Machine Learning and Artificial Intelligence in MX

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Outline

- Aim and idea for the work
- Why machine learning and artificial intelligence
- Training data and METRIX database for exploratory work
- Experimental phasing success
- Molecular replacement success
- Map traceability
- Future plans

Aim

Is there predictive power in crystallographic metrics (multiplicity, completeness, different R values, high and low resolution limit)

If yes, are they useful for anything

If yes then:

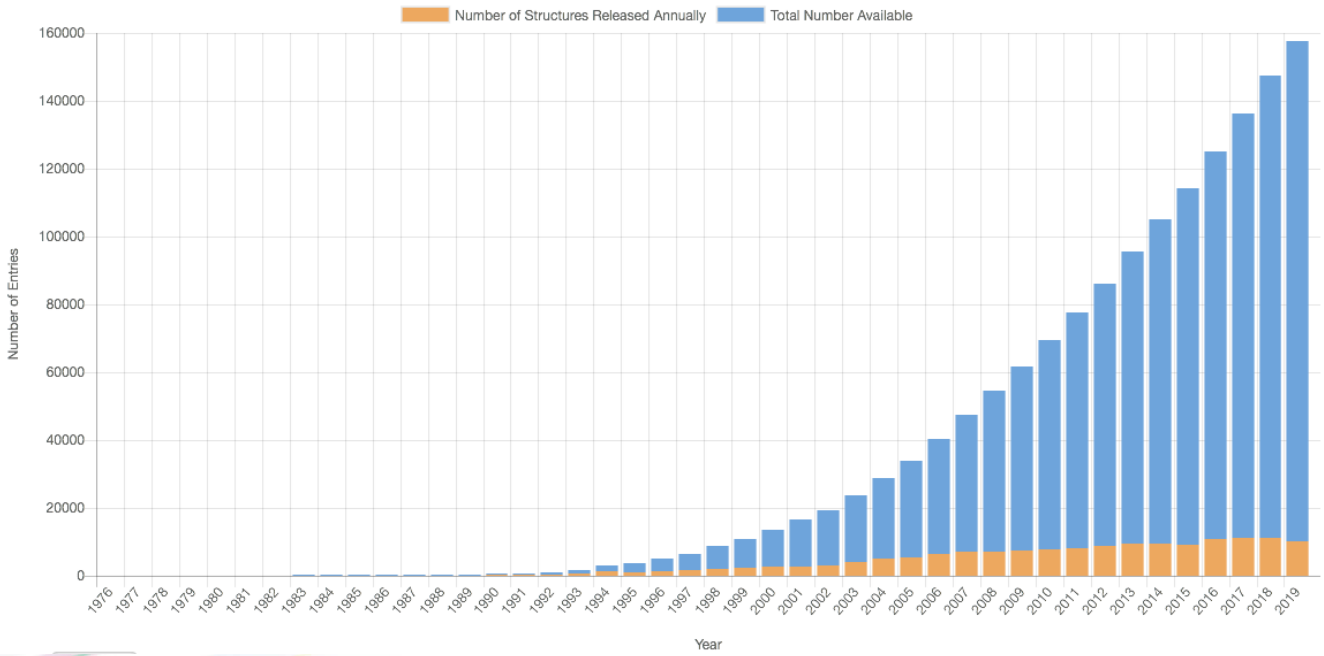
Create a set of tools using machine learning to help users/crystallographers to solve their protein structures.

During data collection, e.g. giving recommendations

During data analysis, e.g. data reduction and phasing

Why machine learning and artificial intelligence

close to 158,000 structures



Problems:

- Inconsistent crystallographic metrics across the PDB
- Most diffraction data not public
- Connection between diffraction data and deposited structure

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Training data and METRIX database

Data sources

JCSG → 507 structures
SGC → 303 structures

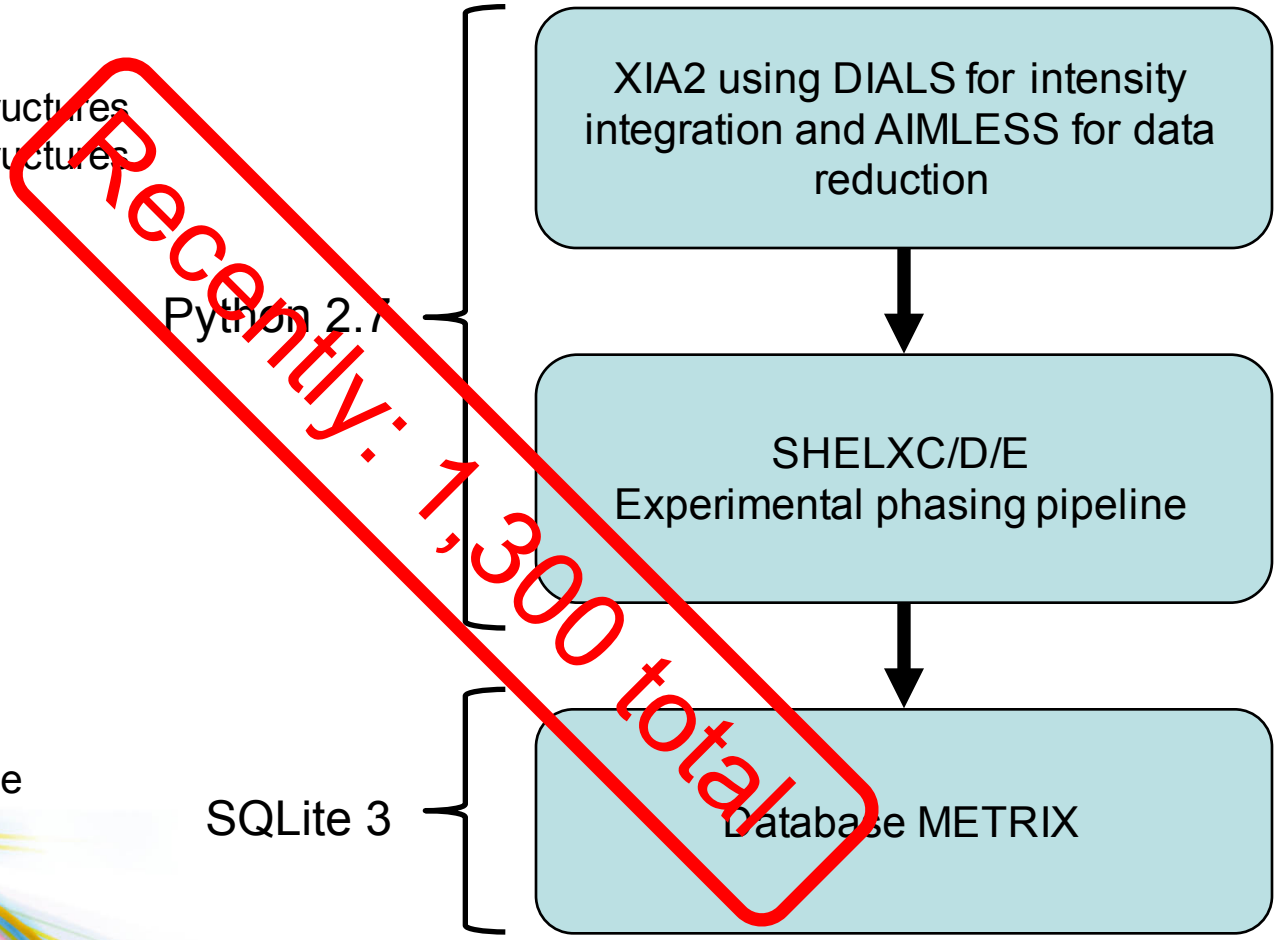
Phasing method:
S/MAD → 446
Native → 364

Resolution range:
1.05 – 3.8Å

Detector type:
CCD, PAD

X-Ray source:
Synchrotron, in-house

Protein:
6 – 100kDa



https://github.com/ccp4/metrix-database

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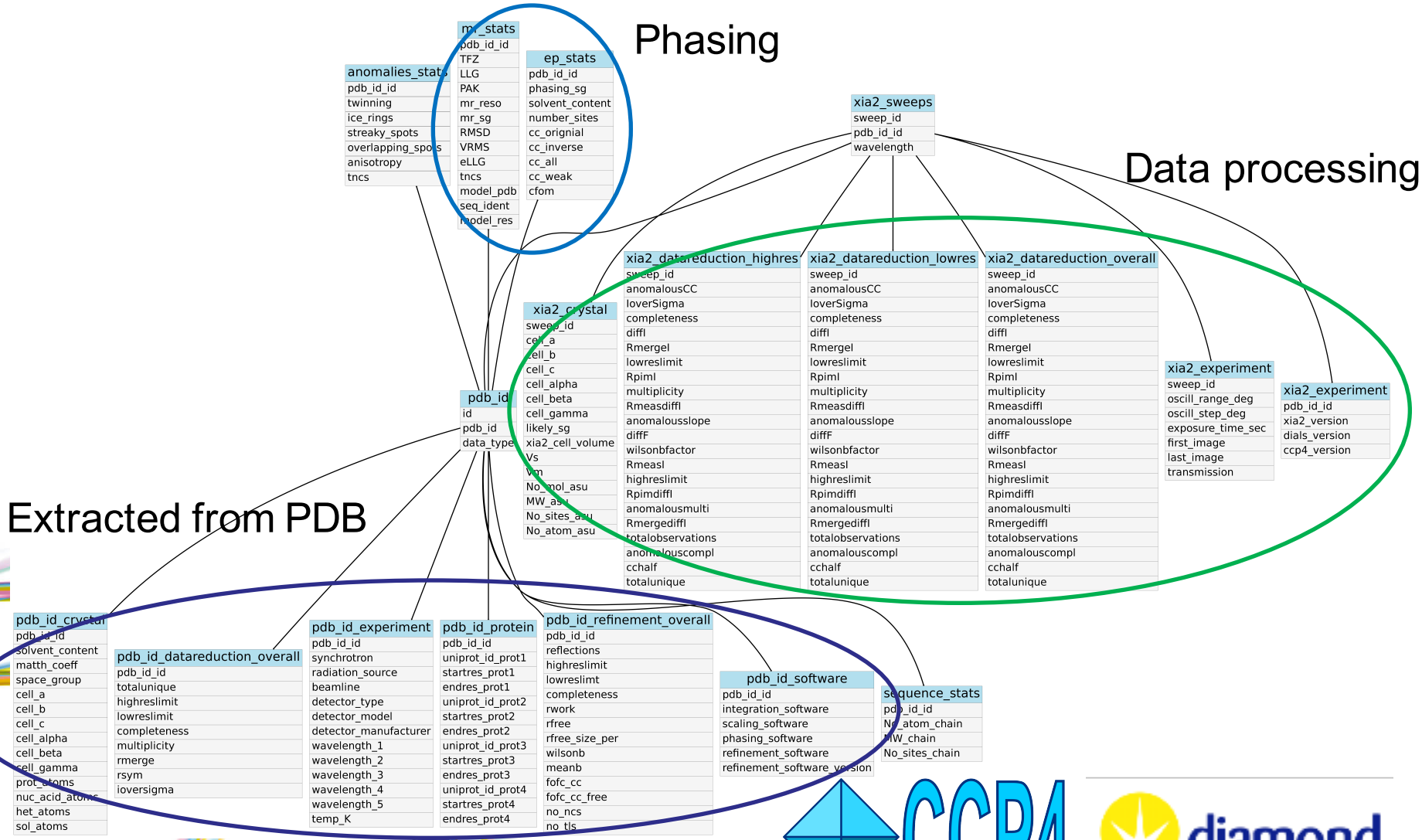
Training data and METRIX database

METRIX content and schema



https://github.com/ccp4/metrix-database

Experimental phasing success

Pre-assessment and classifiers tried

Pre-assessment tried
- Linear Pearson's correlation coefficients
- Recursive feature elimination

Classifiers tried
- Support vector machine with linear kernel
- Support vector machine with RBF kernel
- Decision tree
- Decision tree with Bagging
- Decision tree with AdaBoost
- Random forest
- Extreme random forest

Combined results to identify most important decision making features;
Then retrain all classifiers and assess their performance;
Python 3.x

703 samples; stratified test-train split (20/80)
3-fold cross-validation (20/80 split)

https://github.com/ccp4/metrix_ml

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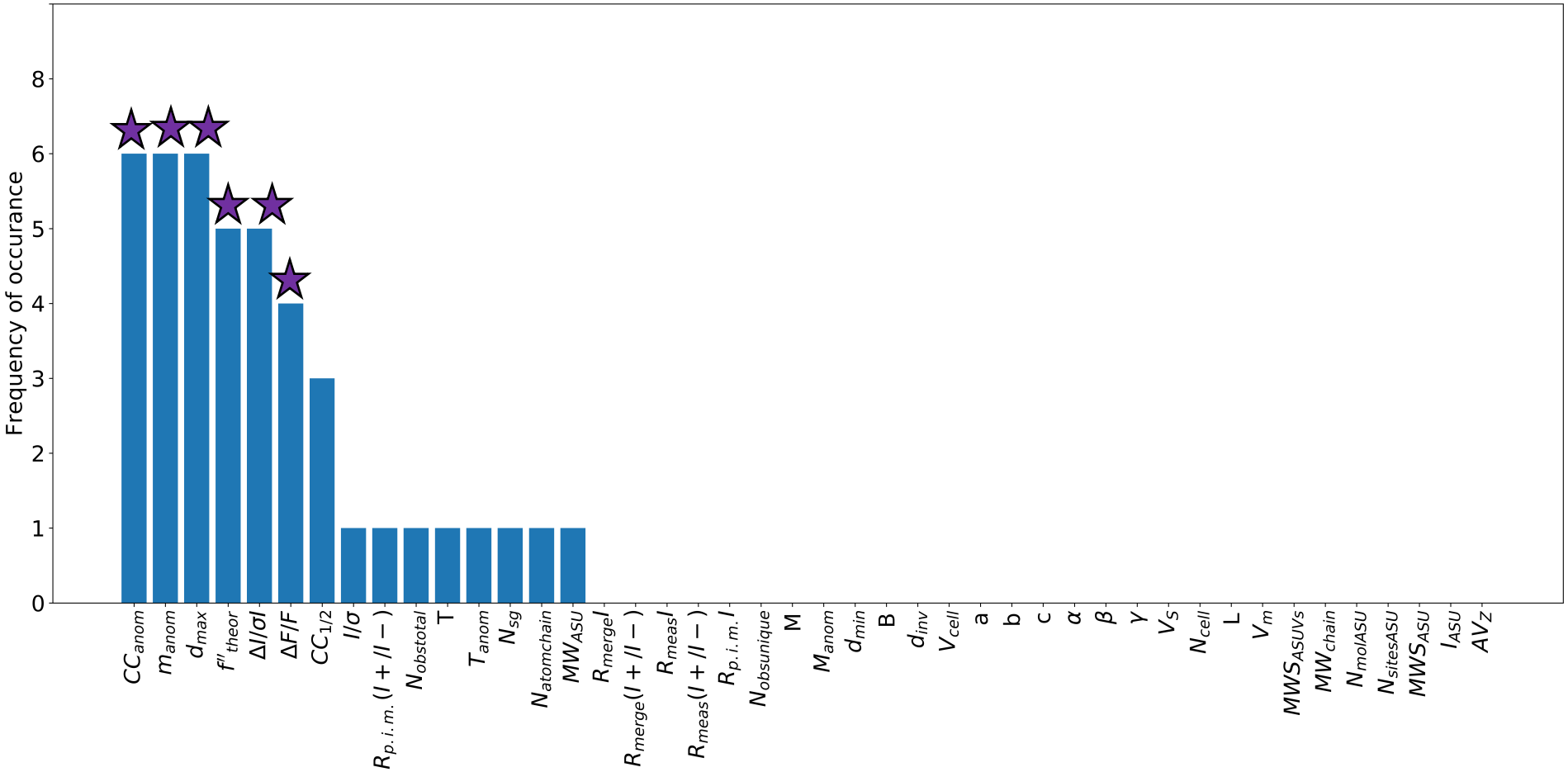
Experimental phasing success

Important decision making features



d_{max} → low resolution cut-off

d_{min} → high resolution cut-off

https://github.com/ccp4/metrix_ml

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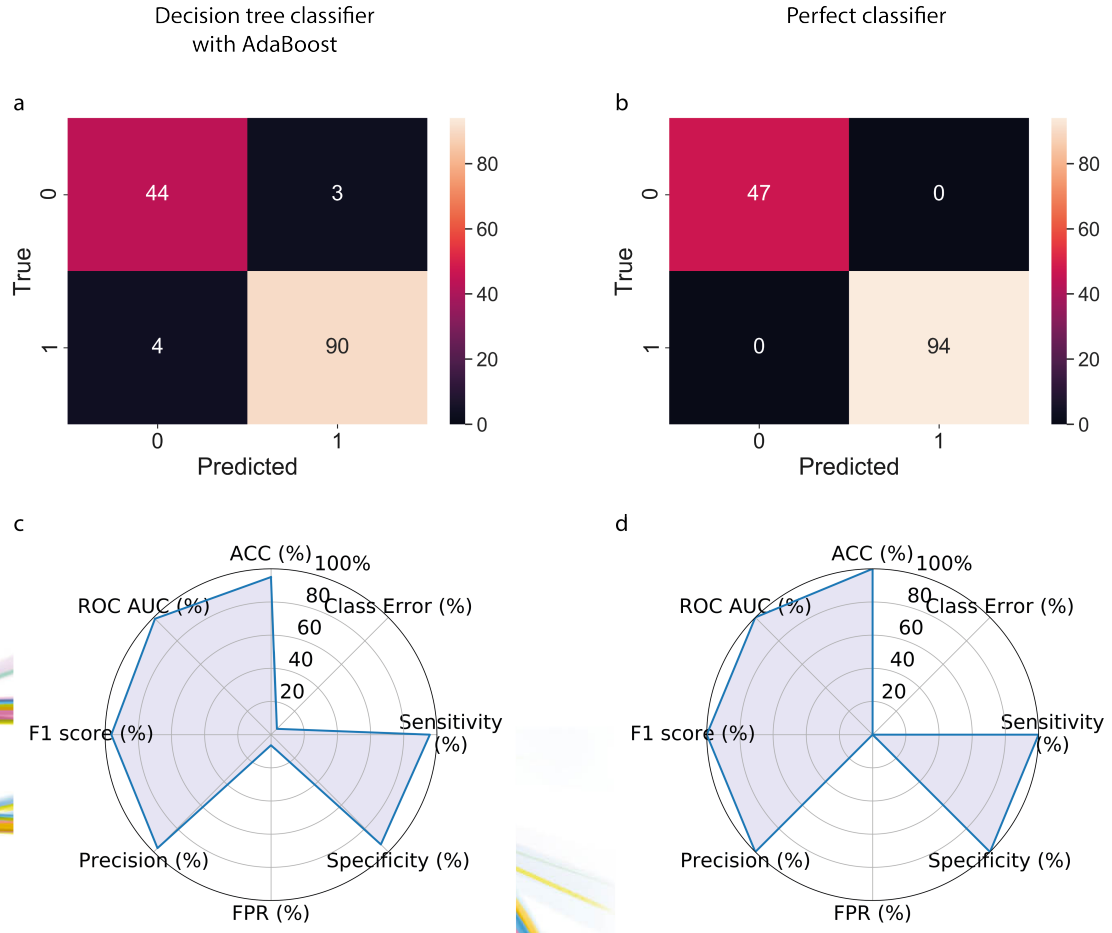
Experimental phasing success

Classifier assessment and performance

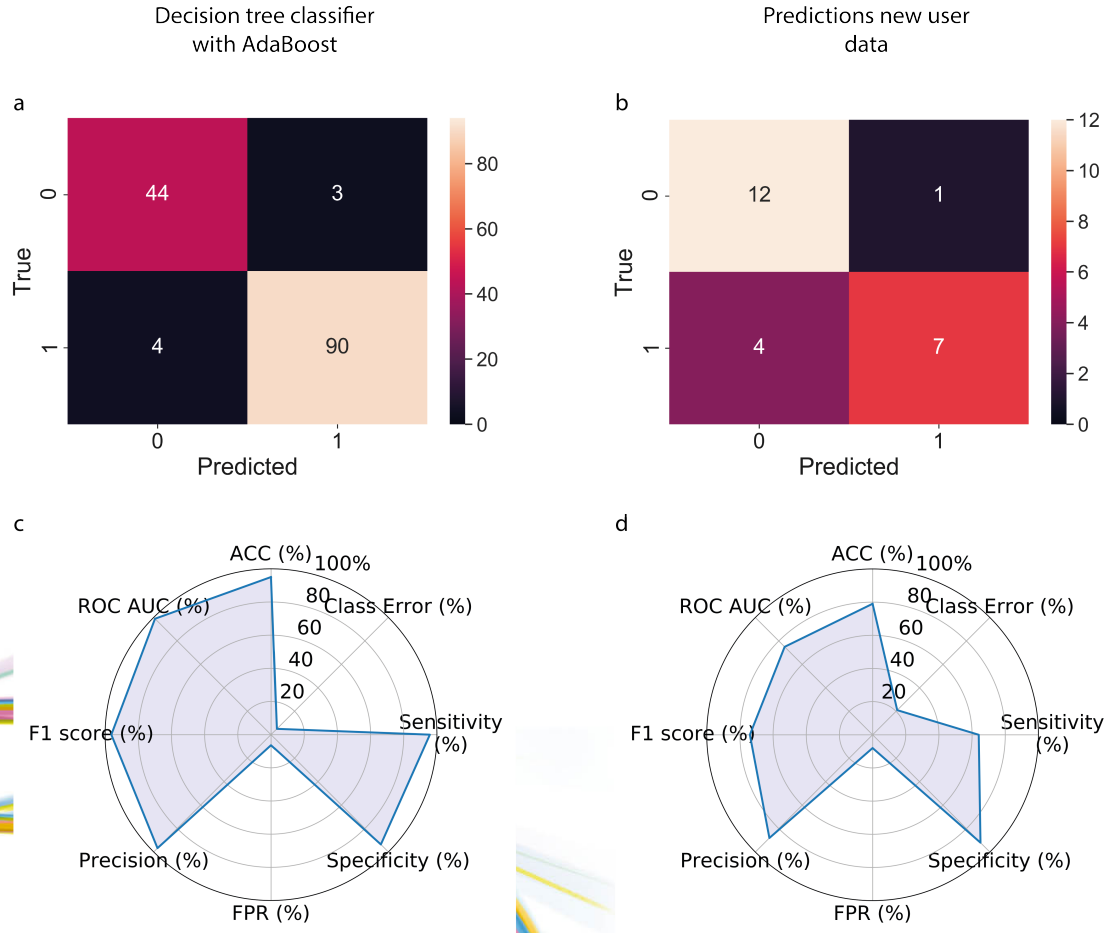


	Decision tree with AdaBoost	Perfect classifier
ACC (%)	95	100
Class Error (%)	5	0
Sensitivity (%)	96	100
Specificity (%)	94	100
FPR (%)	6	0
Precision (%)	97	100
F1 score (%)	96	100
ROC AUC (%)	99	100
TP test set	90	94
TN test set	44	47
FP test set	3	0
FN test set	4	0

https://github.com/ccp4/metrix_ml

Experimental phasing success

Predictions for new user data



	Decision tree with AdaBoost	New user data
ACC (%)	95	79
Class Error (%)	5	21
Sensitivity (%)	96	64
Specificity (%)	94	92
FPR (%)	6	8
Precision (%)	97	88
F1 score (%)	96	74
ROC AUC (%)	99	75
TP test set	90	7
TN test set	44	12
FP test set	3	1
FN test set	4	4

Probability cut-off for class 1: 80%

https://github.com/ccp4/metrix_ml

Molecular replacement success

Pre-assessment and classifiers tried

Pre-assessment tried
- Linear Pearson's correlation coefficients
- Recursive feature elimination

Classifiers tried
- Support vector machine with linear kernel
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- Decision tree
- Decision tree with Bagging
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- Random forest
- Extreme random forest

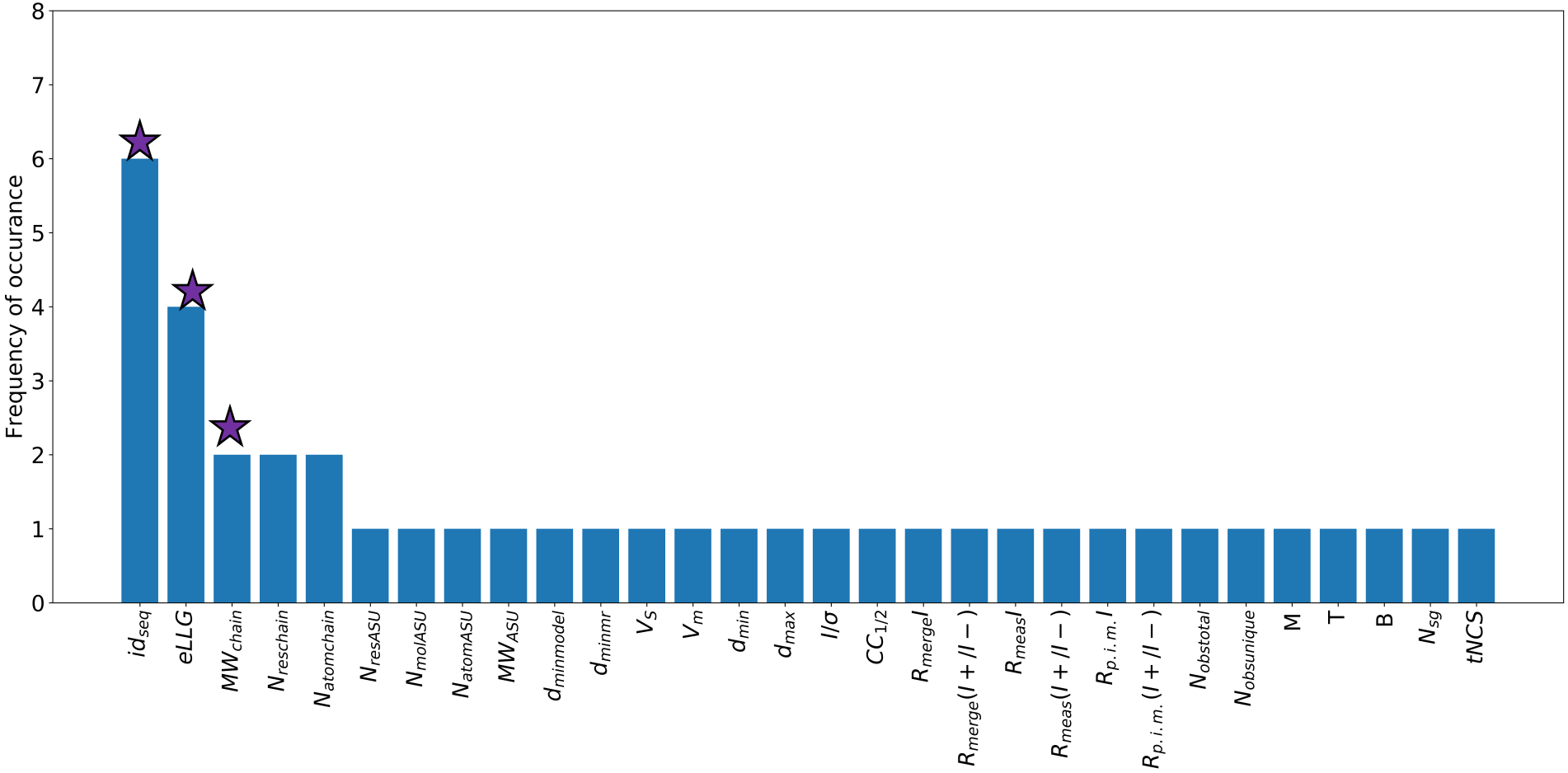
Combined results to identify most important decision making features;
Then retrain all classifiers and assess their performance;
Python 3.x

1020 samples; stratified test-train split (20/80)
3-fold cross-validation (20/80 split)

https://github.com/ccp4/metrix_ml

Molecular replacement success

Important decision making features



https://github.com/ccp4/metrix_ml

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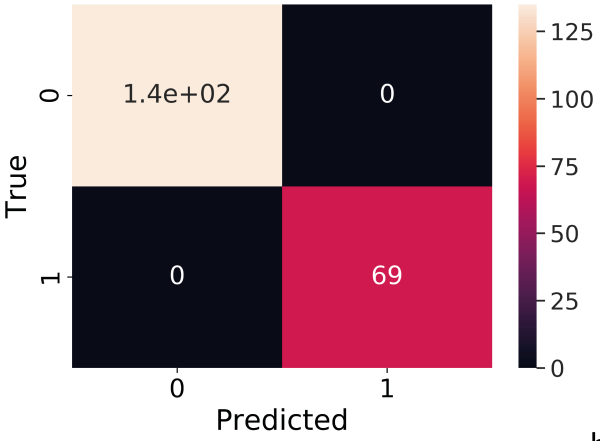
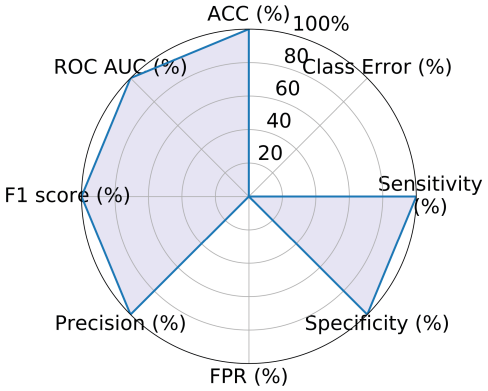
Molecular replacement success

Classifier assessment and performance

Perfect classifier

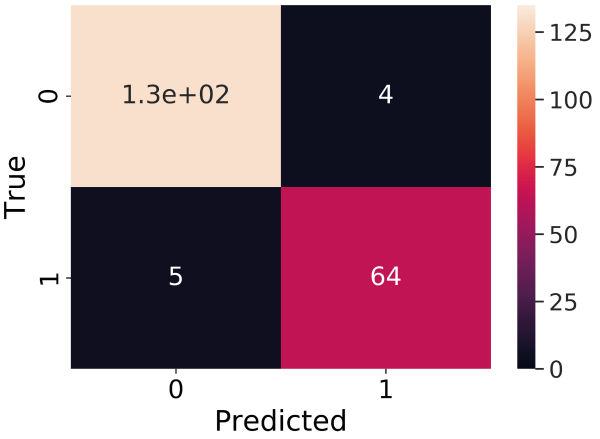


a

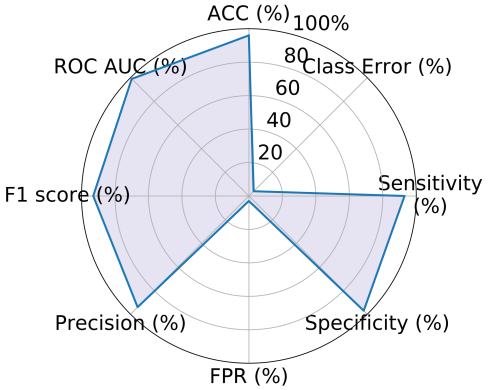


b

Best classifier



c



d

	Decision tree with AdaBoost	Perfect classifier
ACC (%)	96	100
Class Error (%)	4	0
Sensitivity (%)	93	100
Specificity (%)	97	100
FPR (%)	3	0
Precision (%)	94	100
F1 score (%)	93	100
ROC AUC (%)	99	100
TP test set	64	69
TN test set	131	135
FP test set	4	0
FN test set	5	0

https://github.com/ccp4/metrix_ml

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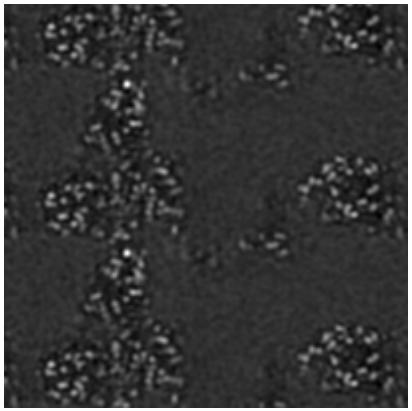
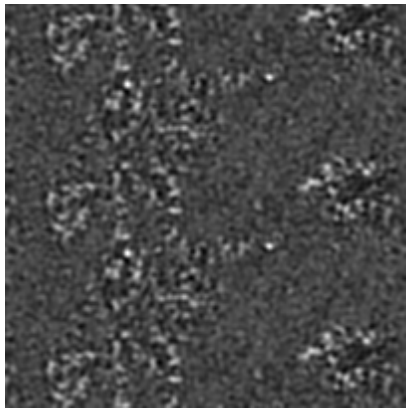
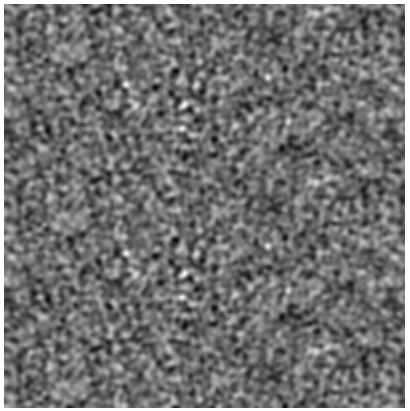
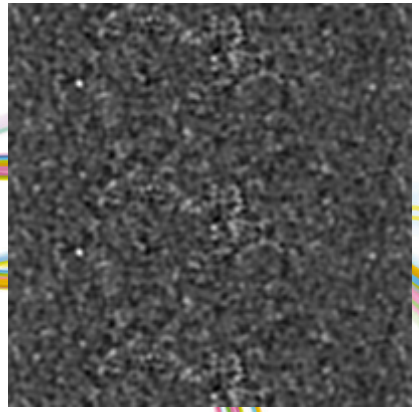
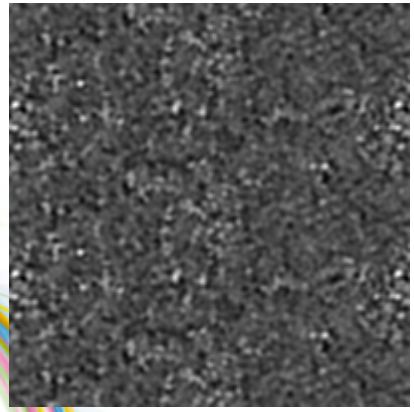
Map traceability

”Good” vs “bad” map PDB entry: 4DNK

solvent flattening backbone tracing	solvent flattening no backbone tracing	no solvent flattening no backbone tracing	
			“good”
			“bad”

https://github.com/DiamondLightSource/python-topaz3

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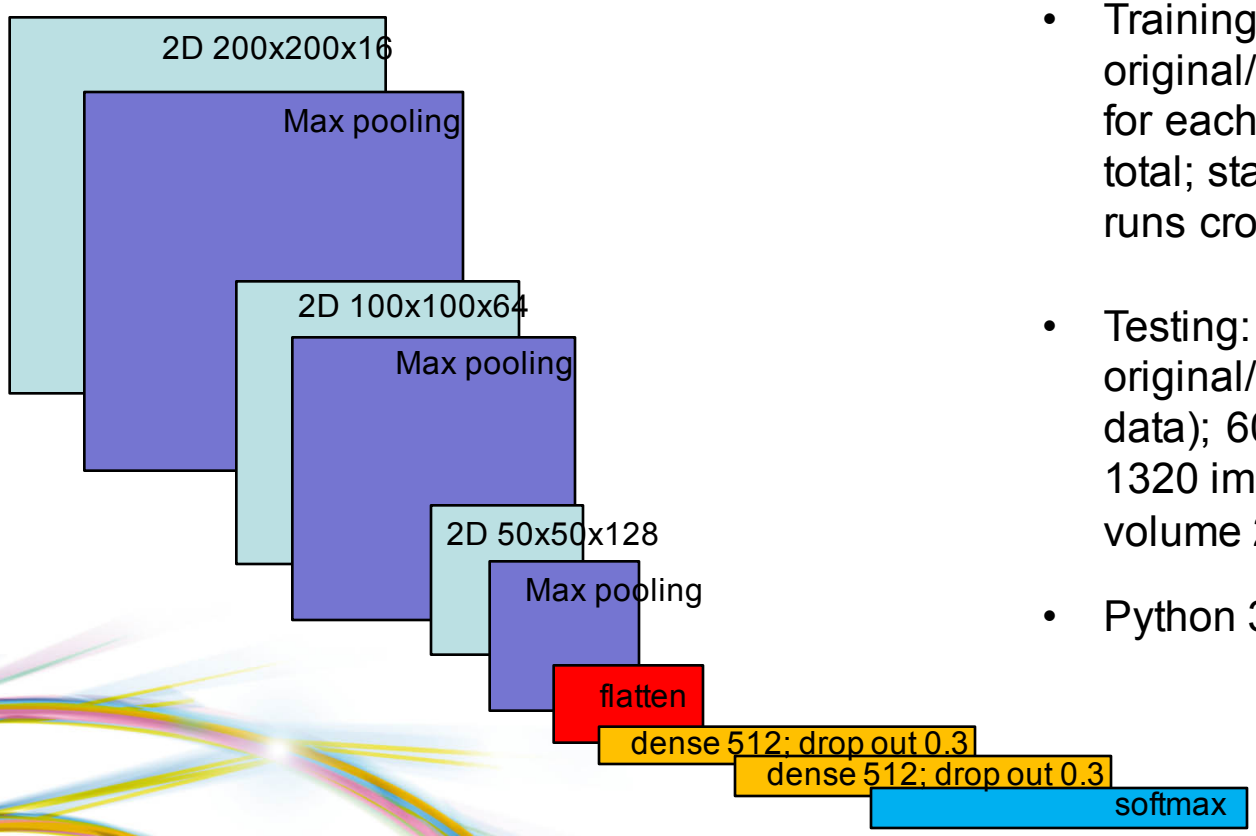
Map traceability

cNN



- Training: 400 maps or 200 original/inverse pairs; 60 slices (20 for each axes); 24,000 images in total; standard volume 200Å^3; 5 runs cross-validation 20/80 split
- Testing: 22 maps or 11 original/inverse pairs (~5% of total data); 60 slices (20 for each axes); 1320 images in total; standard volume 200Å^3
- Python 3.x

https://github.com/DiamondLightSource/python-topaz3

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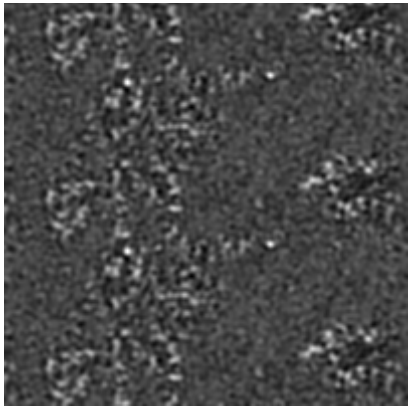
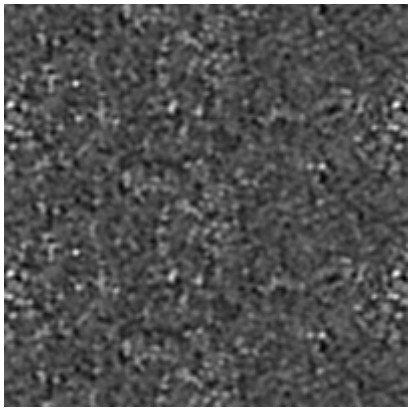
Map traceability

cNN assessment and performance

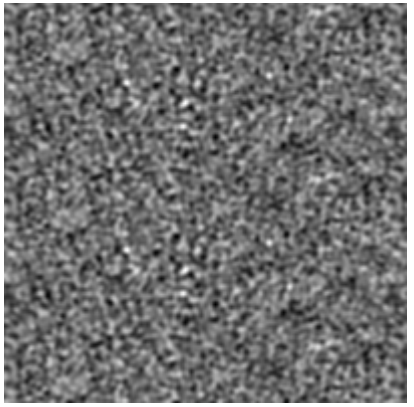
	Train: traced Test: traced	Train: traced Test: solvent flattened, no build
ACC (%)	96	63
Class Error (%)	4	37
Sensitivity (%)	94	67
Specificity (%)	98	58
FPR (%)	2	42
Precision (%)	98	62
TP test set	621	442
TN test set	648	385
FP test set	12	275
FN test set	39	218

solvent flattening
no backbone tracing





no solvent flattening
no backbone tracing



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Future plans

- Molecular replacement or experimental phasing success

–Feedback through Synchweb/ISPyB

–Include other software

- Map traceability

–Applying filters such as Gaussian, mean and median; data augmentation

–deep cNN for image denoising (Deep Image Prior, Ulyanov, D., Vedaldi, A., Lempitsky, V., https://arxiv.org/abs/1711.10925)

–ResNet and others

–From 2D to 3D

- On the side

–General integration into and querying from Synchweb/ISPyB

–Integration into CCP4 or some of its individual programs

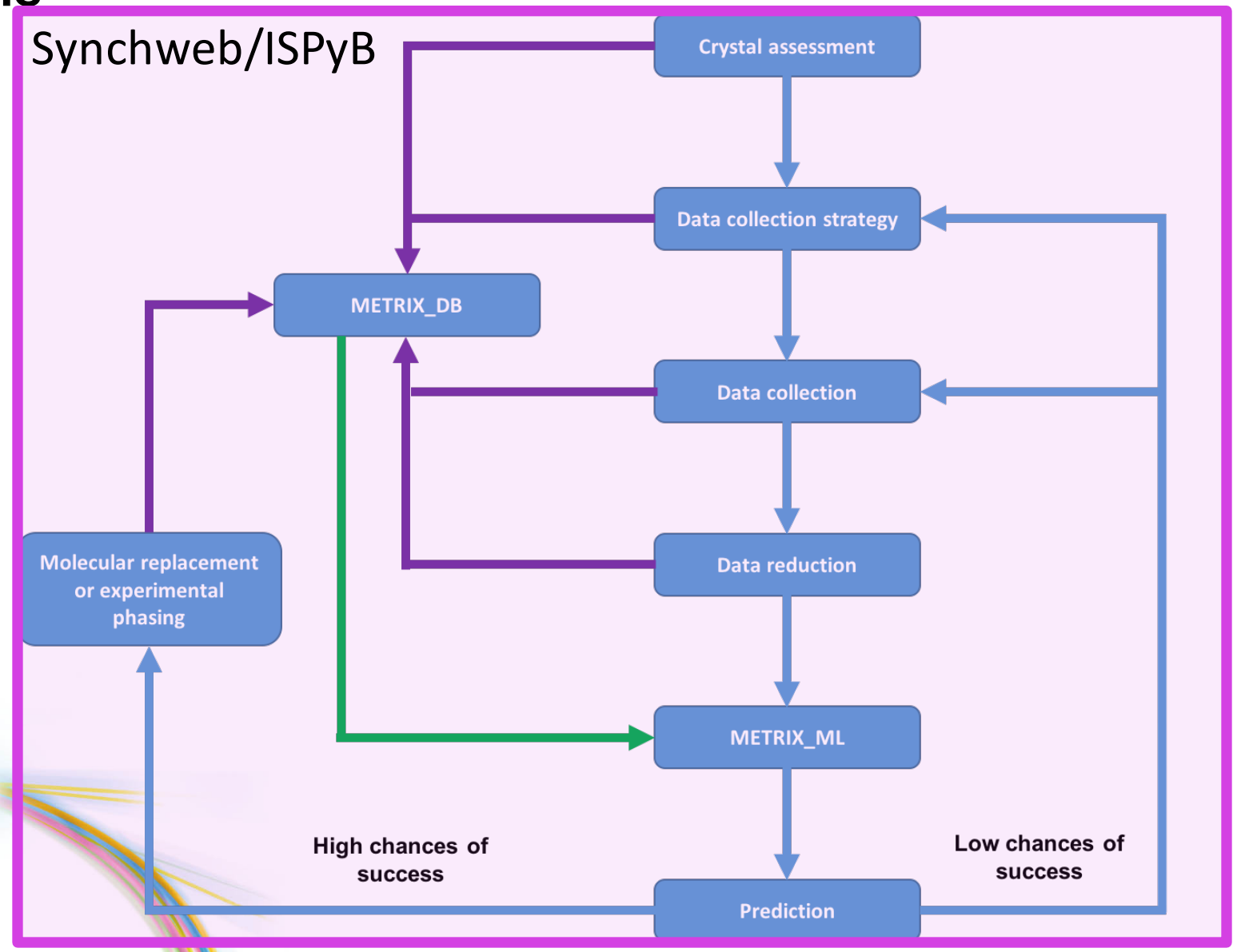
–Expanding crystallographic data analysis framework

–Expanding METRIX, including public access

–Point/space group classifier

–Add other bioinformatics prediction tools

Future plans



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University of Newcastle:
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Vollmar, M., Parkhurst, J. M., Jaques, D., Baslé, A., Murshudov, G. N., Waterman, D. and Evans, G. (2019) IUCrJ, The predictive power of data processing statistics, submitted