Practical Applications for AI in High-Content Analysis: Dose-Response and Quantitative Assays

Featuring Dr. Ilya Goldberg

Presented by

ViQi

Your Webinar Host | **ViQi**

Cloud-based large-scale image analysis software and expertise.

Our partners use ViQi to . . .

➔ Visualize, analyze, annotate, and store over 250 types of image and data formats in one central repository (including individual files over a terabyte in size)

➔ Automate and scale unique research workflows through machine learning and AI (we can help build them or integrate our partners' existing analyses)

➔ Problem-solve complex image and data challenges (we have a team of experts who have been developing this infrastructure for over 15 years starting at UCSB in addition to 20+ years in bio-imaging informatics and AI that Ilya brings to the table)

A series of webinars for experimental biologists

How to use AIs for imaging problems in an experimental setting

Introduction to AI & classification

Live/dead assay

Quantitative assays

Dose-Response

A. **Phenotypic similarity**
B. **Localization**
C. **Morphology as biomarker**

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The Speaker | Dr. Ilya Goldberg

Chief Science Officer, ViQi

Ilya has a long career that lies at the intersection of biology, imaging, and AI.

- Co-founded a startup that used AI to improve diagnosis of lung nodules in CT scans.
- Led research group at the NIH National Institute on Aging: Basic biology of aging, AI for biomedical images,
- At MIT, co-founded the OME project: Infrastructure for large image repositories and analysis.
- PhD in Cell Biology, Johns Hopkins School of Medicine
- Over 60 peer-reviewed scientific articles from time at Johns Hopkins, Harvard, MIT, and NIH in molecular and cell biology, pattern recognition, image informatics and the basic biology of aging.

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Agenda |

What You'll Learn

- Train and evaluate AIs for scoring a continuous morphological process.
- Score a multi-compound screen based on a dose-response standard curve.
- Score any type of phenotypic response without knowing what to look for a priori.

Continuous variables from marginal probabilities: Risk estimation in case-control

Benign

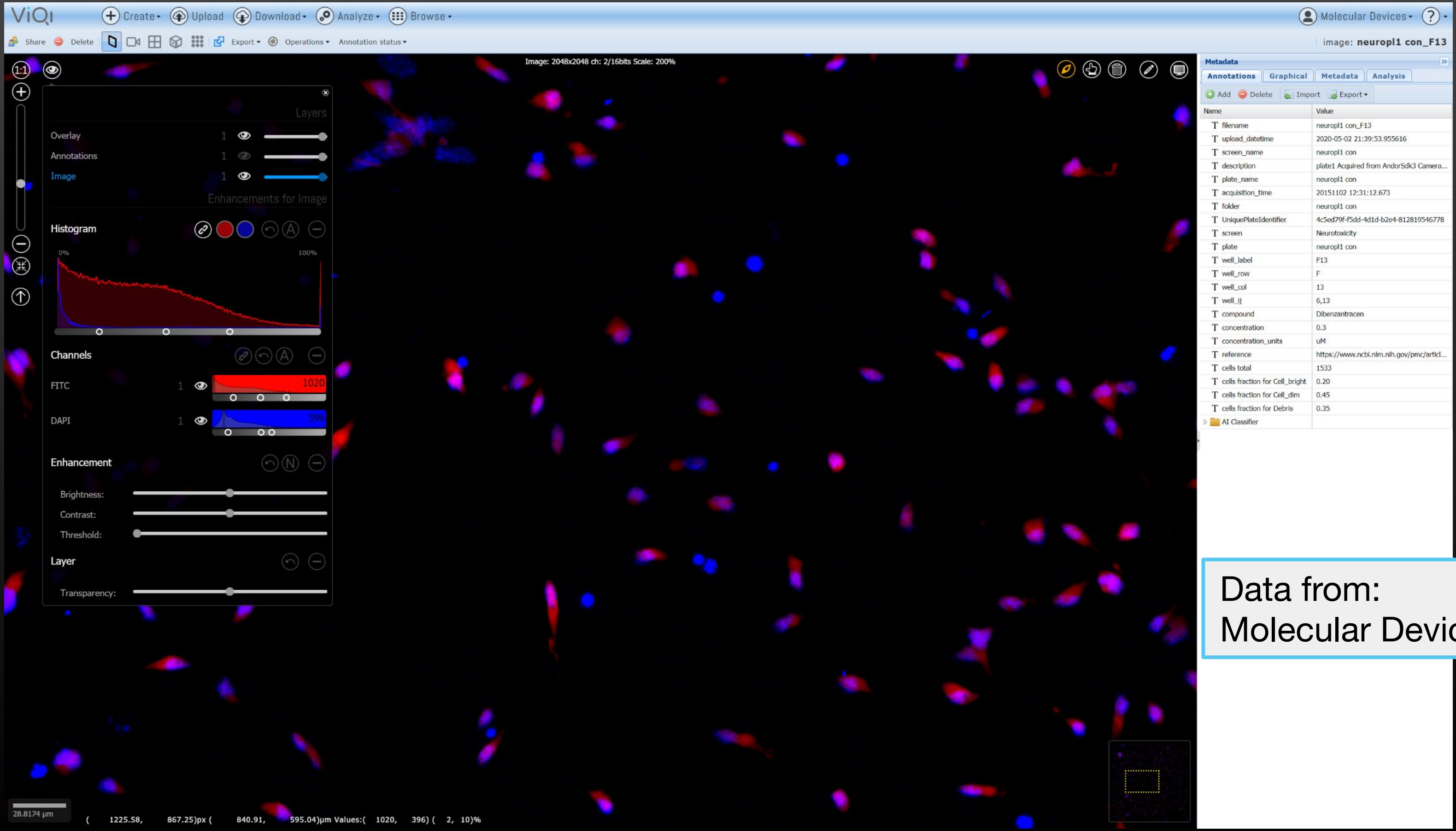
Class	Marginal Probability
Benign	0.85
Malignant	0.15
Malignant probability - "risk"	**0.15**

Malignant

Class	Marginal Probability
Benign	0.1
Malignant	0.9
Malignant probability - "risk"	**0.9**

Typical dose-response setup on an imaging plate

Compounds that affect neurons



Data from:
Molecular Devices

Plate view: Rows, columns, concentrations

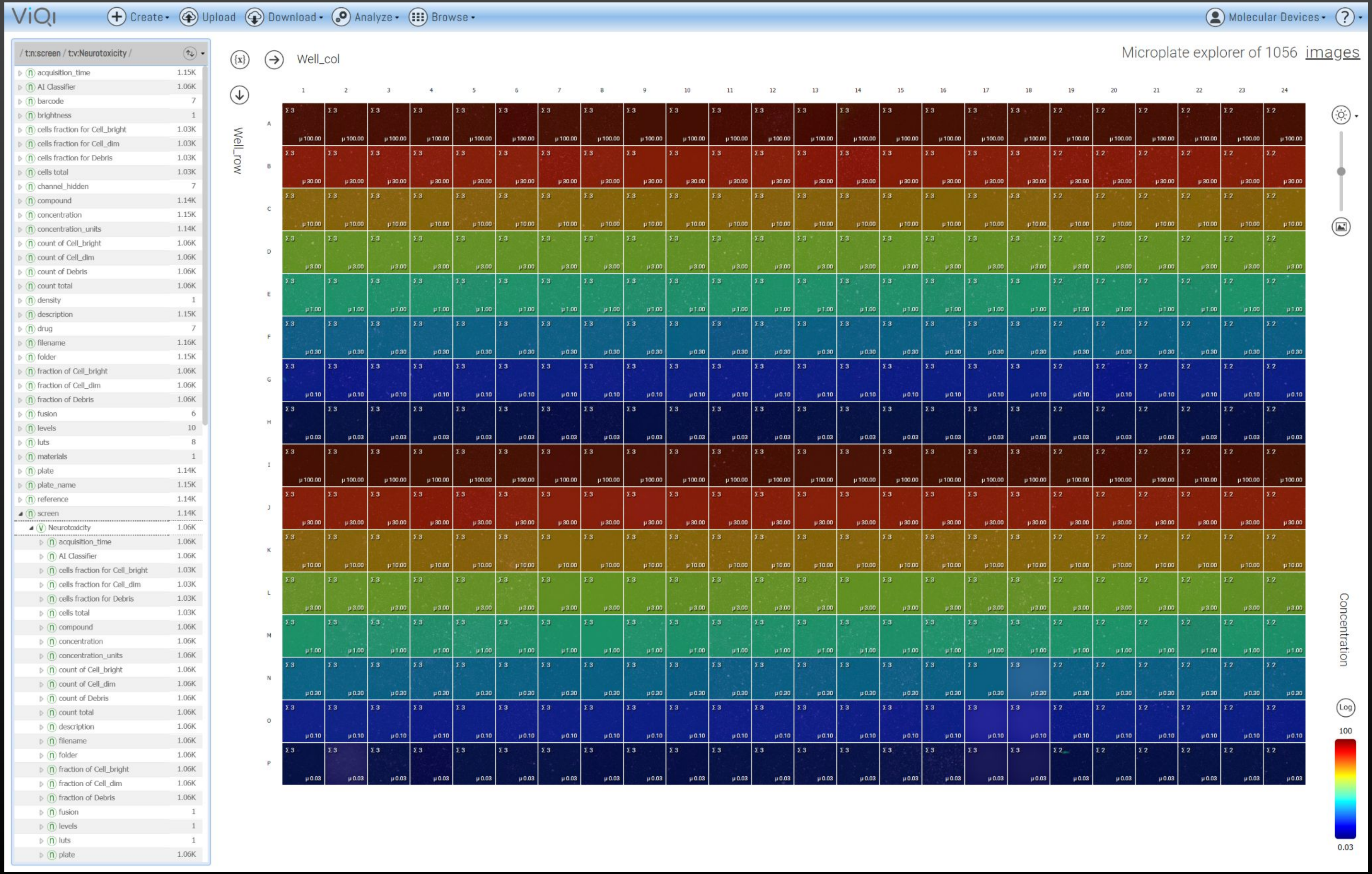


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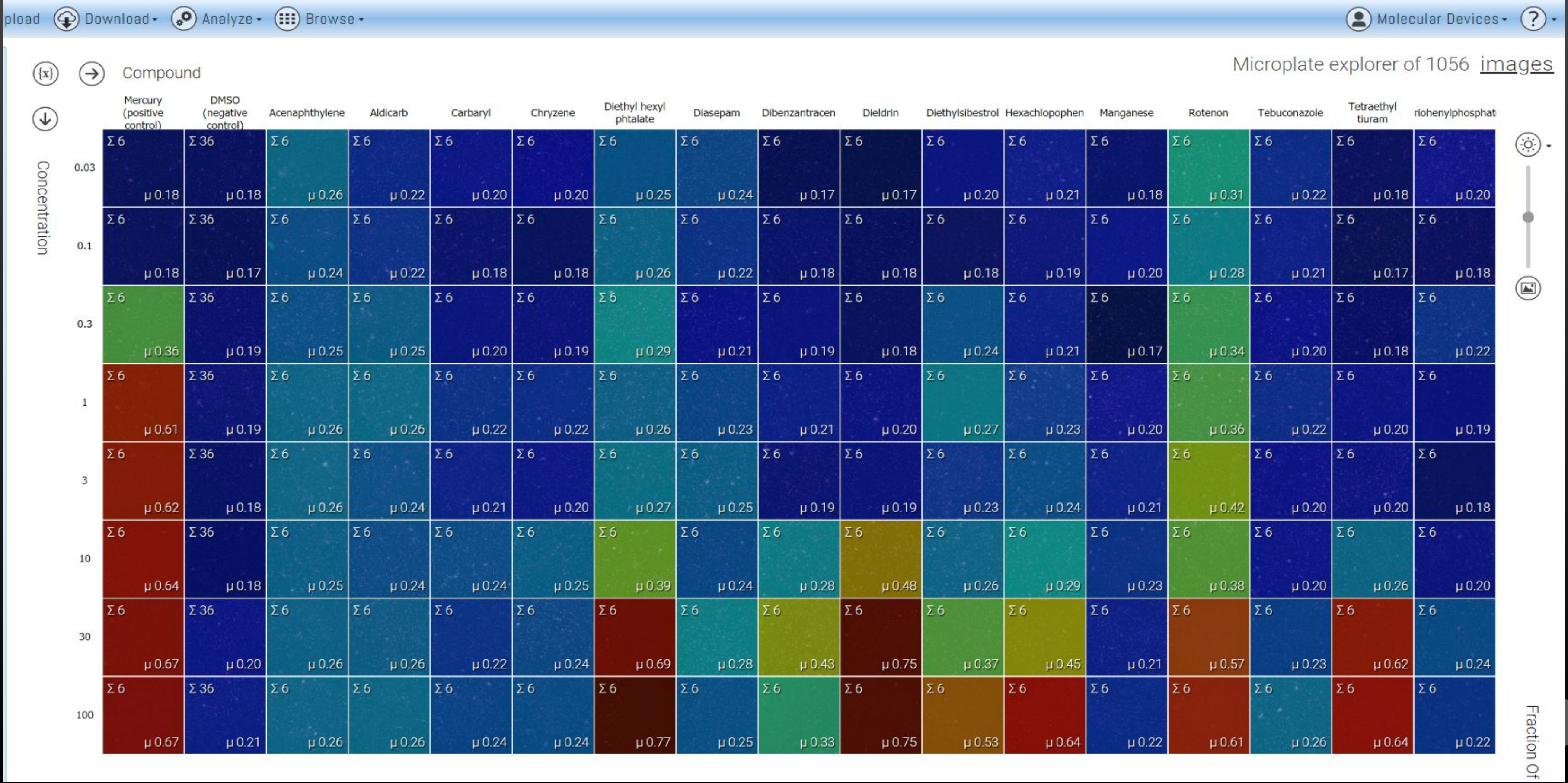
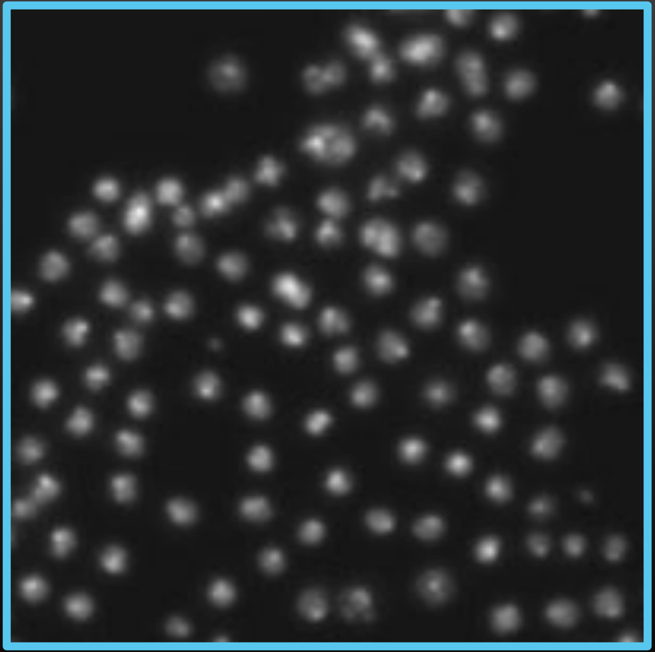
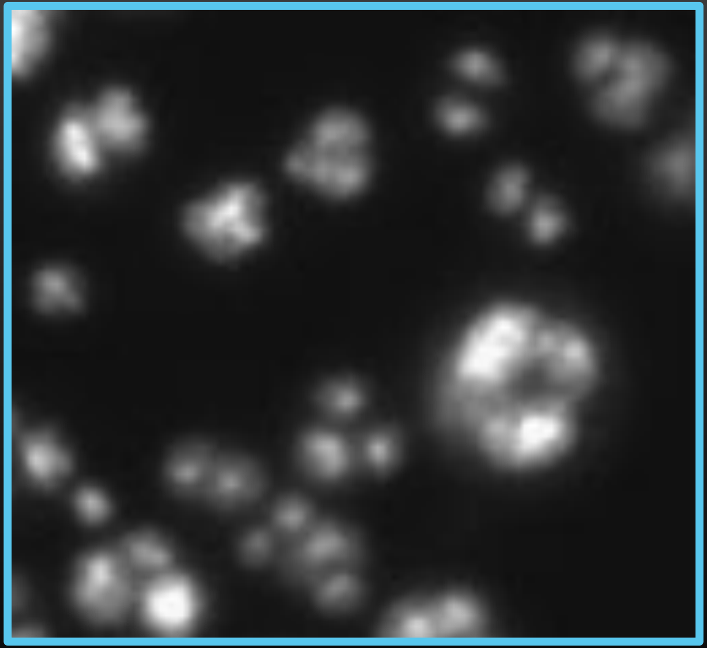
Plate view: Compounds, concentrations and assay results



Binucleate cells: An important target phenotype



Normal



Binucleate

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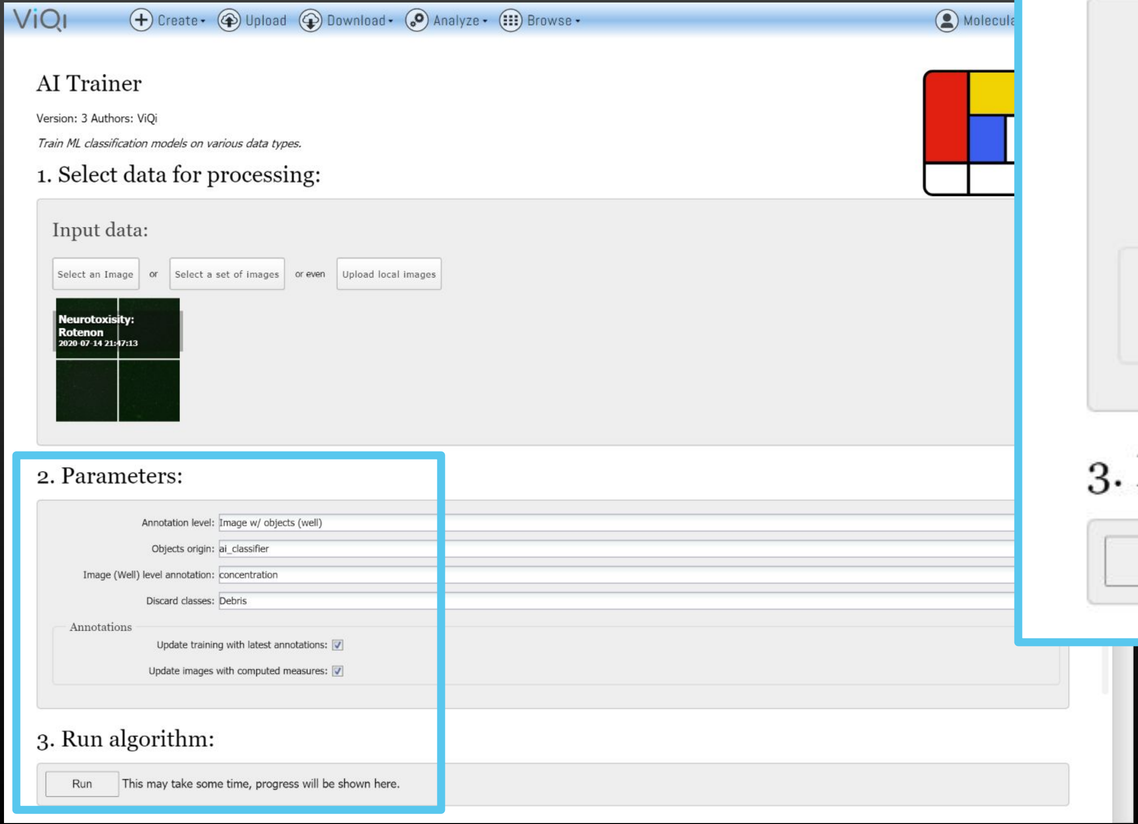
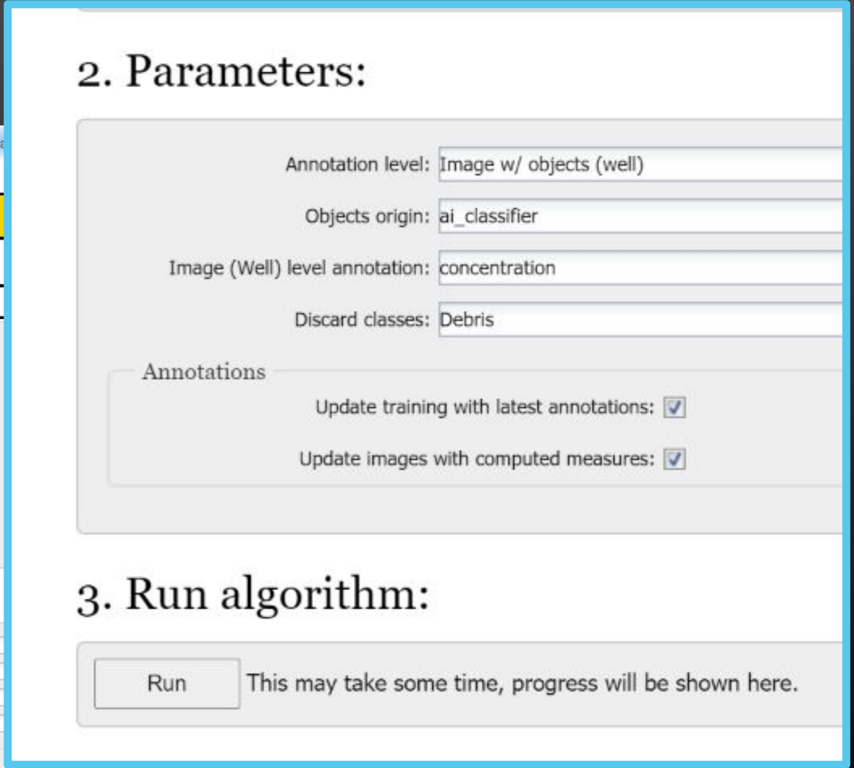
Continuous variables from marginal probabilities: Equivalent dose in dose-response

Class Value	Marginal Probability	Formula
Drug Concentration	Single sample AI Score	Weighted Equivalent Drug Concentration: Drug Concentration X Marginal Probability
0.0	0.001	0.0 X 0.001 = 0.0
0.1	0.001	0.1 X 0.001 = 0.0001
1.0	0.15	1.0 X 0.15 = 0.15
10	0.85	10 X 0.85 = 8.5
100	0.00001	100 X 0.00001 = 0.001
1000	0.00001	1000 X 0.00001 = 0.01
	Equivalent Drug Dose	**8.66**

AI-Trainer user interface





Confusion matrices: Positive controls

Mercury

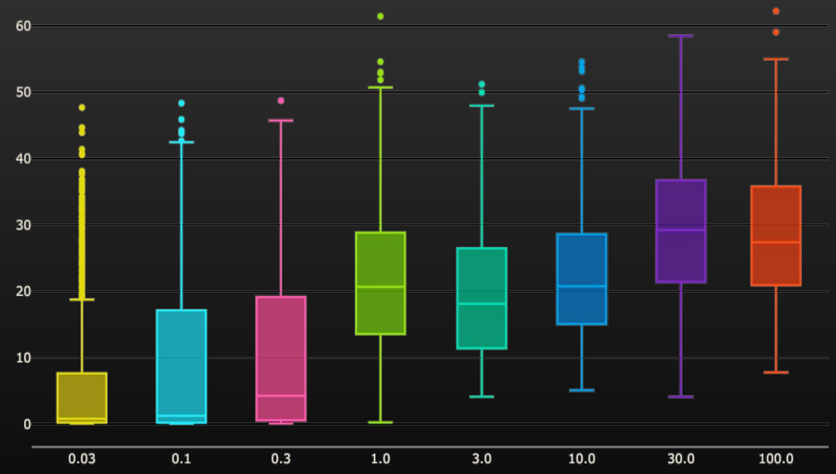
Label	0.03	0.1	0.3	1	3	10	30	100	Accuracy
0.03	358	273	171	56	30	13	43	56	0.358
0.1	334	268	183	61	30	14	56	54	0.268
0.3	105	137	397	112	66	58	57	68	0.397
1	10	23	56	302	248	100	155	106	0.302
3	5	11	33	209	354	155	121	112	0.354
10	7	11	16	153	228	270	177	138	0.27
30	7	14	19	158	69	126	328	279	0.328
100	10	16	12	112	82	110	385	273	0.273

Rotenone

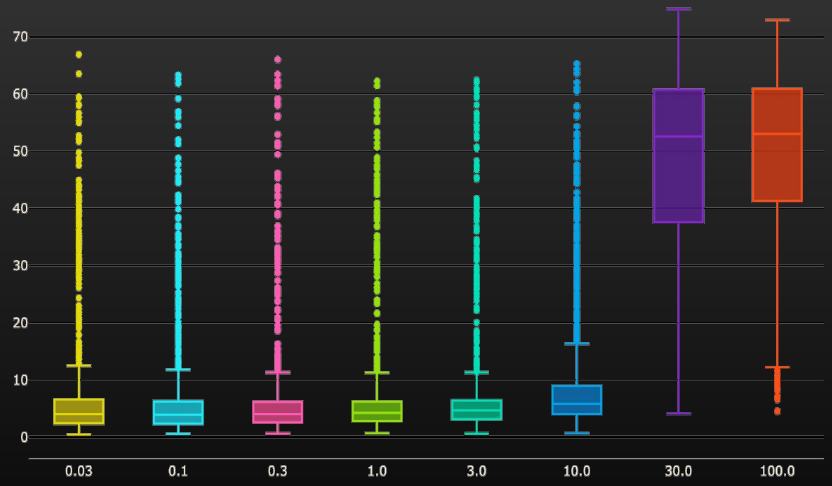
Label	0.03	0.1	0.3	1	3	10	30	100	Accuracy
0.03	161	200	187	121	148	128	25	30	0.161
0.1	224	124	207	124	141	116	34	30	0.124
0.3	130	138	228	193	171	107	13	20	0.228
1	111	88	258	187	166	115	38	37	0.187
3	127	65	214	186	170	148	47	43	0.17
10	131	56	111	121	148	299	93	41	0.299
30	6	0	1	22	38	31	443	459	0.443
100	2	1	1	7	25	19	429	516	0.516

Box plots for cell scores on a continuous scale

Mercury



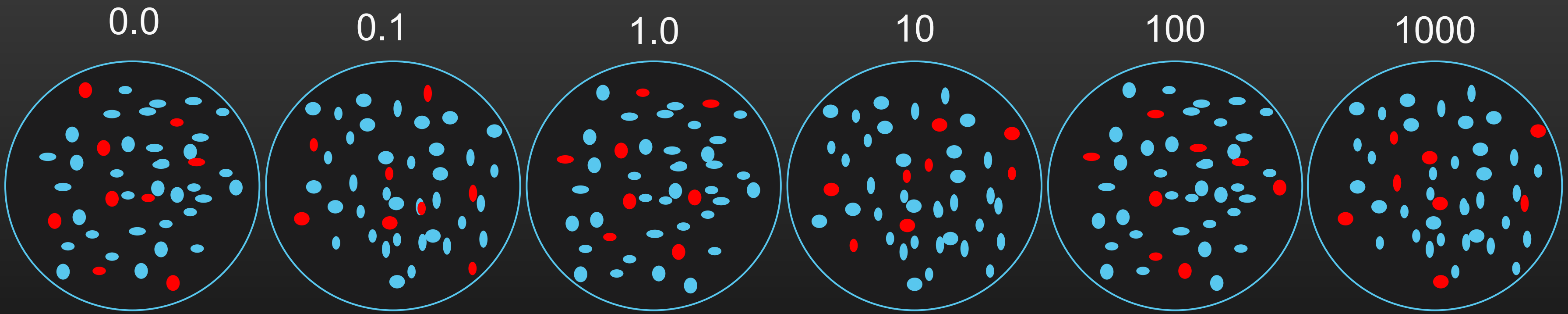
Rotenone



Scoring any phenotype

Cell-based cross-validation

Concentrations:

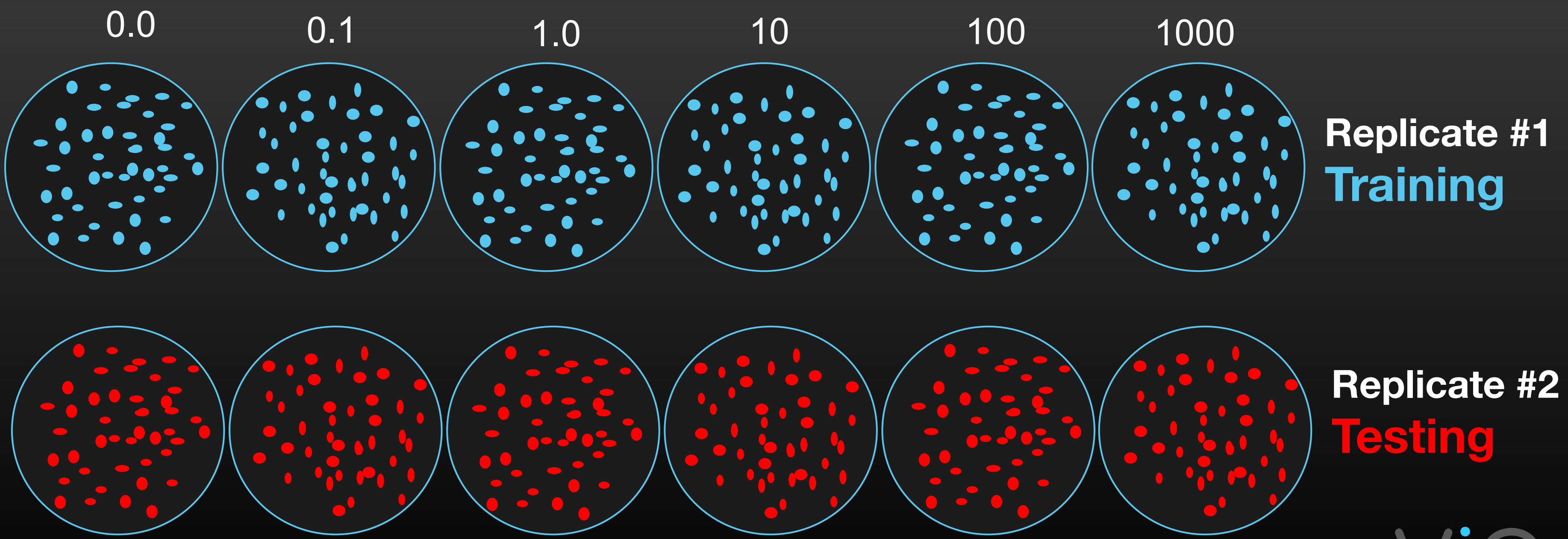


Training

Testing

Replicate-based cross-validation

Concentrations:



Confusion Matrices:
Negative control and non-responder

DMSO

Label	0.03	0.1	0.3	1	3	10	30	100	Accuracy
0.03	90	139	178	69	124	97	72	231	0.09
0.1	115	167	122	50	80	148	100	218	0.167
0.3	123	52	169	42	80	163	135	236	0.169
1	102	135	129	44	94	167	125	204	0.044
3	137	114	115	36	104	162	112	220	0.104
10	107	91	185	81	132	86	73	245	0.086
30	90	77	179	50	109	102	108	285	0.108
100	74	89	143	23	98	111	114	348	0.348

Tebuconazole

Label	0.03	0.1	0.3	1	3	10	30	100	Accuracy
0.03	127	106	99	142	106	152	107	147	0.129
0.1	101	110	102	119	119	189	110	136	0.112
0.3	99	116	109	149	106	140	103	138	0.114
1	107	112	104	148	141	131	123	120	0.15
3	124	110	130	143	100	136	126	117	0.101
10	131	117	102	135	123	118	134	126	0.12
30	106	118	85	143	120	145	120	149	0.122
100	123	110	112	126	121	132	119	143	0.145

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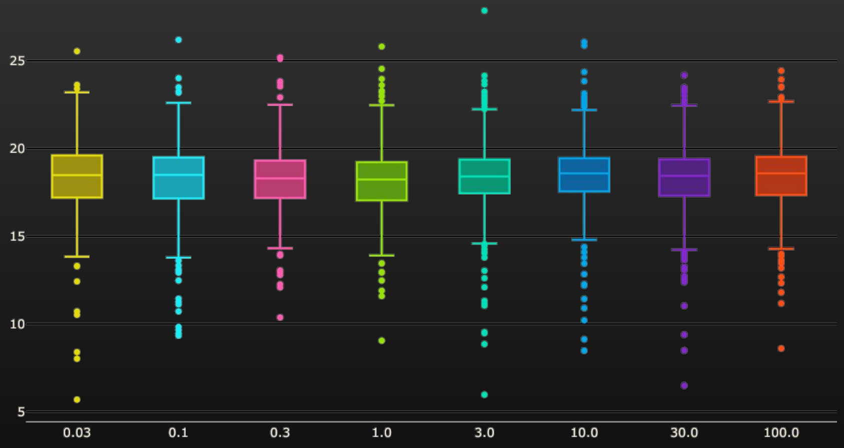
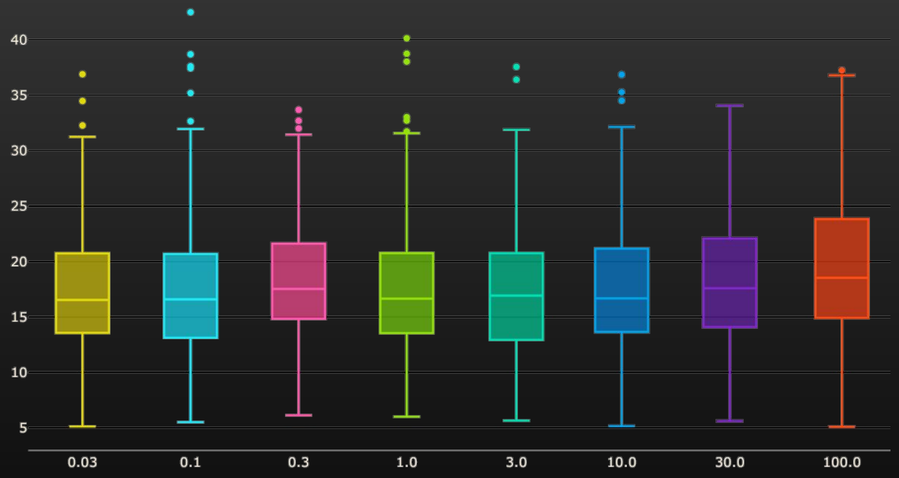
Box plots: Negative control and non-responder

DMSO



Tebuconazole



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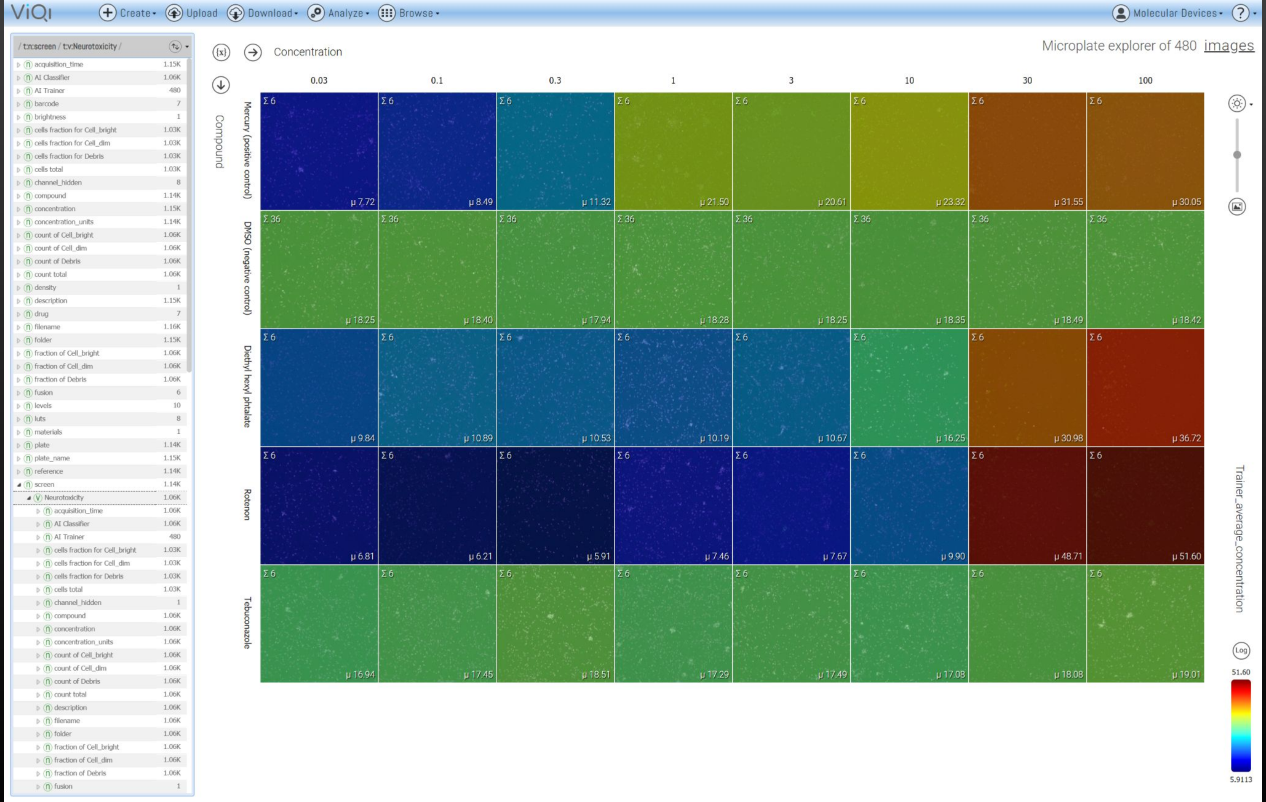
Assay summary for per-compound AIs



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Parting thoughts

- **You don't need preconceived notions about the phenotypes you expect in order to use AIs for quantitative assays. You don't even need to know if there will be an effect or not. The AI will tell you.**

- **With automated AI training, using AIs is conceptually more similar to typical experimental considerations compared to conventional image processing.**
  - Use positive controls or standard curves to train AIs. Always compare to negative controls.
  - Account for sample bias and sample variability when training.
  - Don't allow controls to contaminate your unknowns when validating and testing your AI.

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Would you like to learn more?

Contact us at info@viqi.org or visit viqi.org

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