

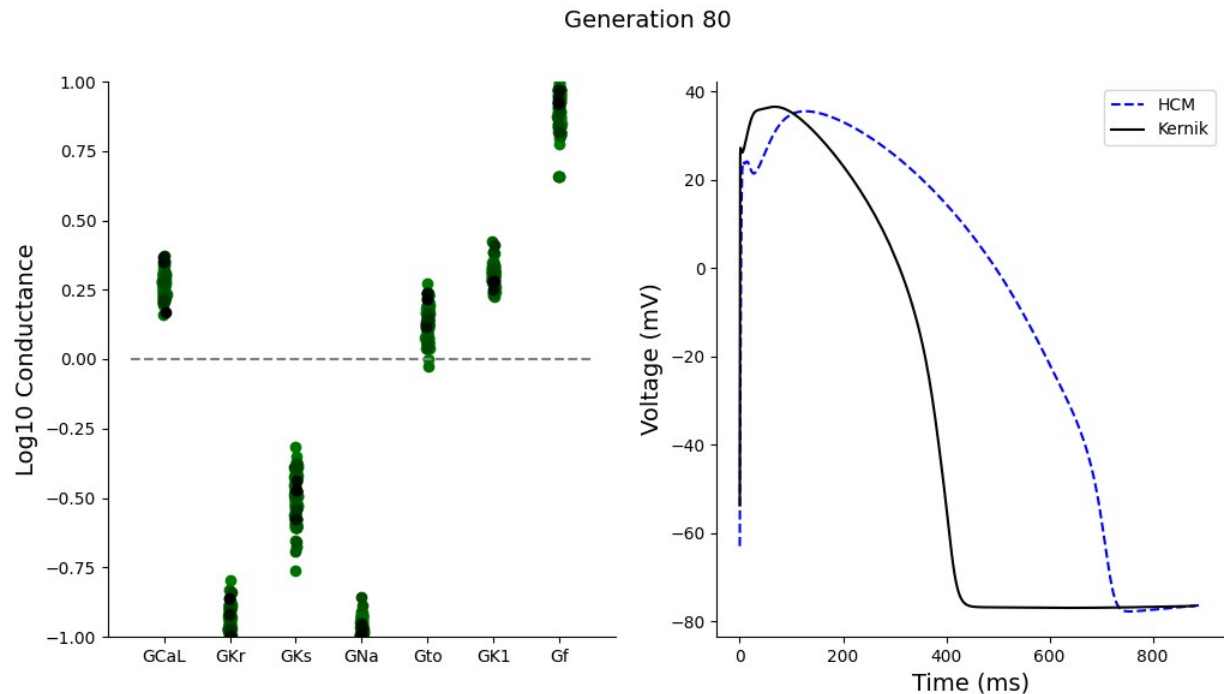


Hypertrophic Cardiomyopathy Project

Lab Meeting 26th October 2022

GA algorithm

```
feature_targets = { 'dvd_t_max': [6.56, 6.84, 7.12],  
                    'peak': [25.64, 28.26, 30.88],  
                    'apa': [82.12, 86.24, 90.36],  
                    'apd50': [505.11, 595.9, 686.69],  
                    'apd90': [668.07, 711.75, 755.43],  
                    'mdp': [-61.52, -59.62, -57.72],  
                    }
```





Data Comparison: Currents

	Surgical samples (Santini et al.)	GA fit	MYH7 mut (Han et al.)	ACTN2 mut (Prondzynski et al.)	MYBPC3 or TPM1 mut (Prajapati et al.)	MYL2 mut (Zhou et al.)
I_{CaL}	Increase	Increase	Increase	Increase	Increase	Decrease
I_{Kr}	Decrease	Decrease	-	-	-	-
I_{Ks}	Decrease	Decrease	-	-	-	-
I_{Na}	Increase (INaL)	Decrease	Increase	No change	-	-
I_{to}	Decrease	Increase	-	-	Decrease	-
I_{K1}	Decrease	Increase	Increase (IK total)	-	No change	-
I_f	-	Increase	-	-	-	-



Data Comparison: APD and Ca^{2+}

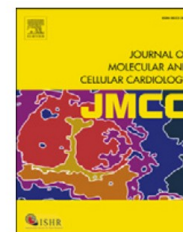
	Surgical samples (Santini et al.)	MYH7 mut (Han et al.)	ACTN2 mut (Prondzynski et al.)	TnT mut (Wang et al.)	MYL2 mut (Zhou et al.)
Ca^{2+} transient	Slower	Slower	Slower	Slower	Slower
$[\text{Ca}^{2+}]_i$	Increase	Increase	-	Increase	Decrease
APD	Prolonged	Prolonged	Prolonged	Reduced	-
CaMKII	Increase	-	-	-	-
NCX	Reduced	-	-	Reduced	-



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Journal of Molecular and Cellular Cardiology

journal homepage: www.elsevier.com/locate/yjmcc



Original article

Mechanisms of pro-arrhythmic abnormalities in ventricular repolarisation and anti-arrhythmic therapies in human hypertrophic cardiomyopathy

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Late Sodium Current Inhibition Reverses Electromechanical Dysfunction in Human Hypertrophic Cardiomyopathy

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	I_{NaL}	I_{CaL}	I_{to}	I_{K1}	I_{Kr}	I_{Ks}
human HCM	Increase	Increase	Decrease	Decrease	Decrease	Decrease

	APD	Ca^{2+} transient	$[Ca^{2+}]_i$	NCX	CaMKII
human HCM	Prolonged	Slower	Increase	Reduced	Increase



Computational Model

Model: **Ord**

Construction of HCM population by applying the electrical remodelling to the CTRL population: scaling conductances

	I_{NaL}	I_{CaL}	I_{to}	I_{K1}	I_{Kr}	I_{Ks}	J_{up}	J_{rel}	I_{NCX}	K_{TRPN}	I_{NaK}	I_{Nab}
HCM (%)	+165	+40	-70	-30	-45	-45	-25	-20	+30	-50	-30	+165

Modification of the cell radius to reproduce the +90% increase in cell volume reported in the experiments.