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Machine Learning for Chemists

– Gaussian Processes –

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19 February 2024

Outline

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Introduction to Regression

Uncertainty of Predictions

The “big idea” behind Gaussian Processes

Examples of GPs used in the wild

Live Demo!

Regression

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Answers a question that asks for a number.

Answers a question that asks for a number.

How much does this pet weigh?

Answers a question that asks for a number.

How much does this pet weigh?

This pet weighs **8 lbs**

Answers a question that asks for a number.

How much does this pet weigh?

This pet weighs **26 lbs**

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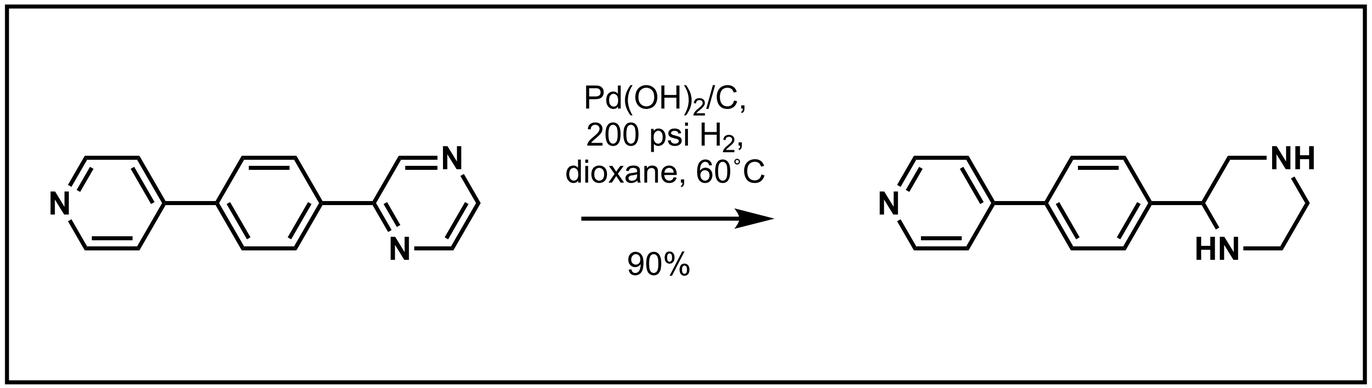
Answers a question that asks for a number.

What is the yield for this reaction?



The yield of this reaction is **90%**

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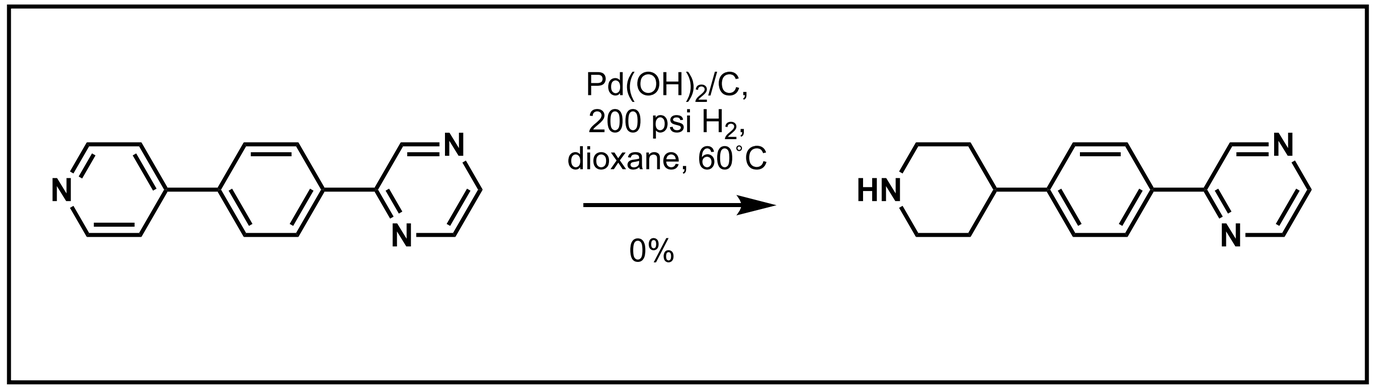
Answers a question that asks for a number.

What is the yield for this reaction?



The yield of this reaction is **0%**

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Confusion Matrix

What we predicted (predictions) \ What actually happened (ground truth)	High Yielding	Not High Yielding
High Yielding	True Positive	False Positive
Not High Yielding	False Negative	True Negative

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN} \qquad \text{Precision} = \frac{TP}{TP + FP} \qquad \text{Recall} = \frac{TP}{TP + FN} \qquad \text{F-Score} = \frac{2 \cdot TP}{TP + TN + FP}$$

Metrics quantify how far away from reality the predictions are.

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Common Regression Metrics:

Mean Absolute Error (MAE)

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Mean Absolute Error (MAE)

Absolute Error = | What actually happened – What we predicted |

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Common Regression Metrics:

Mean Absolute Error (MAE)

Absolute Error = | What actually happened – What we predicted |

	Exp 1	Exp 2	Exp 3
Ground truth	80%	25%	5%
Prediction	45%	30%	5%
Absolute Error			

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Common Regression Metrics:

Mean Absolute Error (MAE)

Absolute Error = | What actually happened – What we predicted |

	Exp 1	Exp 2	Exp 3
Ground truth	**80%**	25%	5%
Prediction	**45%**	30%	5%
Absolute Error	**35%**		

Abs Error Exp 1 = | **80%** – **45%** | = **35%**

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Common Regression Metrics:

Mean Absolute Error (MAE)

Absolute Error = | What actually happened – What we predicted |

	Exp 1	Exp 2	Exp 3
Ground truth	80%	**25%**	5%
Prediction	45%	**30%**	5%
Absolute Error	35%	**5%**	

Abs Error Exp 2 = | **25%** – **30%** | = **5%**

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Common Regression Metrics:

Mean Absolute Error (MAE)

Absolute Error = | What actually happened – What we predicted |

	Exp 1	Exp 2	Exp 3
Ground truth	80%	25%	**5%**
Prediction	45%	30%	**5%**
Absolute Error	35%	5%	**0%**

Abs Error Exp 3 = | **5%** – **5%** | = **0%**

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Common Regression Metrics:

Mean Absolute Error (MAE)

Absolute Error = | What actually happened – What we predicted |

	Exp 1	Exp 2	Exp 3
Ground truth	80%	25%	5%
Prediction	45%	30%	5%
Absolute Error	**35%**	**5%**	**0%**

$$\text{Mean Abs Error} = \frac{35\% + 5\% + 0\%}{3} = \textbf{13.3\% yield}$$

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Common Regression Metrics:

Root Mean Squared Error (RMSE)

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Common Regression Metrics:

Root Mean Squared Error (RMSE)

Squared Error = (What actually happened – What we predicted)^2

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Common Regression Metrics:

Root Mean Squared Error (RMSE)

Squared Error = (What actually happened – What we predicted)^2

	Exp 1	Exp 2	Exp 3
Ground truth	**80%**	25%	5%
Prediction	**45%**	30%	5%

Squared Error **1225%**

Sqrd Error Exp 1 = (**80%** – **45%**)^2 = **1225%**

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Common Regression Metrics:

Root Mean Squared Error (RMSE)

Squared Error = (What actually happened – What we predicted)^2

	Exp 1	Exp 2	Exp 3
Ground truth	80%	**25%**	5%
Prediction	45%	**30%**	5%
Squared Error	1225%	**25%**	

Sqrd Error Exp 2 = (**25%** – **30%**)^2 = **25%**

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Common Regression Metrics:

Root Mean Squared Error (RMSE)

Squared Error = (What actually happened – What we predicted)^2

	Exp 1	Exp 2	Exp 3
Ground truth	80%	25%	**5%**
Prediction	45%	30%	**5%**
Squared Error	1225%	25%	**0%**

Sqrd Error Exp 3 = (**5%** – **5%**)^2 = **0%**

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Common Regression Metrics:

Root Mean Squared Error (RMSE)

Squared Error = (What actually happened – What we predicted)^2

	Exp 1	Exp 2	Exp 3
Ground truth	80%	25%	5%
Prediction	45%	30%	5%
Squared Error	**1225%**	**25%**	**0%**

$$\text{Mean Squared Error} = \frac{1225\% + 25\% + 0\%}{3}$$

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Common Regression Metrics:

Root Mean Squared Error (RMSE)

Squared Error = (What actually happened – What we predicted)^2

	Exp 1	Exp 2	Exp 3
Ground truth	80%	25%	5%
Prediction	45%	30%	5%
Squared Error	**1225%**	**25%**	**0%**

$$\text{Root Mean Squared Error} = \sqrt{\frac{1225\% + 25\% + 0\%}{3}} = \textbf{20.4\% yield}$$

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Common Regression Metrics:

R^2 Error

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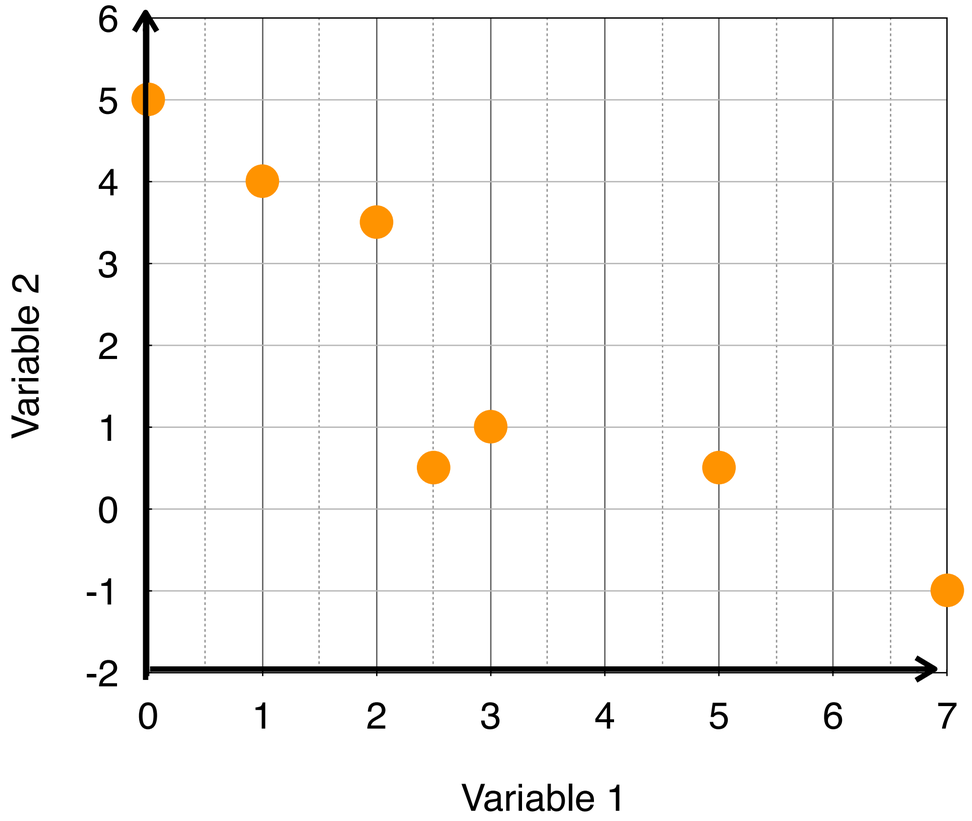
Common Regression Metrics:

R^2 Error

Recall from early graphing



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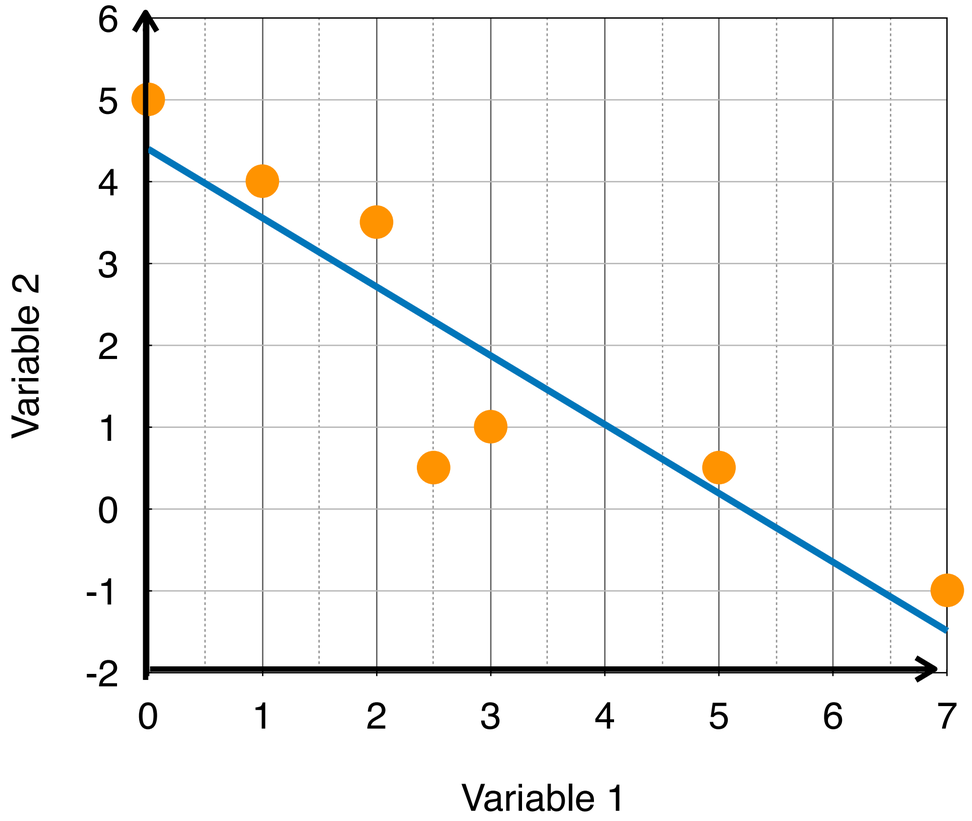
Common Regression Metrics:

R^2 Error

Recall from early graphing



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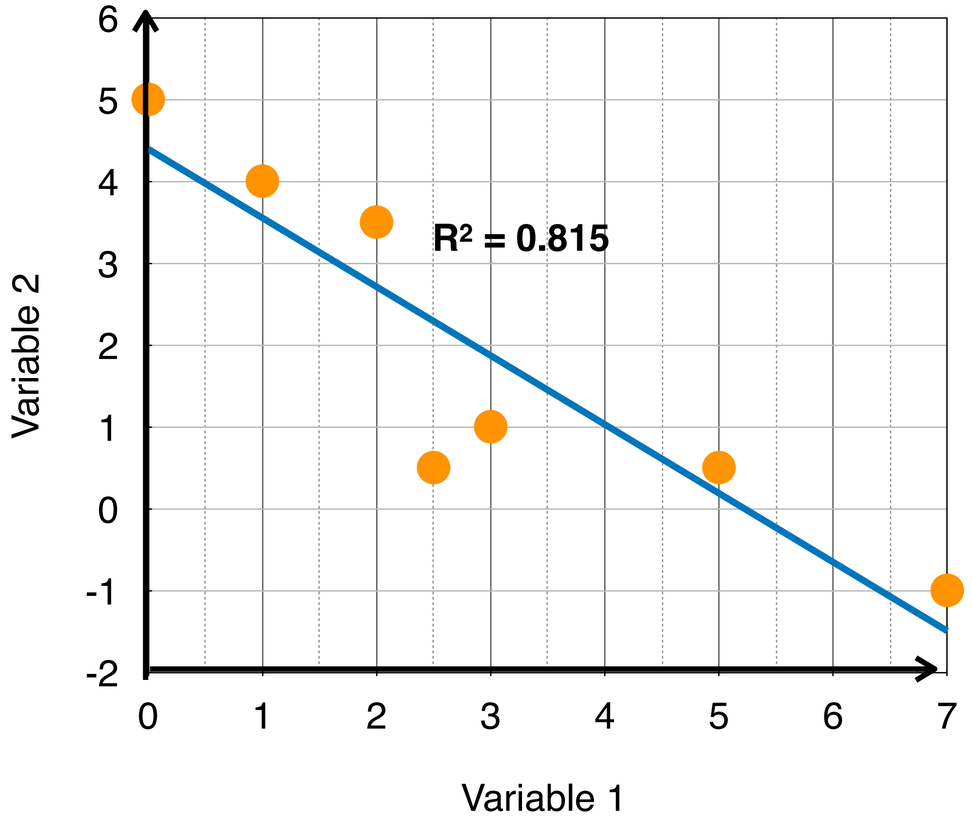
Common Regression Metrics:

R^2 Error

Recall from early graphing



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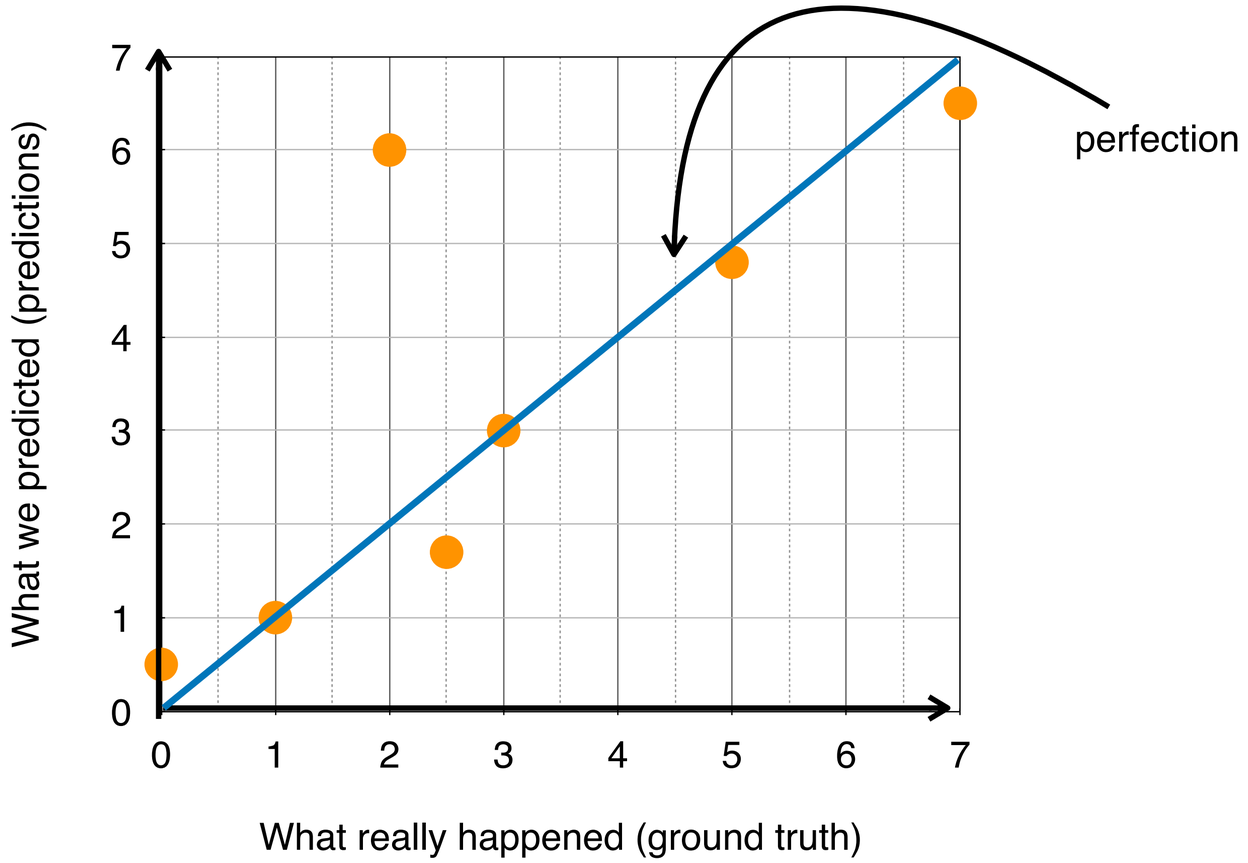
Common Regression Metrics:

R^2 Error

How well does the line y = x fit the data?



Answers a question that asks for a number AND answers with its confidence.

How much does this pet weigh?

How sure of your answer are you?

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Answers a question that asks for a number AND answers with its confidence.

How much does this pet weigh?

How sure of your answer are you?

This pet weighs **8 lbs**

I’m not very sure (lots of fluff).

± 4 lbs

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Answers a question that asks for a number AND answers with its confidence.

How much does this pet weigh?

How sure of your answer are you?

This pet weighs **26 lbs**

I'm very sure (I've seen lots of corgis).

± 0.5 lbs

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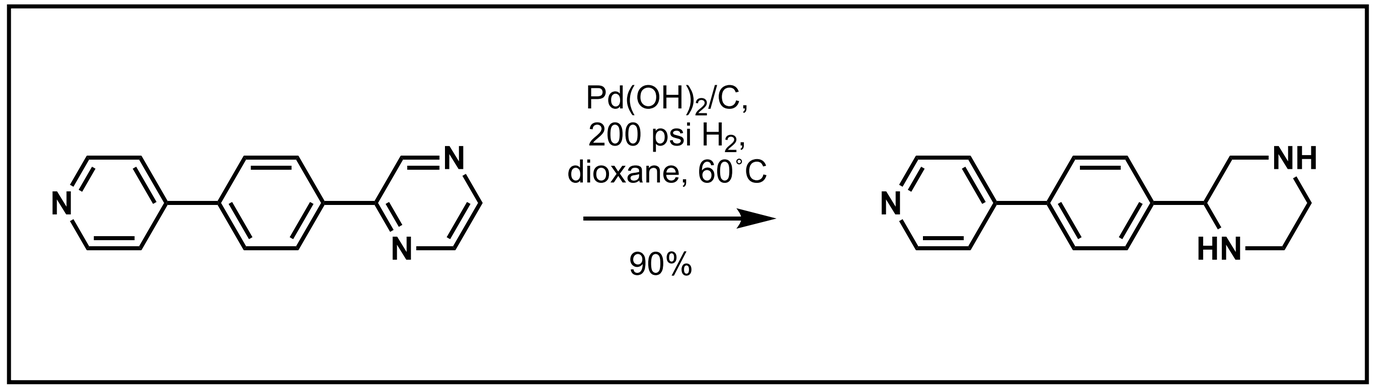
Answers a question that asks for a number AND answers with its confidence.

What is the yield of this reaction?

How sure of your answer are you?

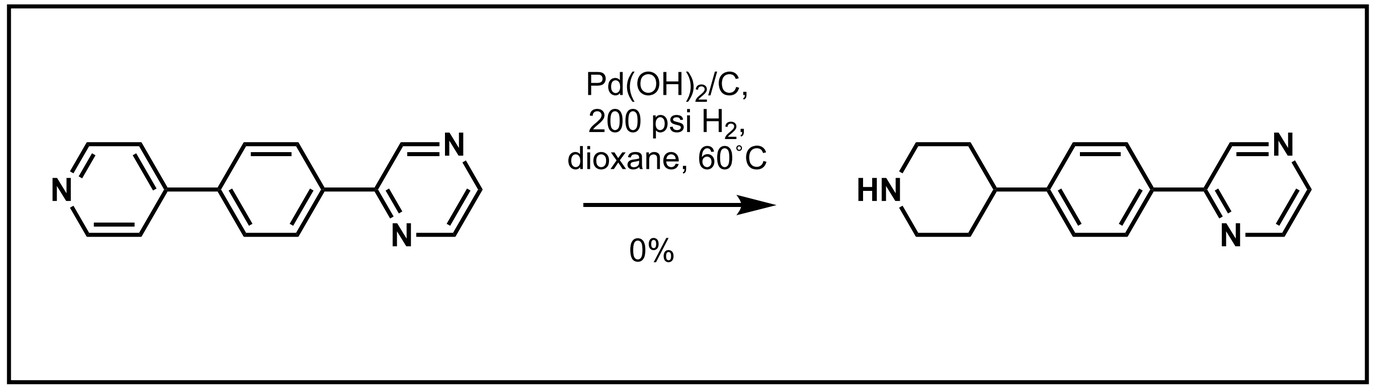


The yield of this reaction is **90% ± 10%**

Answers a question that asks for a number AND answers with its confidence.

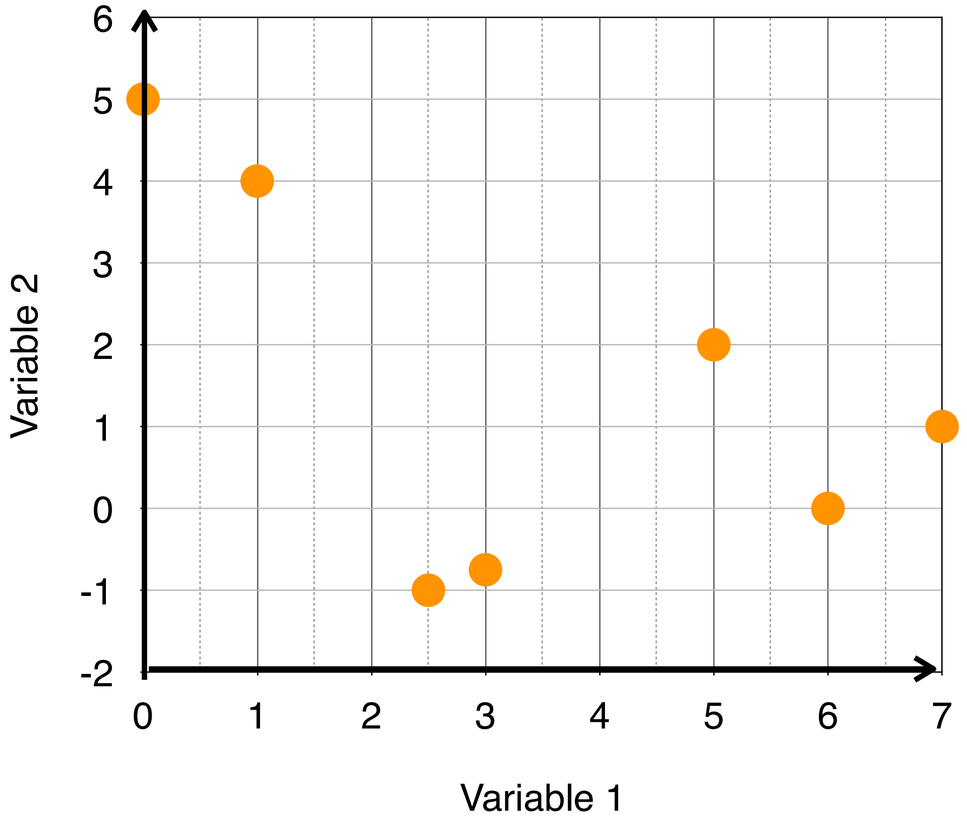
What is the yield of this reaction?

How sure of your answer are you?

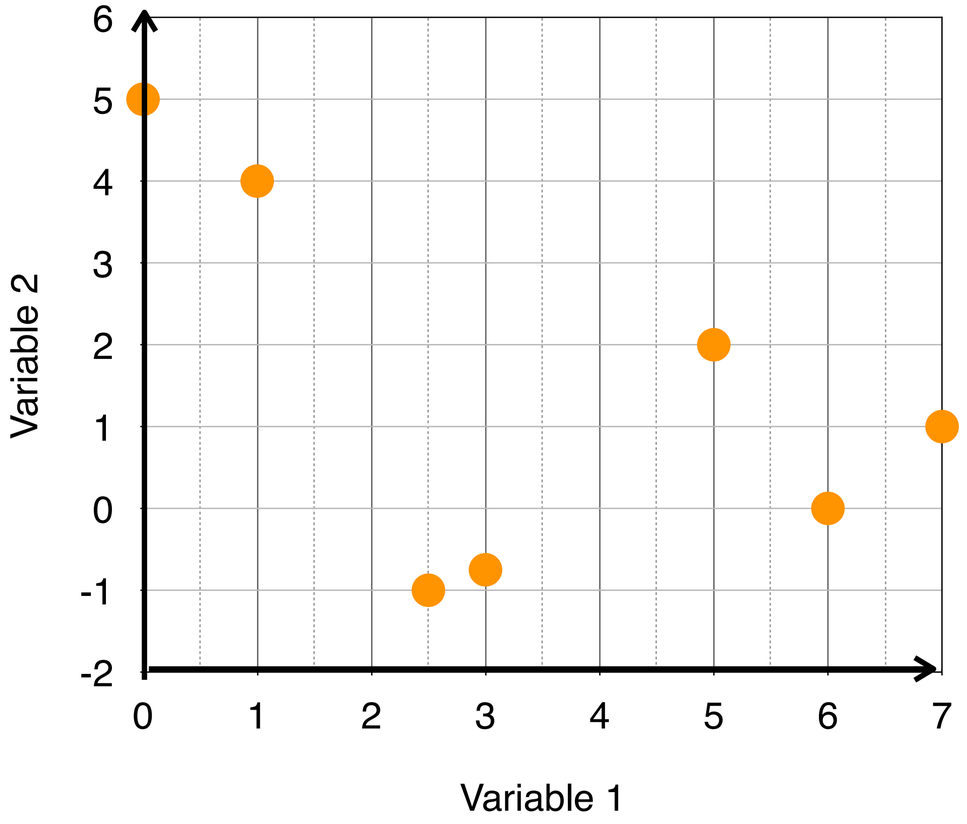


The yield of this reaction is **0% ± 50%**

Our Typical Workflow for Regression

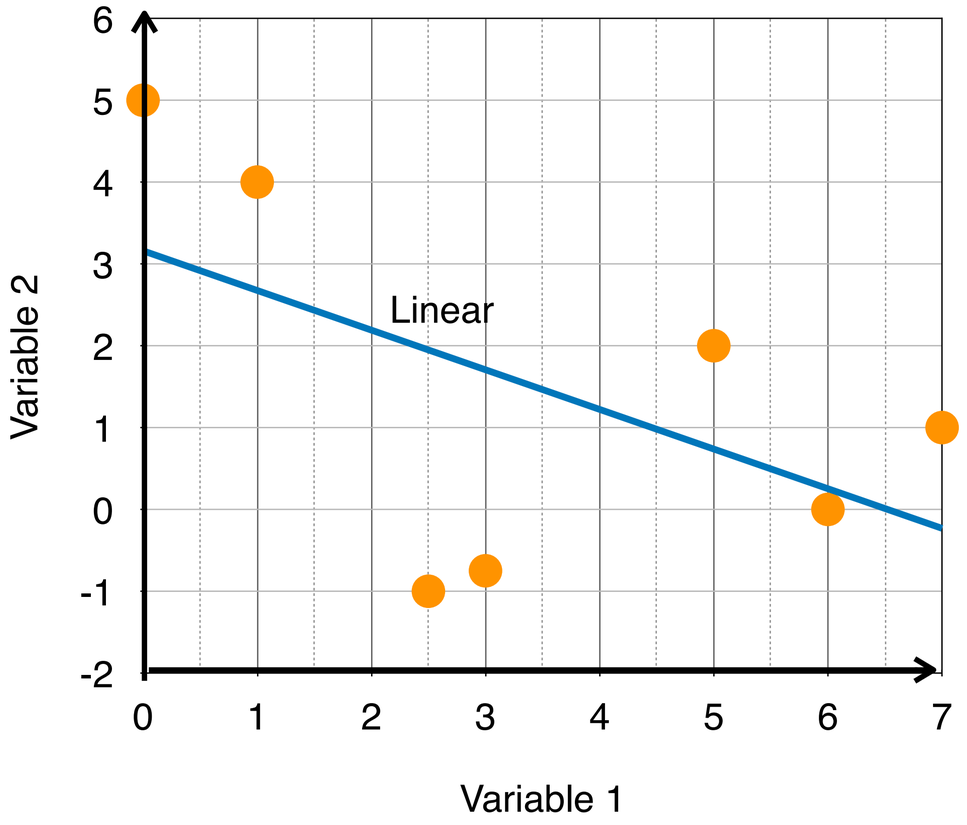


Our Typical Workflow for Regression



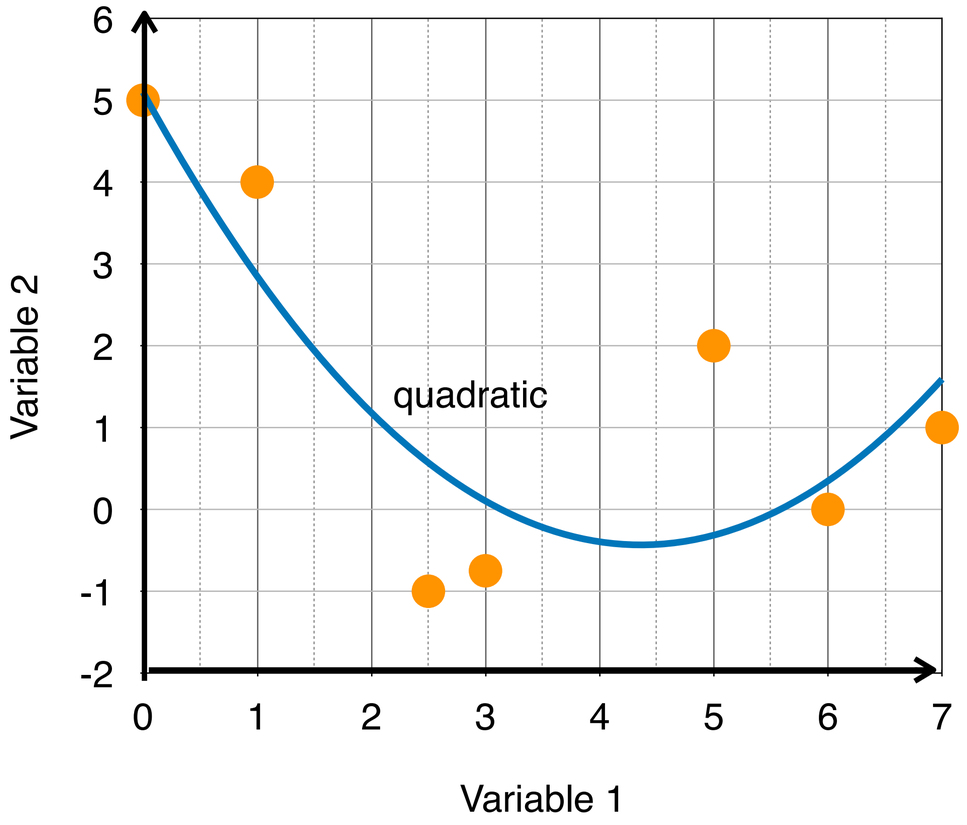
We have data → Single style of function to fit data

Our Typical Workflow for Regression



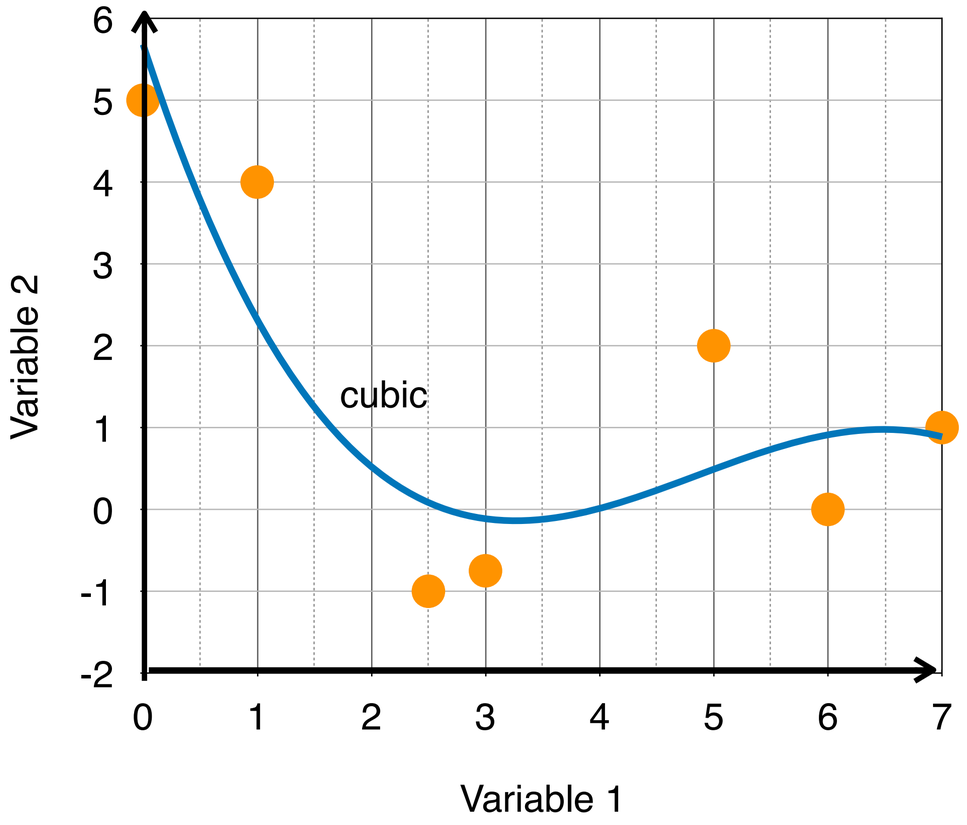
We have data → Single style of function to fit data

Our Typical Workflow for Regression



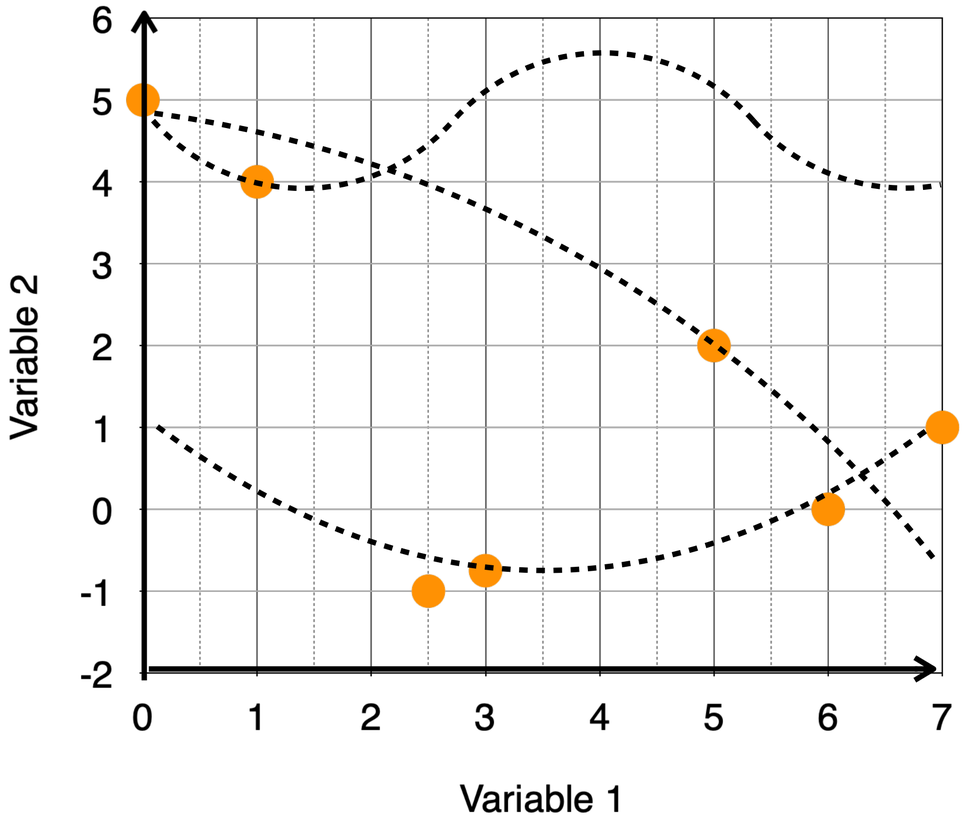
We have data → Single style of function to fit data

Our Typical Workflow for Regression



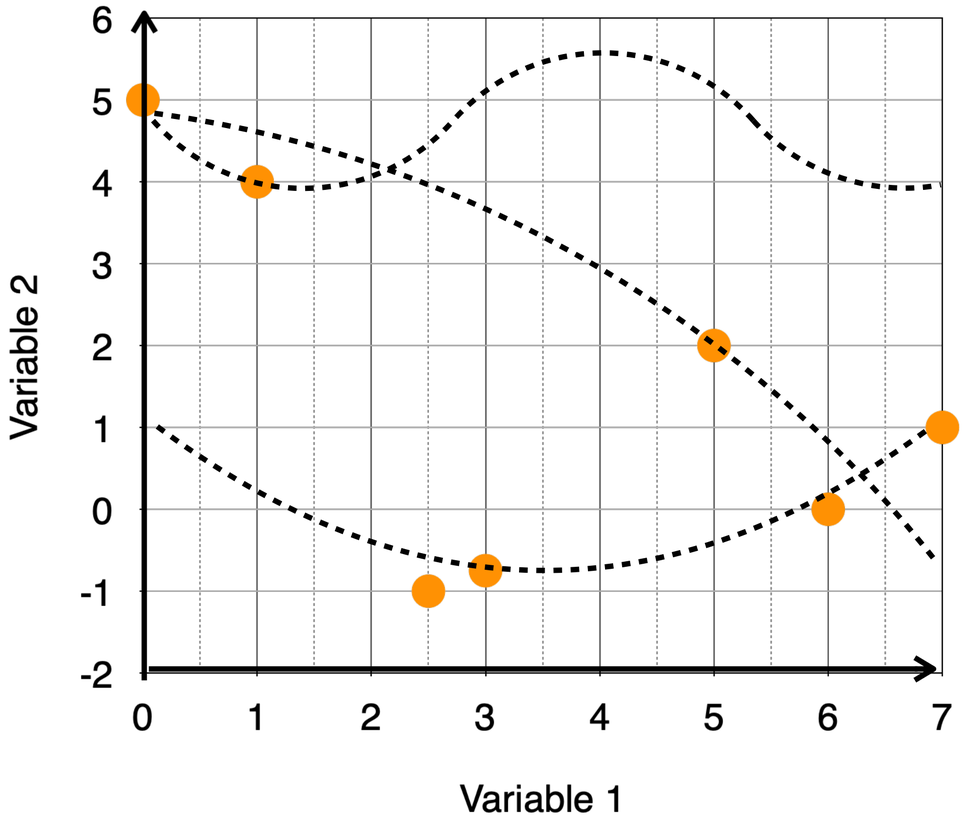
We have data → Single style of function to fit data

The Big Idea



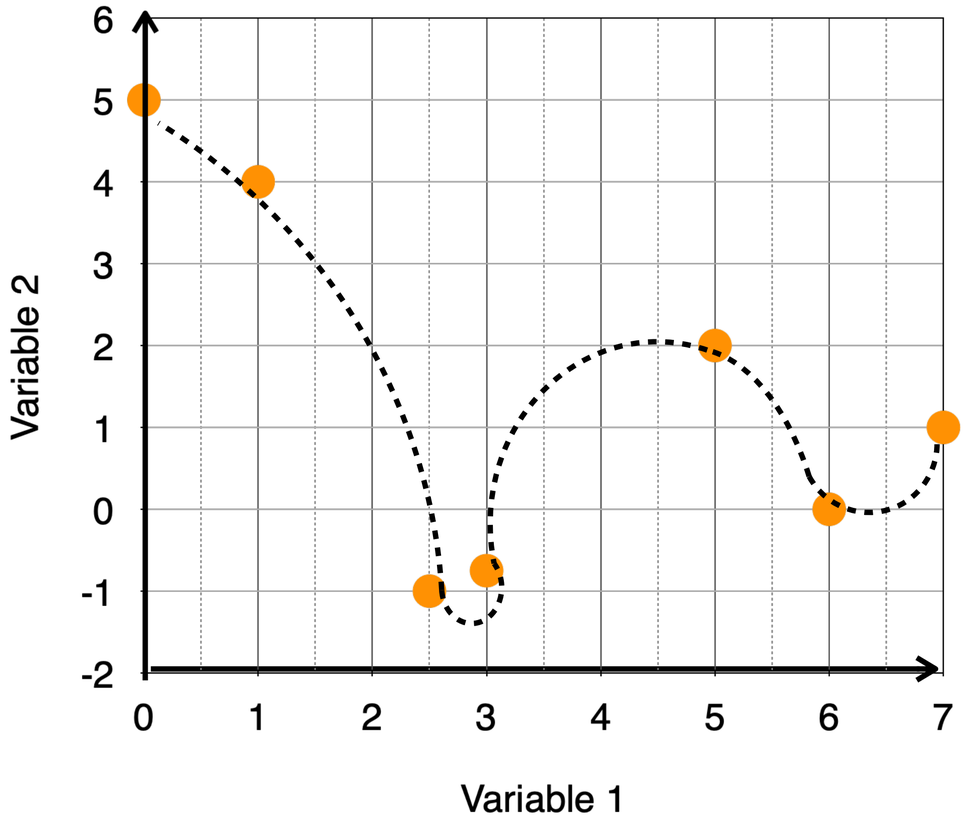
We have data → All possible functions that fit the data

The Big Idea



We have data → All possible functions that **go through ALL our points**

The Big Idea



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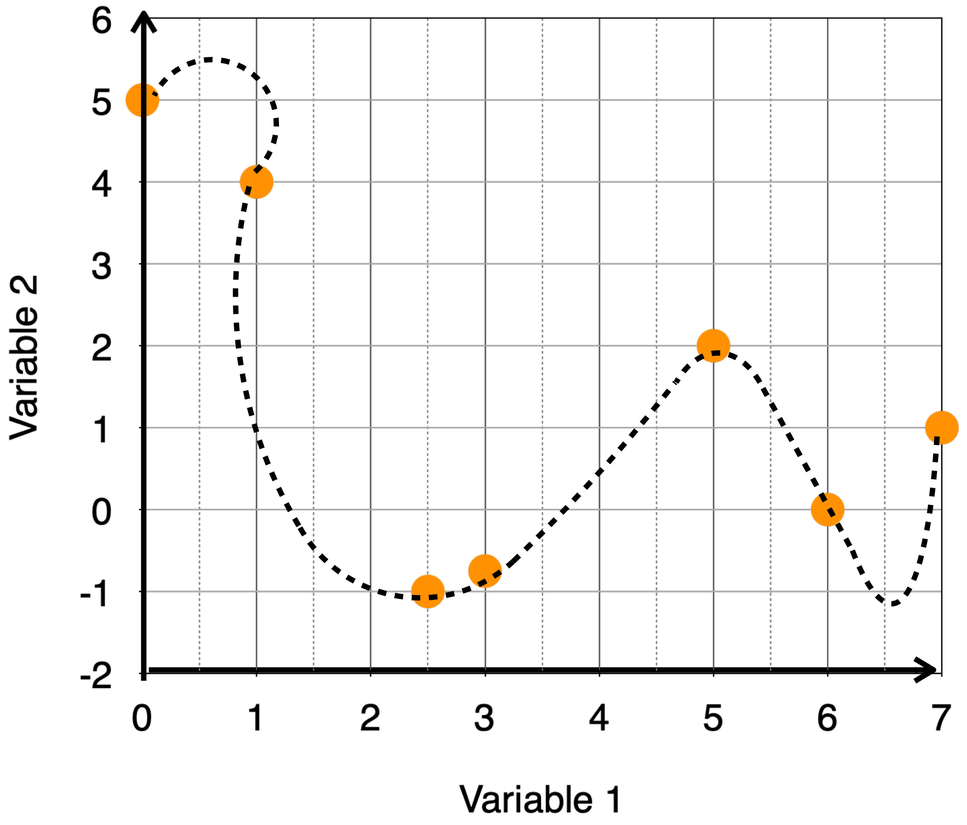

We have data → All possible functions that **go through ALL our points**

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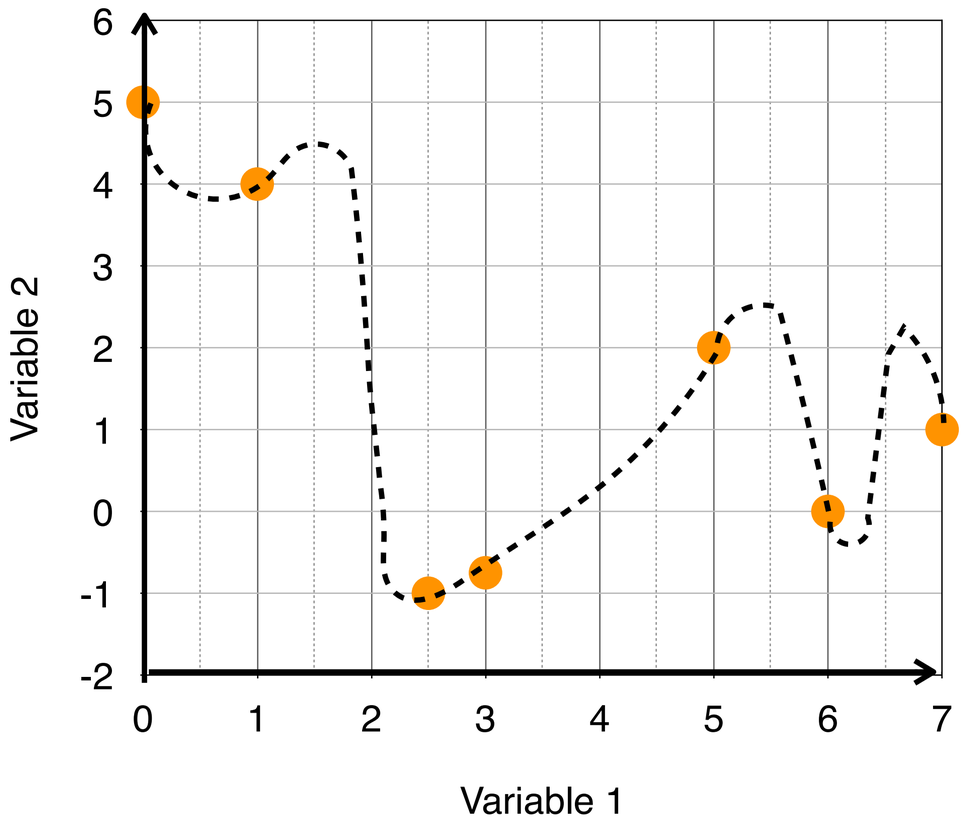
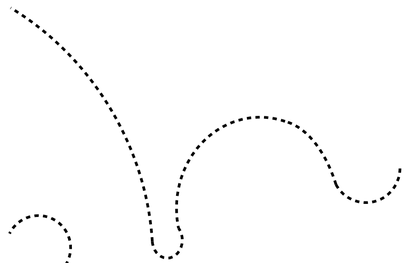
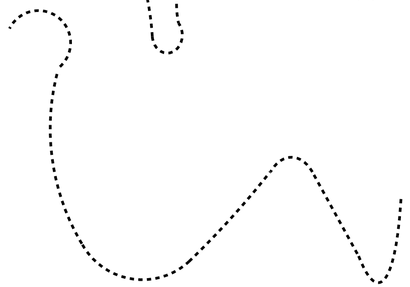
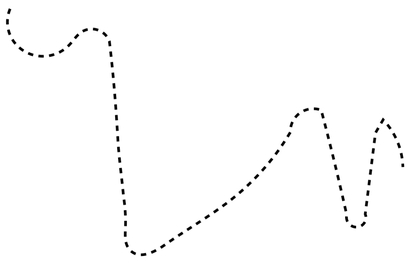
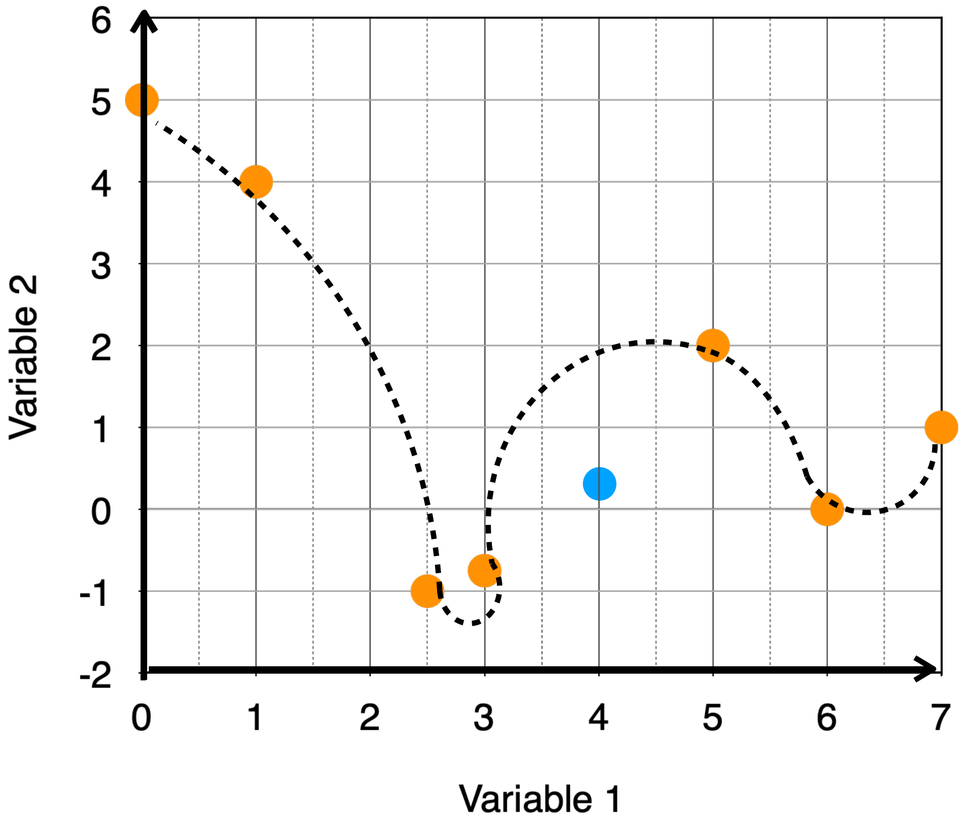


We have data → All possible functions that **go through ALL our points**

The Big Idea

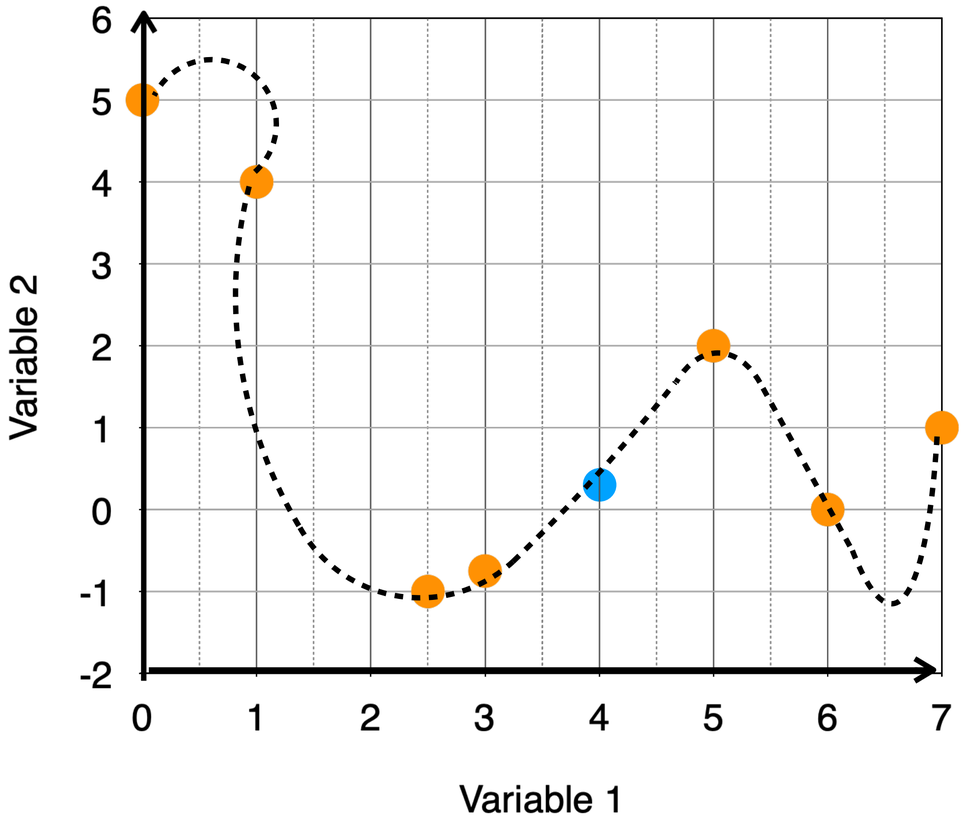
Possible Function	Probability
	5%
	3%
	4%
⋮	

The Big Idea



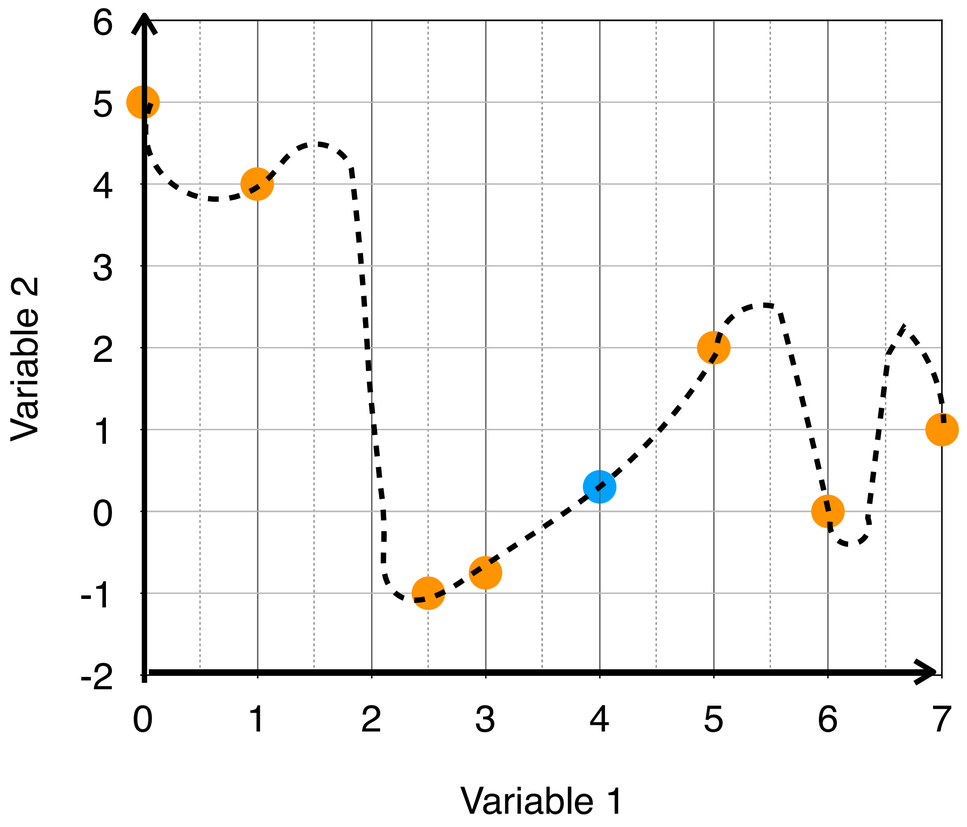
Add new data point → Update the probabilities

The Big Idea



Add new data point → Update the probabilities

The Big Idea



Add new data point → Update the probabilities

The Big Idea

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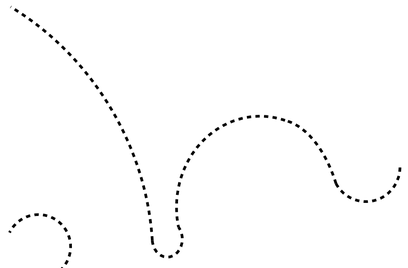
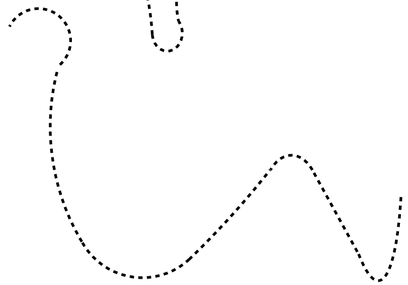
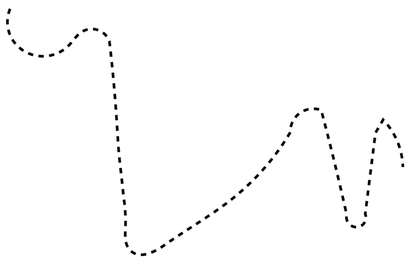
Possible Function	Probability
	**0%**
	3%
	7%
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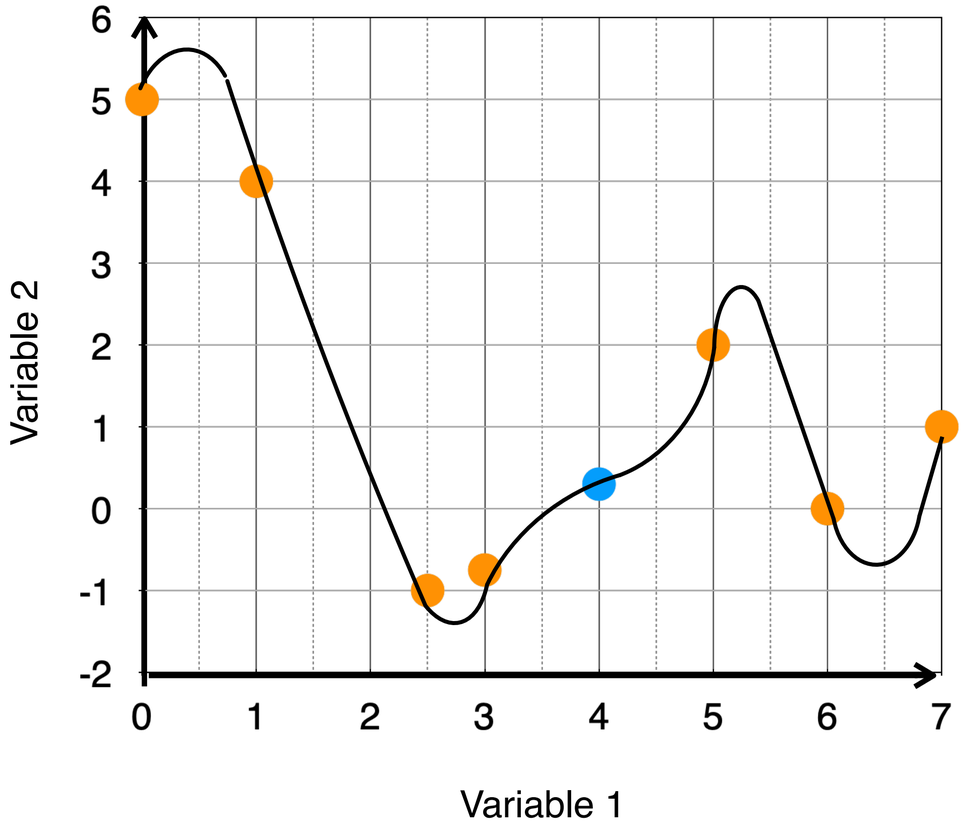
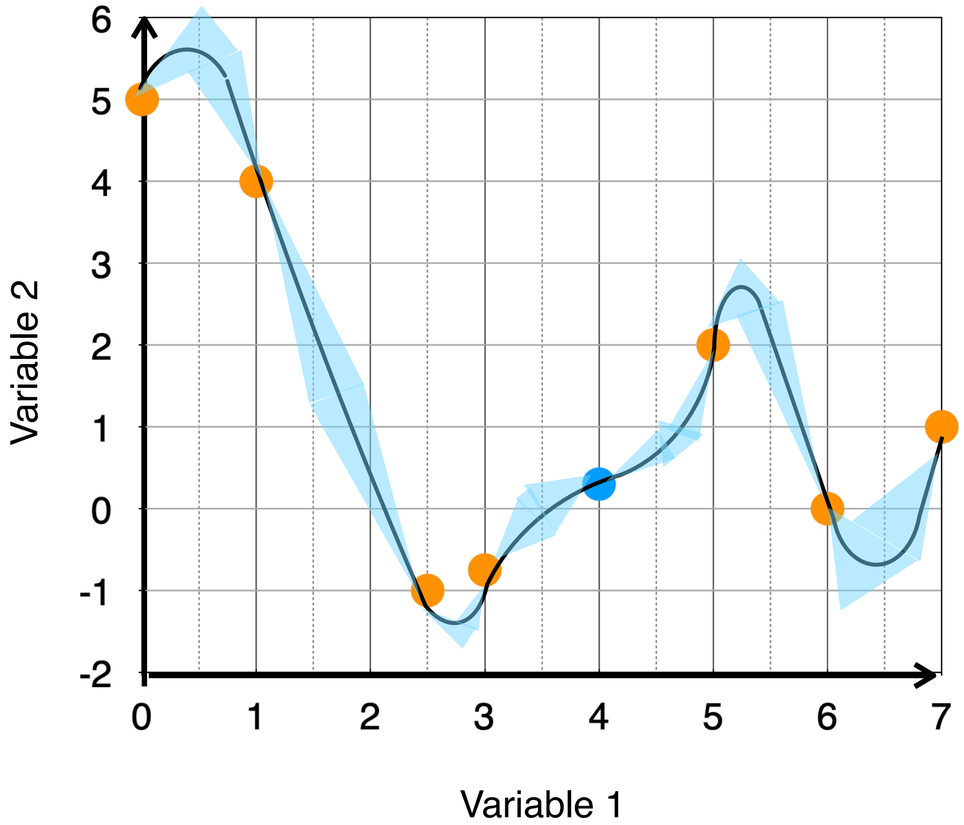
The Big Idea



Weighted average of the possible functions → Mean = most probable value

https://distill.pub/2019/visual-exploration-gaussian-processes/

The Big Idea



Weighted average of the possible functions

Mean = most probable value

Standard Deviation = uncertainty of each prediction
(based on values of other probable functions)

https://distill.pub/2019/visual-exploration-gaussian-processes/

A Challenge for Gaussian Processes

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Gaussian Processes work best for continuous processes.

https://2020blogfor.github.io/posts/2020/04/kf_gp/

A Challenge for Gaussian Processes

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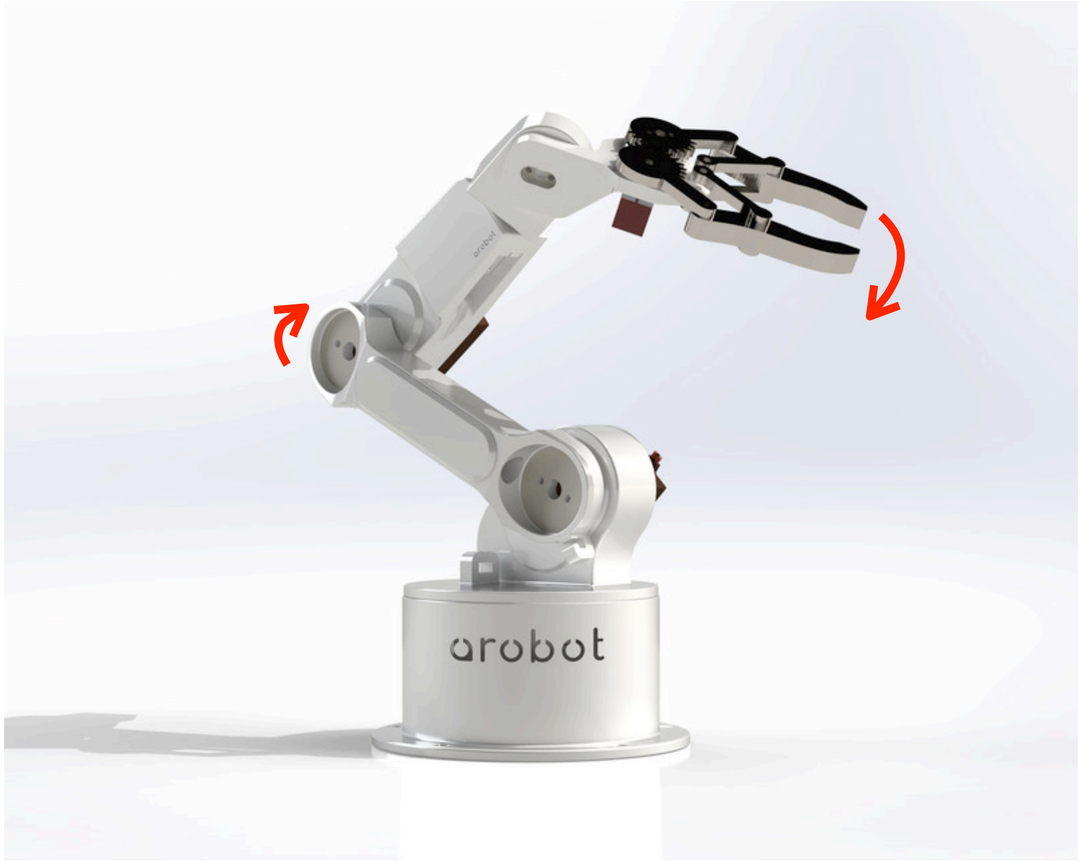
Gaussian Processes work best for continuous processes.



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A Challenge for Gaussian Processes

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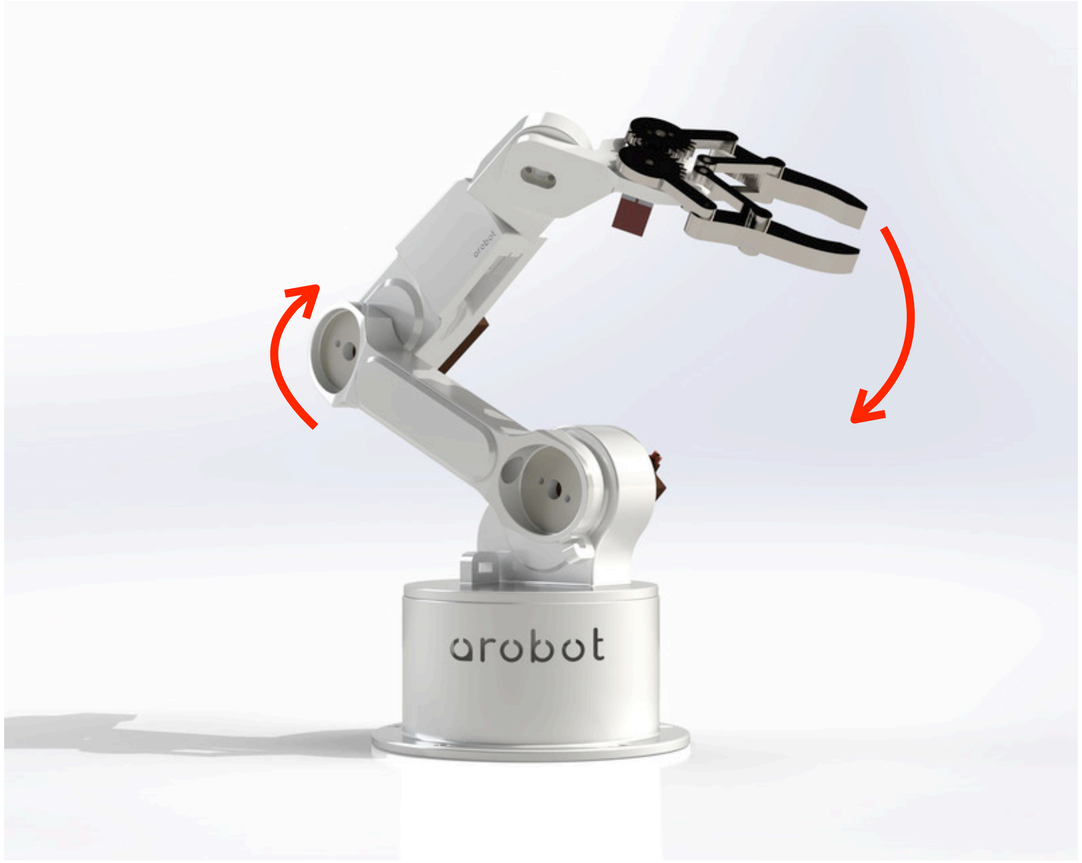
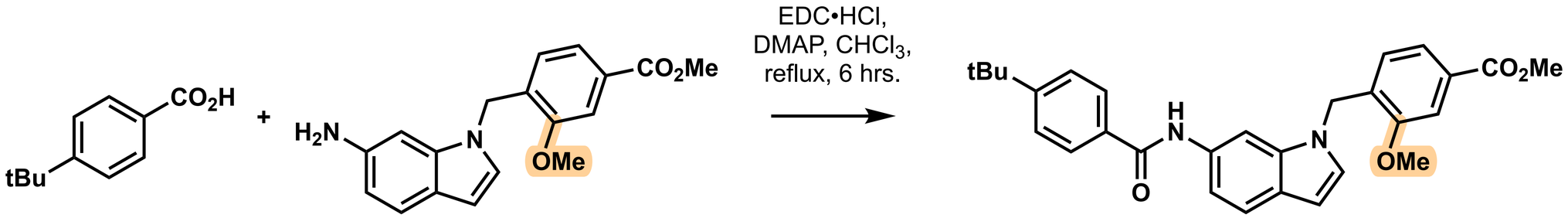
Gaussian Processes work best for continuous processes.



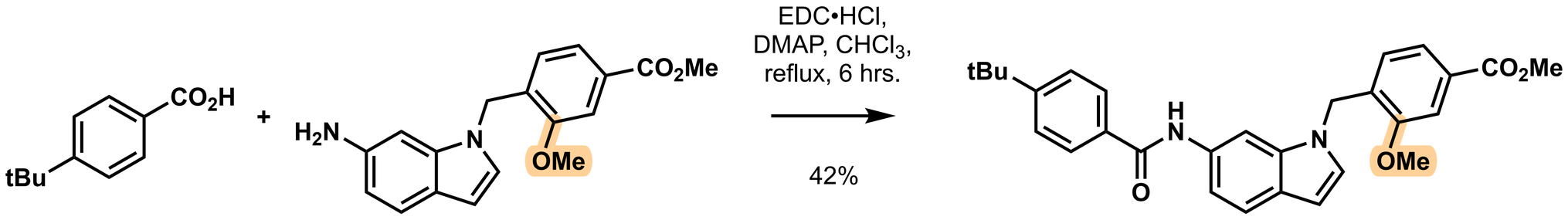
https://2020blogfor.github.io/posts/2020/04/kf_gp/

Discontinuous processes much harder to model



Liu *et al. Chem. Sci.* **2023**, *14*, 10835.

Discontinuous processes much harder to model



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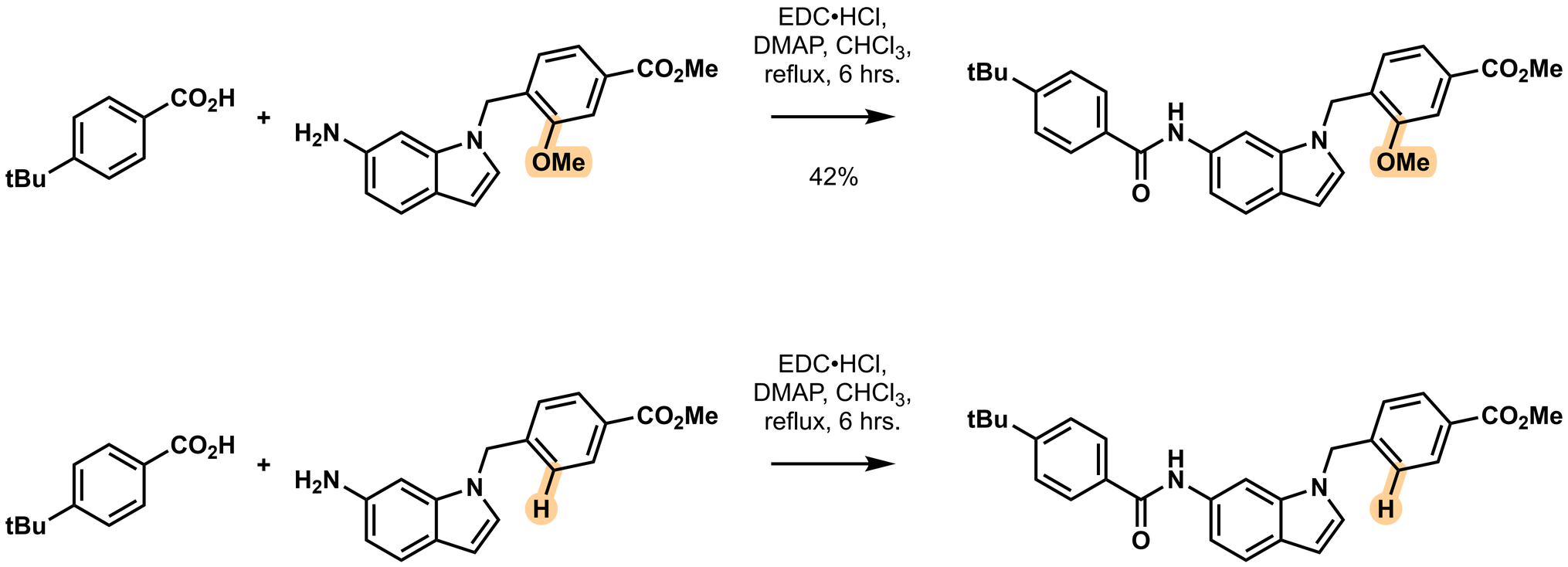
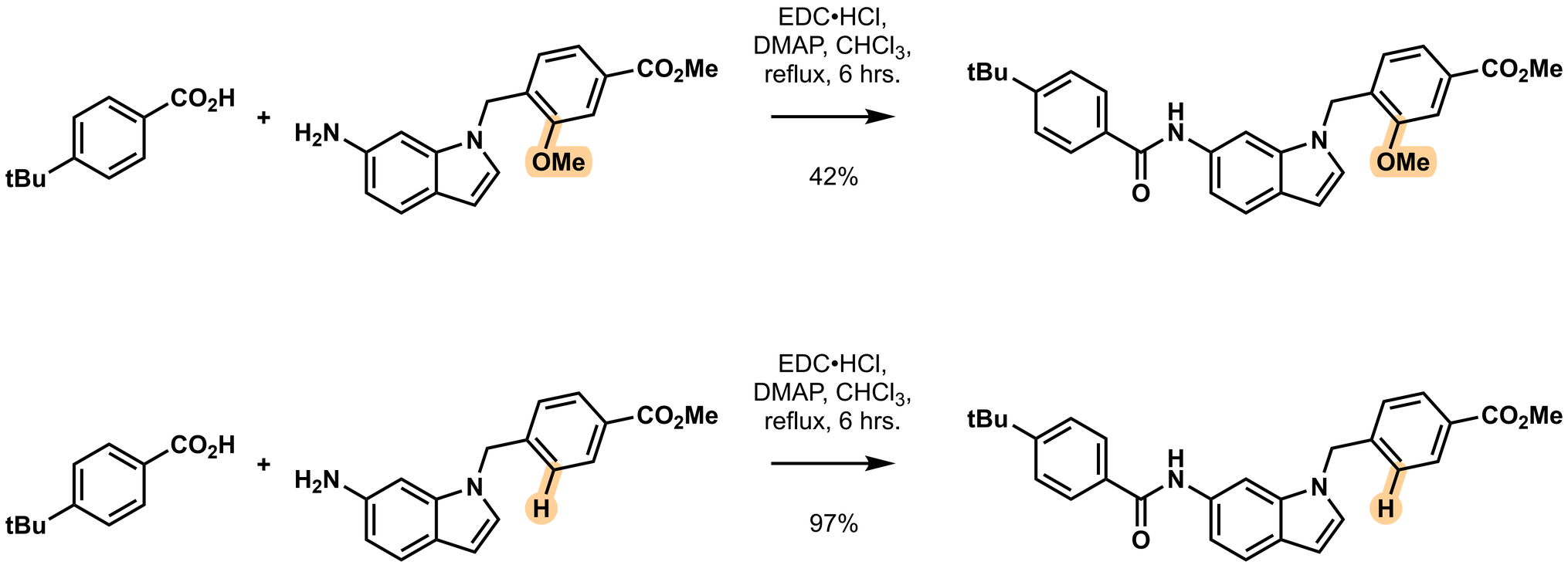
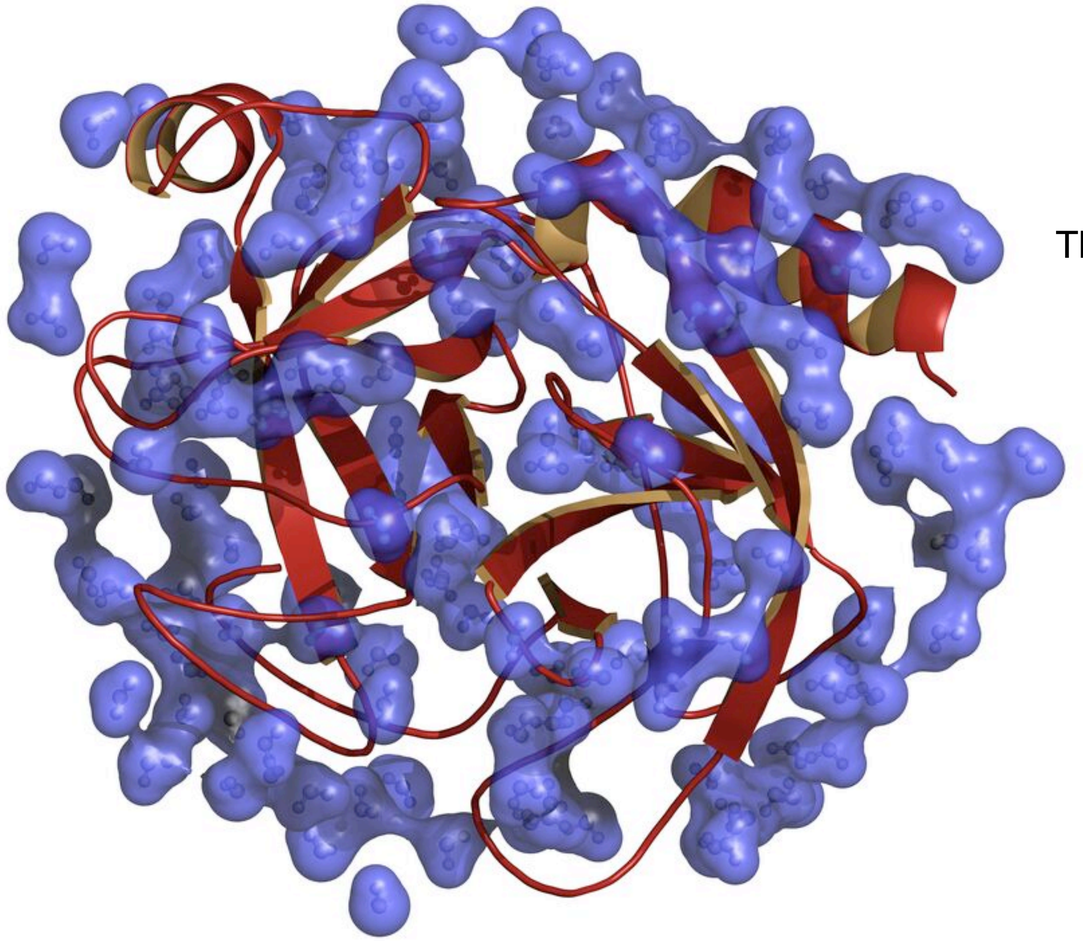
Discontinuous processes much harder to model



Discontinuous processes much harder to model



Enzymes!



There are a lot of enzymes in the world.

There are a lot of enzymes with unknown function.

A lot of metabolites made from unknown enzymes.

Can we predict unknown reactivity?

Some Real World Examples of Gaussian Processes

Does this enzyme catalyze this reaction?

Mellor *et al. ACS Synth. Biol.* **2016**, *5*, 518.

Some Real World Examples of Gaussian Processes

Is there affinity between the enzyme and the starting materials?

Mellor *et al. ACS Synth. Biol.* **2016**, *5*, 518.

Some Real World Examples of Gaussian Processes

Is there affinity between the enzyme and the starting materials?

predicting K_M

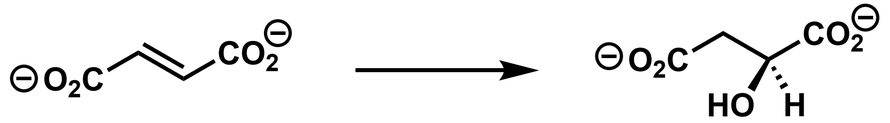
Mellor *et al. ACS Synth. Biol.* **2016**, *5*, 518.

Some Real World Examples of Gaussian Processes

Is there affinity between the enzyme and the starting materials?

predicting K_M

MYRALRLLARSRPLVRAPAAALASAPGLGGAAVPSFWPPNAARMASQNSFRIEYDTFGEL
KVPNDKYYGAQTVRSTMNFKIGGVTERMPTPVIKAFGILKRAAAEVNQDYGLDPKIANAI
MKAADEVAEGKLNDHFPLVVWQTGSGTQTNMNVNEVISNRAIEMLGGELGSKIPVHPNDH
VNKSQSSNDTFPTAMHIAAAIEVHEVLLPGLQKLHDALDAKSKEFAQIIKIGRTHTQDAV PLTL
TGLPFVTAPNKFEALAAHDALVELSGAMNTTACSLMKIANDIRFLGSGPRSGLGELILPE
NEPGSSIMPGKVNPTQCEAMTMVAAQVMGNHVAVTVGGSNGHFELNVFKPMMIKNVLHSA
RLLGDASVSFTENCVVGIQANTERINKLMNESLMLVTALNPHIGYDKAAKIAKTAHKNGS
TLKETAIELGYLTAEQFDEWVKPKDMLGPK



fumarate (*S*)-malate

Mellor *et al. ACS Synth. Biol.* **2016**, *5*, 518.

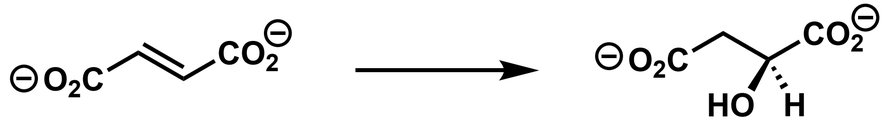
Some Real World Examples of Gaussian Processes

Is there affinity between the enzyme and the starting materials?

predicting K_M

MYRALRLLARSRPLVRAPAAALASAPGLGGAAVPSFWPPNAARMASQNSFRIEYDTFGEL
KVPNDKYYGAQTVRSTMNFKIGGVTERMPTPVIKAFGILKRAAAEVNQDYGLDPKIANAI
MKAADEVAEGKLNDHFPLVVWQTGSGTQTNMNVNEVISNRAIEMLGGELGSKIPVHPNDH
VNKSQSSNDTFPTAMHIAAAIEVHEVLLPGLQKLHDALDAKSKEFAQIIKIGRTHTQDAV PLTL
TGLPFVTAPNKFEALAAHDALVELSGAMNTTACSLMKIANDIRFLGSGPRSGLGELILPE
NEPGSSIMPGKVNPTQCEAMTMVAAQVMGNHVAVTVGGSNGHFELNVFKPMMIKNVLHSA
RLLGDASVSFTENCVVGIQANTERINKLMNESLMLVTALNPHIGYDKAAKIAKTAHKNGS
TLKETAIELGYLTAEQFDEWVKPKDMLGPK

fumarate hydratase sequence



fumarate (*S*)-malate

K_M = 5 x 10^{-6} M

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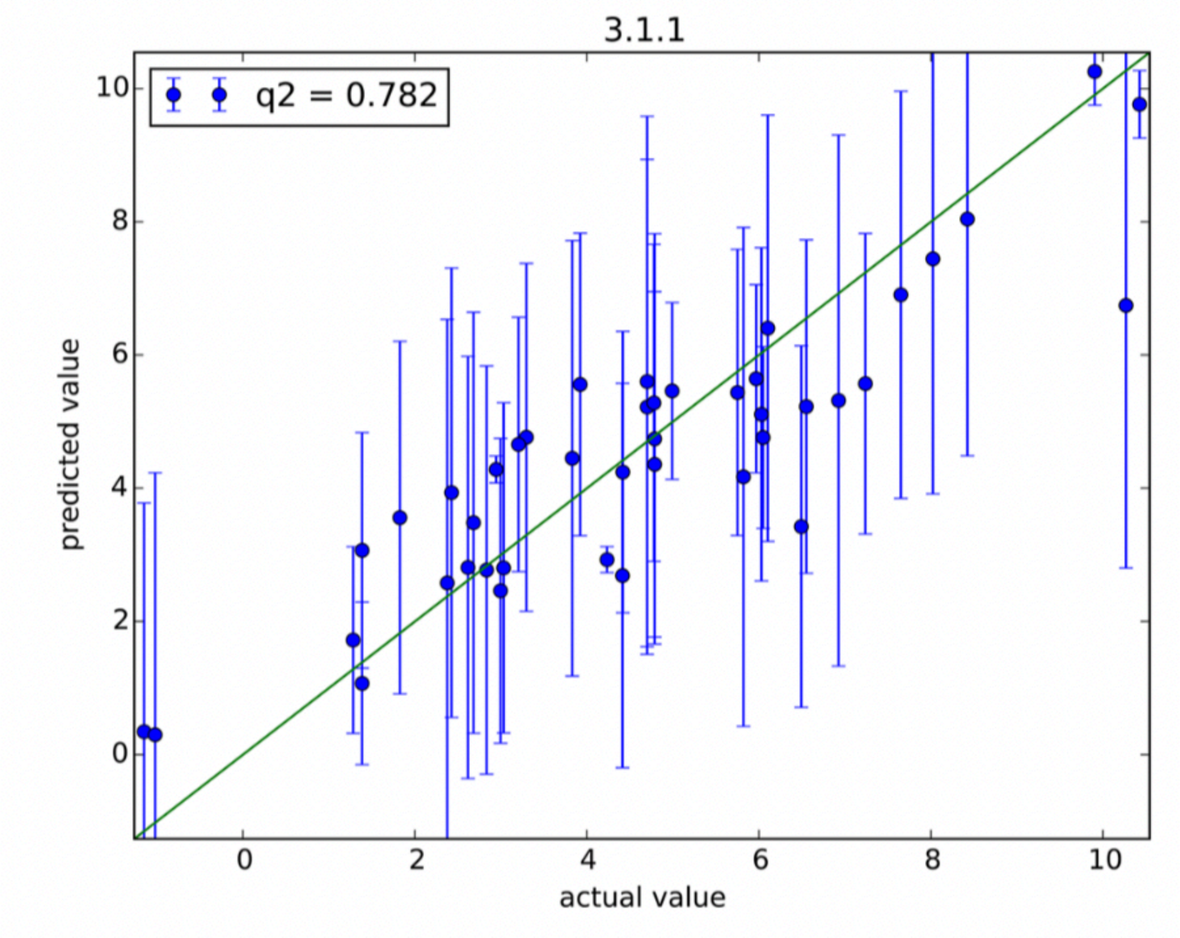
Some Real World Examples of Gaussian Processes



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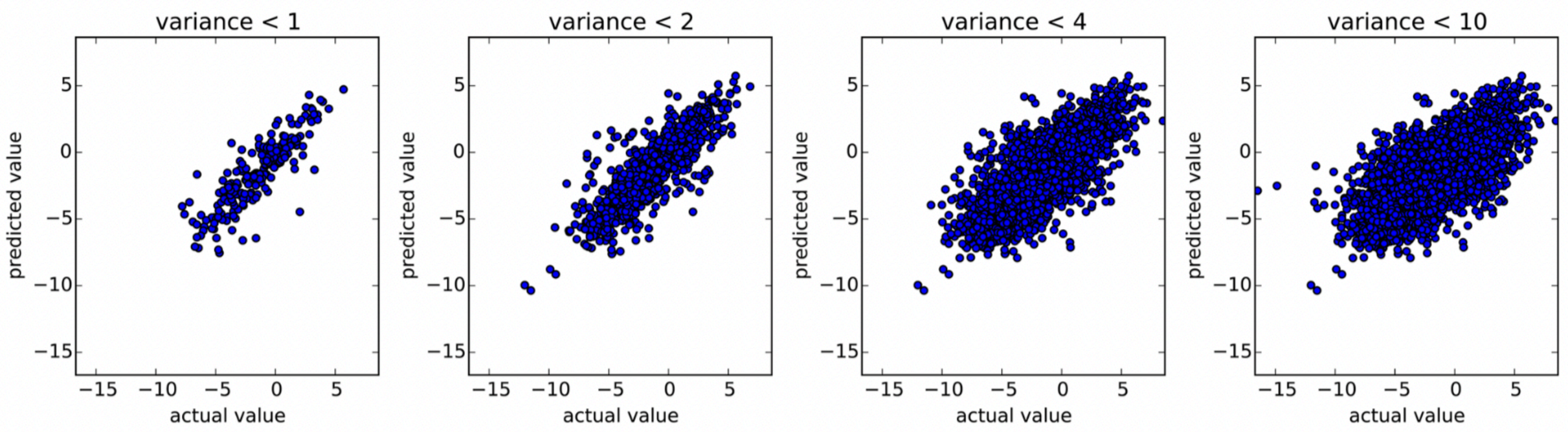
Some Real World Examples of Gaussian Processes



Mellor *et al. ACS Synth. Biol.* **2016**, *5*, 518.

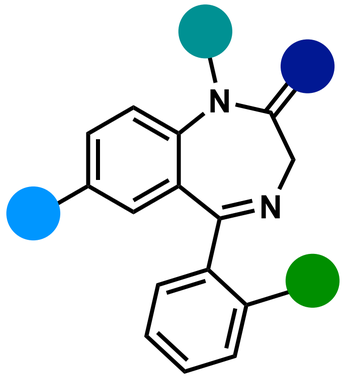
UNIVERSITY OF CAMBRIDGE

ADME Property optimization

Absorption, Distribution, Metabolism, Excretion

Obrezanova *et al. J. Chem. Inf. Model.* **2007**, *47*, 2007.

Some Real World Examples of Gaussian Processes



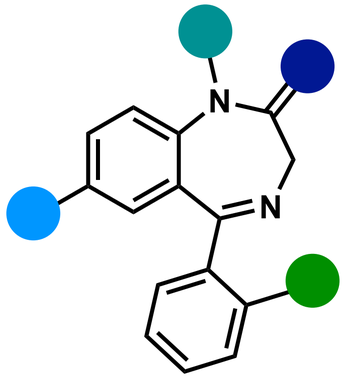
245 benzodiazepines

predicting in vitro
binding affinities (pIC_{50})

Table 1. BZD Set with Molecular Indices Descriptors

		Our Results[a]					
		training set			test set		
method	desc.	RMSE	R^2	r_{corr}^2	RMSE	R^2	r_{corr}^2
PLS	3[b]	0.63	0.32	0.32	0.52	0.51	0.53
GP-Basic	38	0.53	0.51	0.52	0.52	0.51	0.53
GP-FVS	15	0.53	0.51	0.52	0.52	0.52	0.54
GP-Opt	9	0.47	0.62	0.62	0.55	0.47	0.51
GP-Nest	38	0.44 (0.14)[c]	0.67	0.68	0.46 (0.15)[c]	0.63	0.65

Obrezanova *et al. J. Chem. Inf. Model.* **2007**, *47*, 2007.



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Burden Results[5]

		training set			test set		
method	desc.	SEF[d]	R^2	r_{corr}^2	SEP[e]	R^2	r_{corr}^2
MLR	39	0.18		0.47	0.20		0.32
ANN	22	0.13		0.73	0.14		0.66
BRANN	39	0.12		0.75	0.12		0.71
GPmodel	39	0.12		0.76	0.14		0.66
GPlinear	39	0.12		0.78	0.13		0.71

[a] Training set 208 compounds, test set 37 compounds. [b] Number of PLS components. [c] In brackets: RMSE for unit interval scaled Y values. [d] SEF = Standard error of fit. [e] SEP = Standard error of prediction.

The actual data split into training and test sets used to model BZD by Burden[5] was not available to us.

Obrezanova *et al. J. Chem. Inf. Model.* **2007**, *47*, 2007.