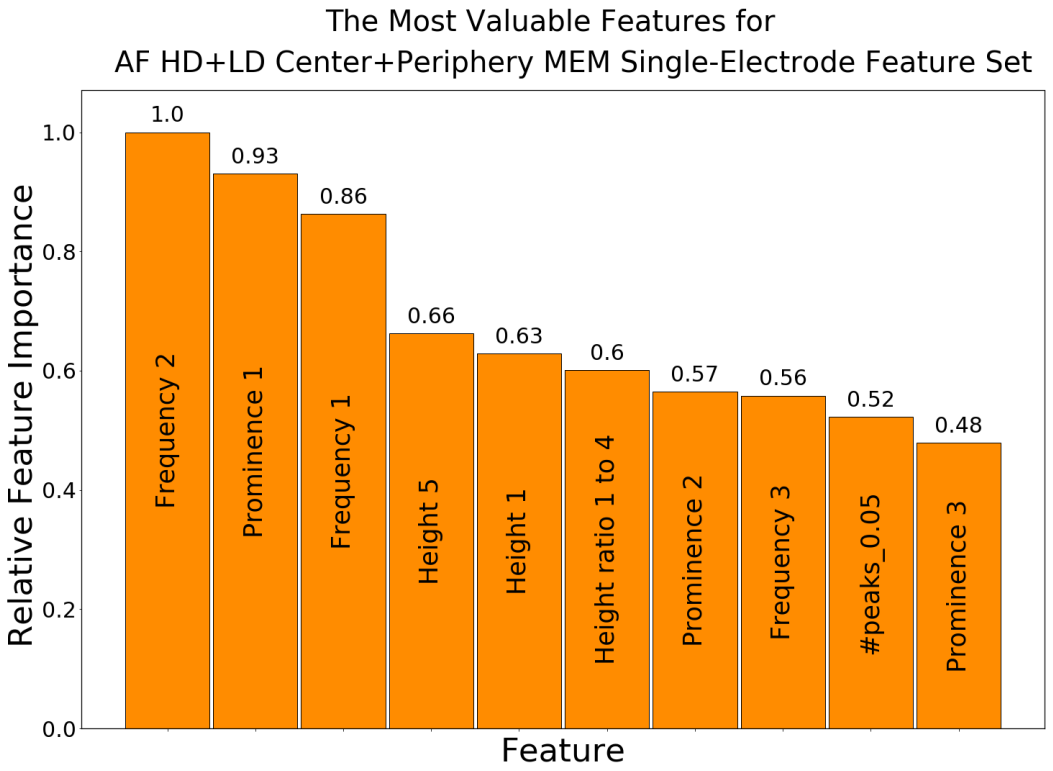
Supplementary Figure IV. The Comparison between the Most Valuable Features for Center vs Center plus Periphery Annotation.



Abbreviations as in **Supplementary Figure IV**.

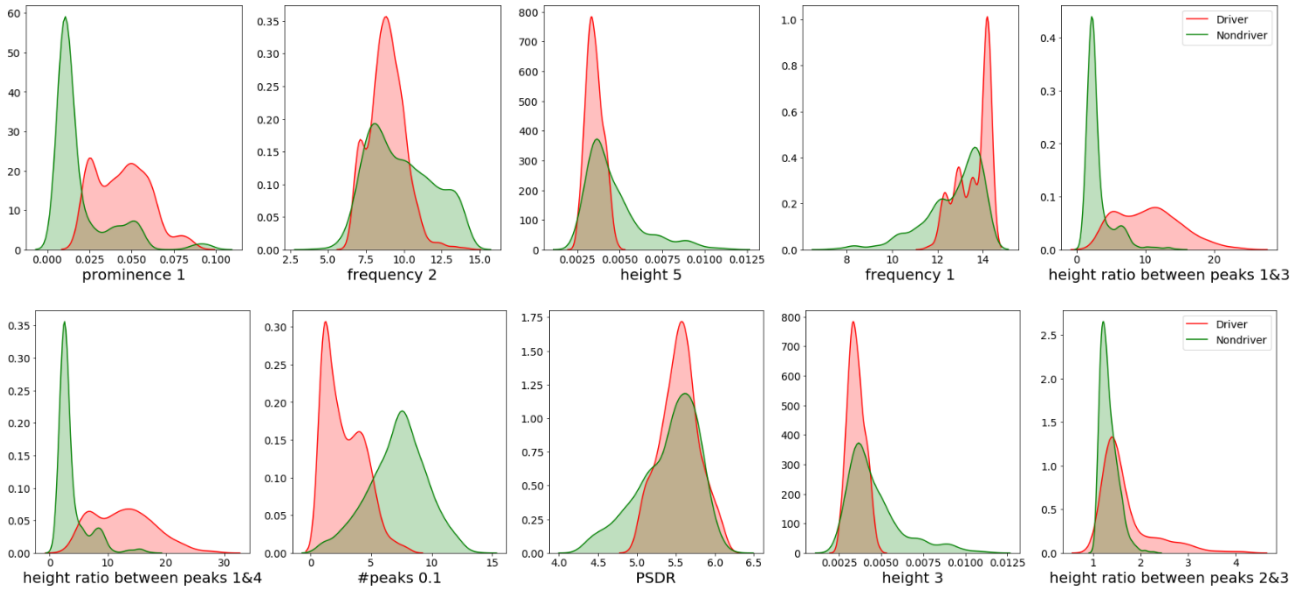
Supplementary Figure V. The Comparison between the Most Valuable Features for Center vs Center plus Periphery Annotation of LD+HD Single-Electrode Dataset.





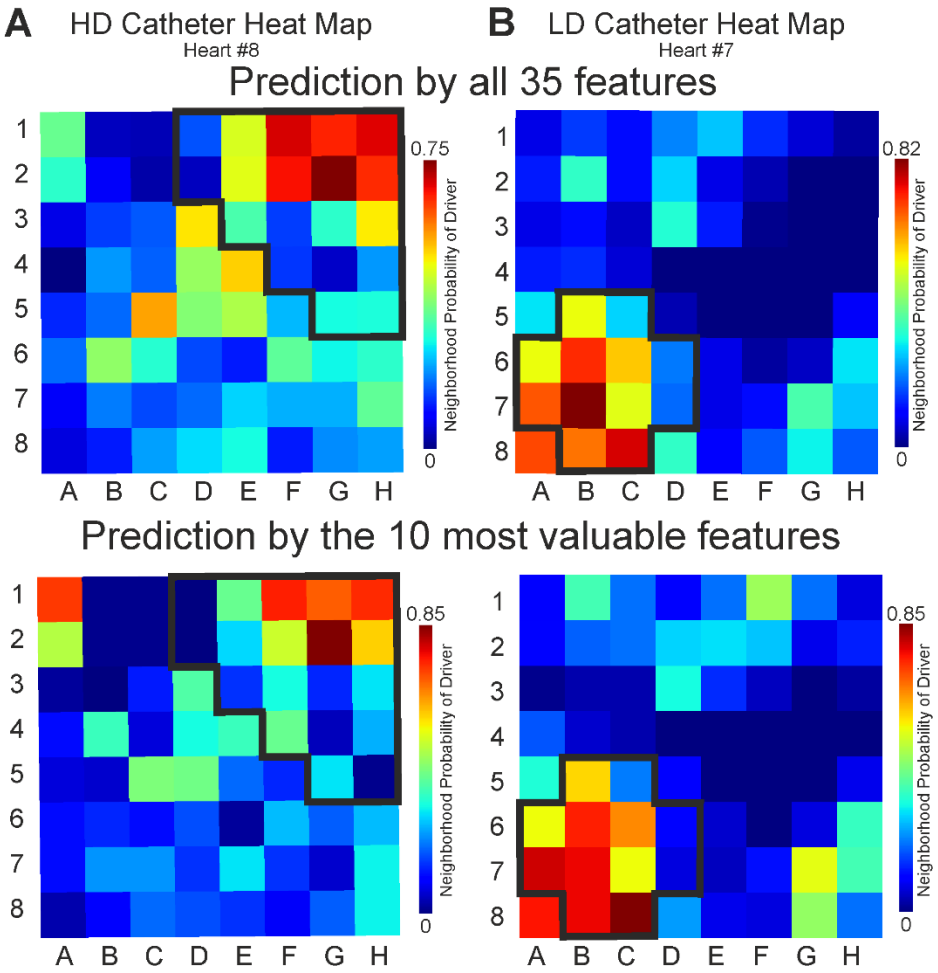
Abbreviations as in **Supplementary Figure IV**.

Supplementary Figure VI. Distributions of 10 the Most Important Features for Hold-Out Recording from Heart #8.



PSDR – Peak to Standard Deviation Ratio.

Supplementary Figure VII. The Comparison between ML Probability Prediction Heat Maps by All vs 10 the Most Valuable Driver Features



(A) Higher-density (HD) catheter and (B) Lower-density (LD) catheter. Ground truth driver region (center plus periphery) is outlined by black bold line. The color bar encodes probability of an electrode to be a driver.