

■ Electronic Supplementary Information (ESI)

Coupled Molecular Design Diagrams to Guide Safer Chemical Design with Reduced Likelihood of Perturbing the NRF2-ARE Antioxidant Pathway and Inducing Cytotoxicity

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Contents

	Page S
1 NRF2-ARE Assays Testing Range	2
2 Activity Comparison between ATG_NRF2 and Tox21_ARE assay	2
3 Exploratory Statistics	3

1 NRF2-ARE Assays Testing Range

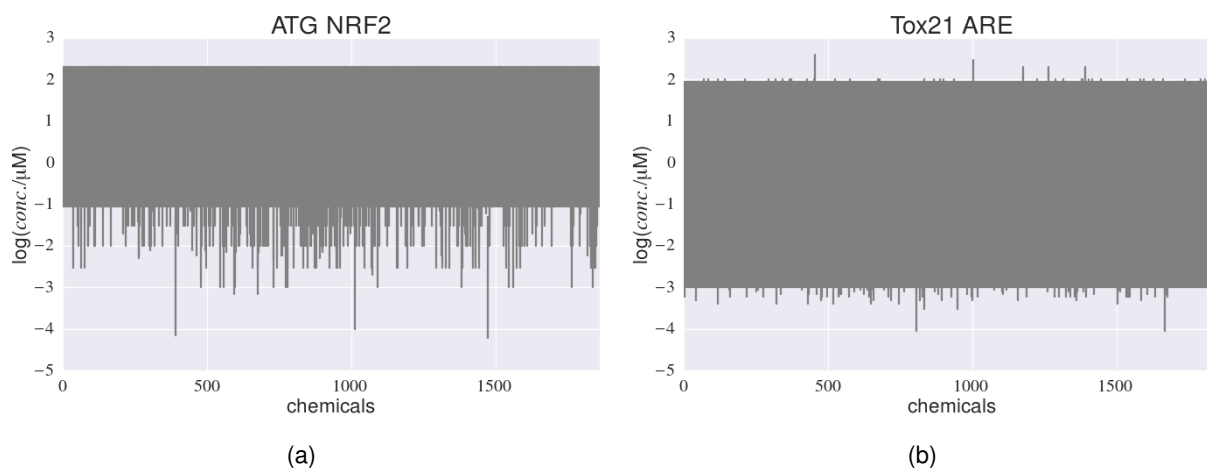


Figure S 1: Concentration range for tested chemicals

2 Activity Comparison between ATG_NRF2 and Tox21_ARE assay

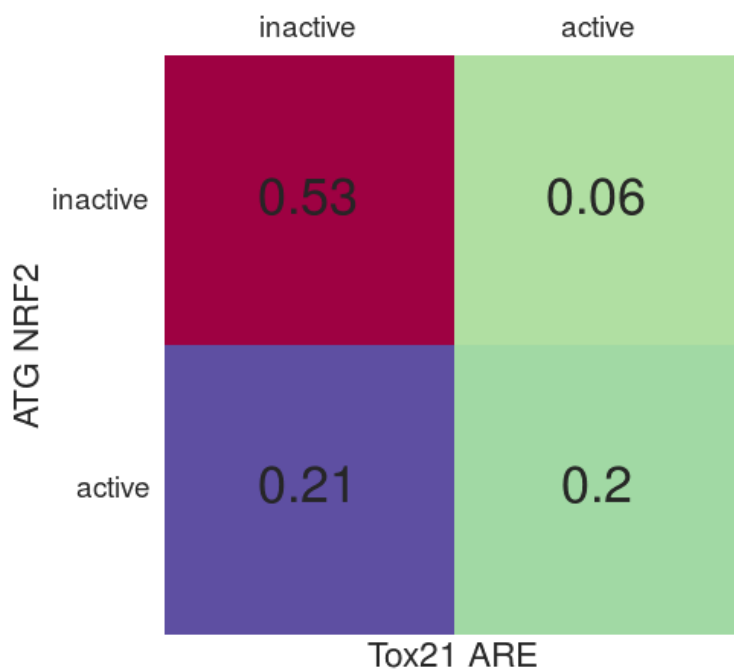


Figure S 2: Confusion matrix for ATG_NRF2 and Tox21_ARE activity

Chemicals corresponding to the diagonal elements in the matrix were chosen for this study.

3 Exploratory Statistics

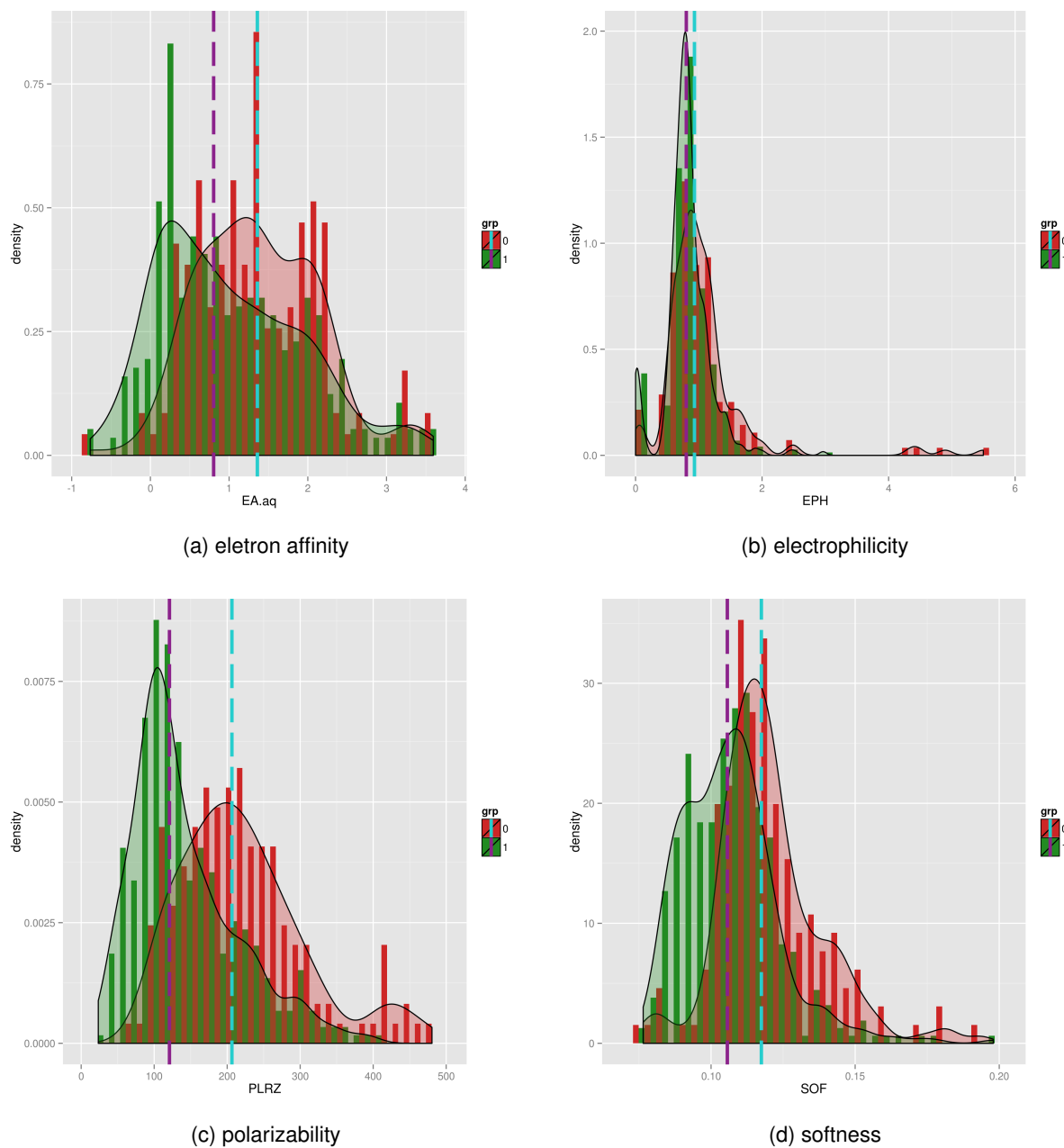


Figure S 3: Histograms for the chemicals by groups. 1 : inactive; 0 : active. Verical dotted line : median for a group distribution. to be continued on the next page

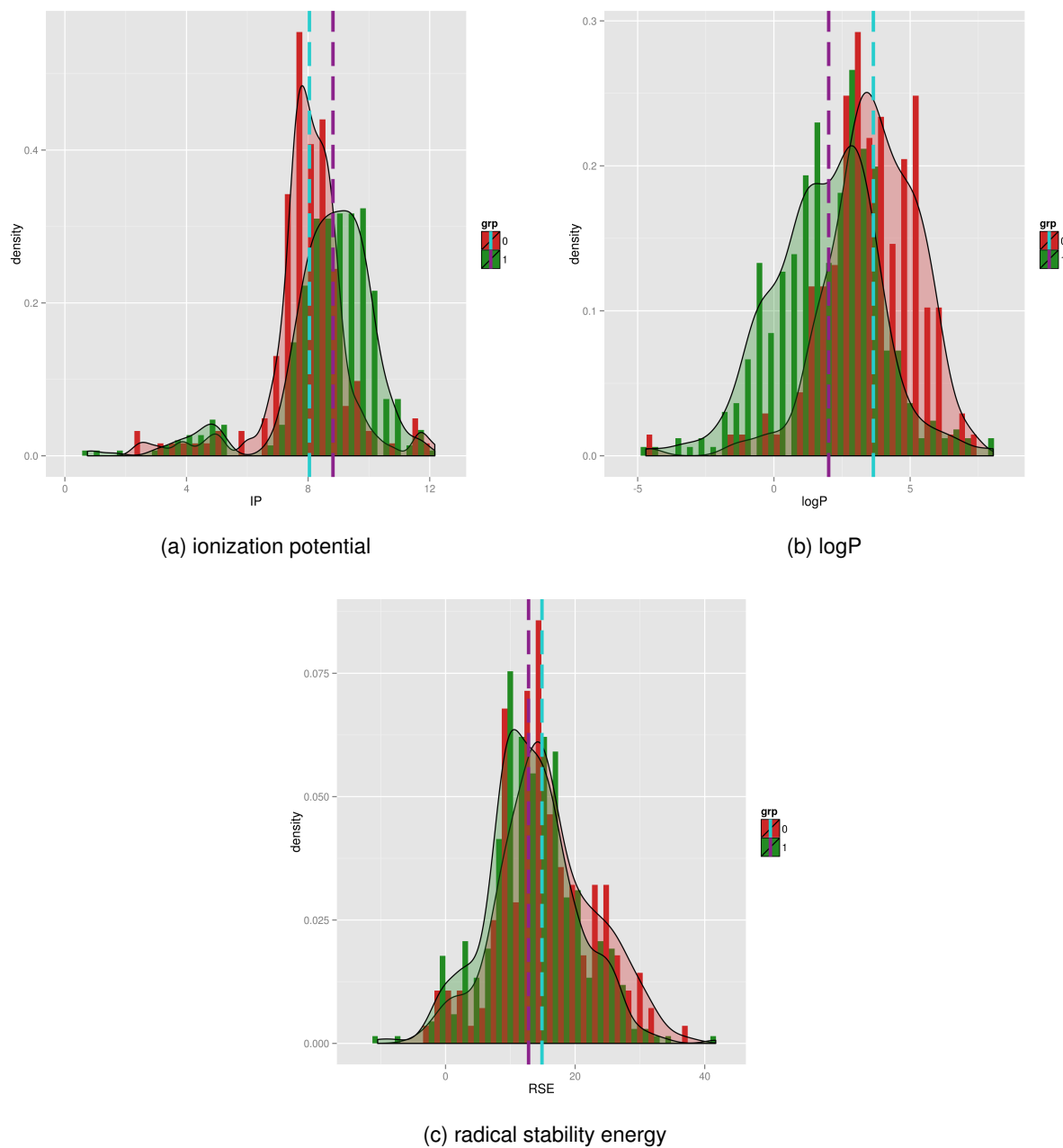


Figure S 3: continued. Histograms for the chemicals by groups.

Table S 1: ROC AUC for design variables

design variable	ROC AUC	design variable	ROC AUC
EA.aq	0.65	PLRZ	0.76
EPH	0.62	SOF	0.75
IP	0.67	logP	0.75
RSE	0.58		