

Individual specific effects in myotonic dystrophy and other diseases

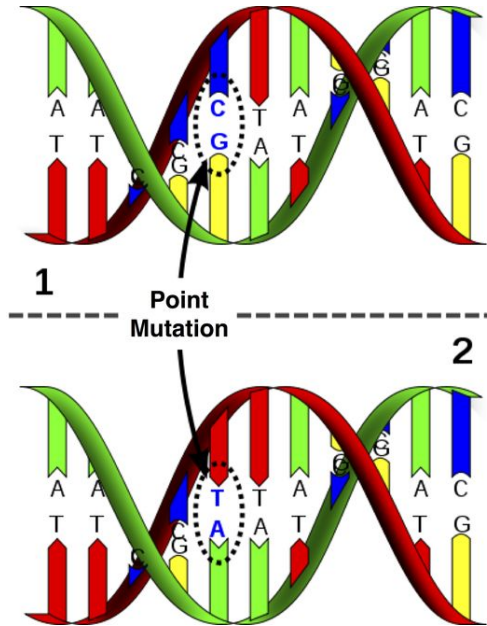
Adam Kurkiewicz
EPSRC PhD studentship application

Myotonic dystrophy

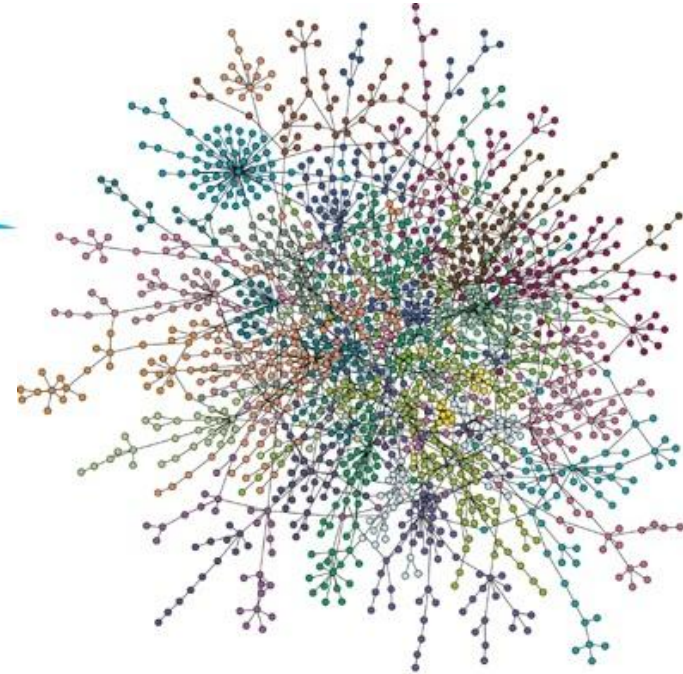


Single-Gene Disease

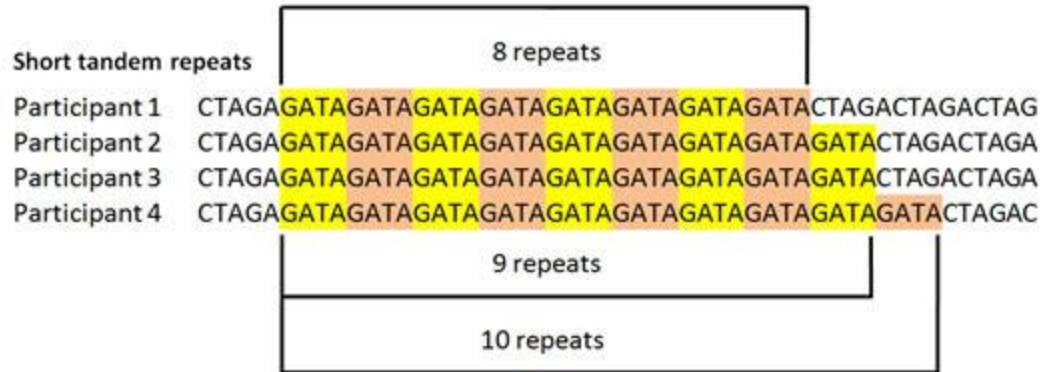
Complex Disease



Myotonic Dystrophy

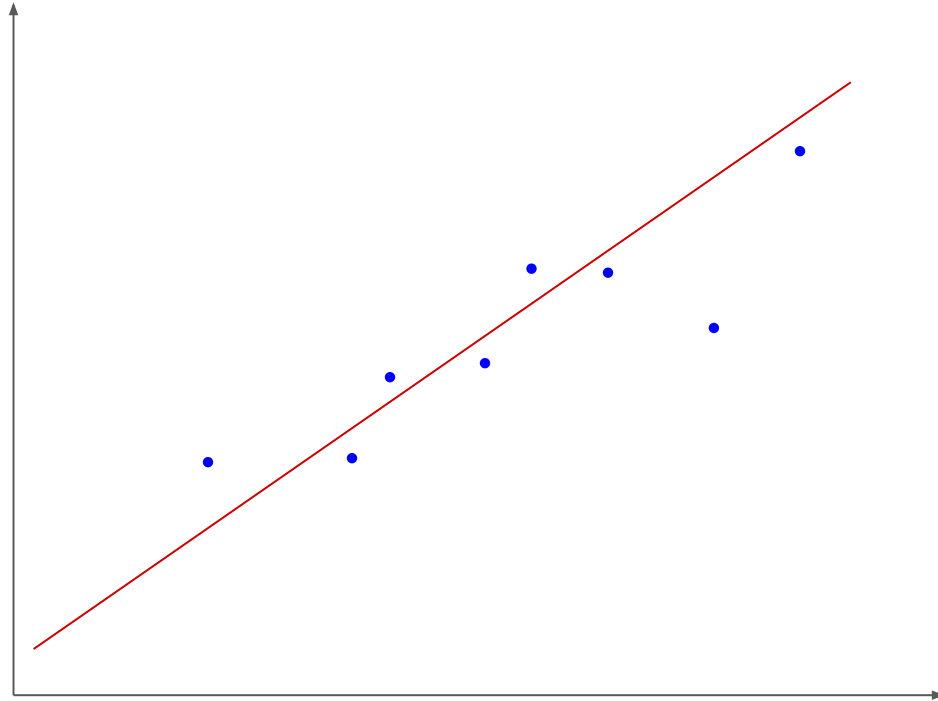


Short Tandem Repeats



Genotype to phenotype correlations in myotonic dystrophy

**Disease
severity**



Length of STR

Myotonic Dystrophy

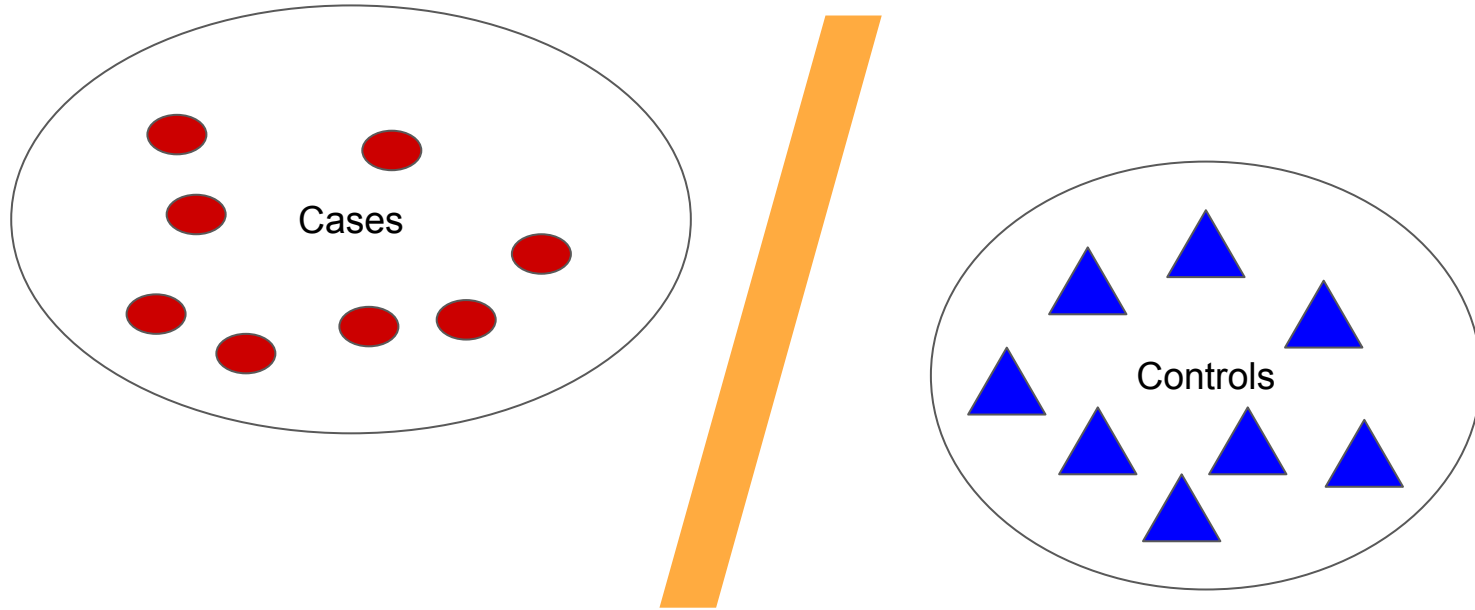
1. World class research at Glasgow University.
2. Relatively well-understood single-gene character.
3. The length of STR contributes to severity of disease.



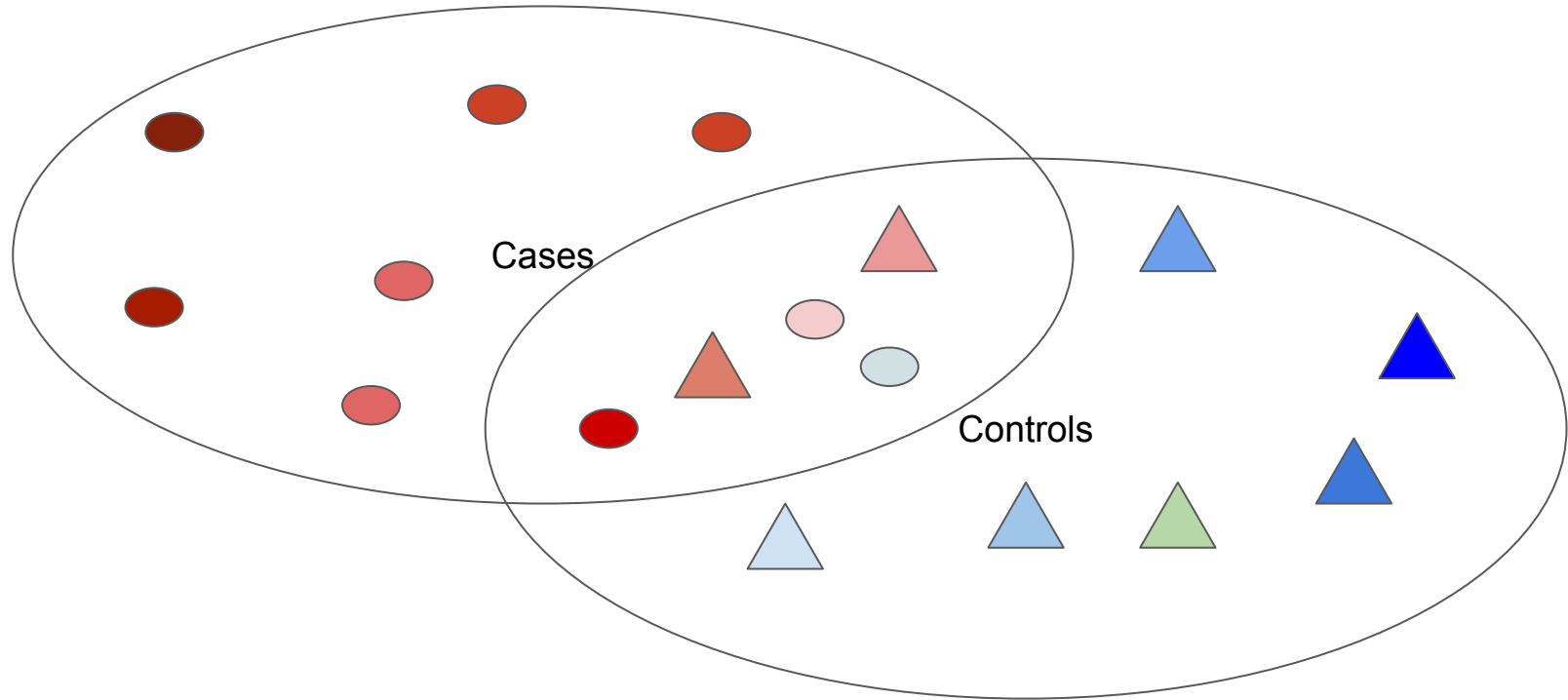
Myotonic Dystrophy



Case / Control Paradigm

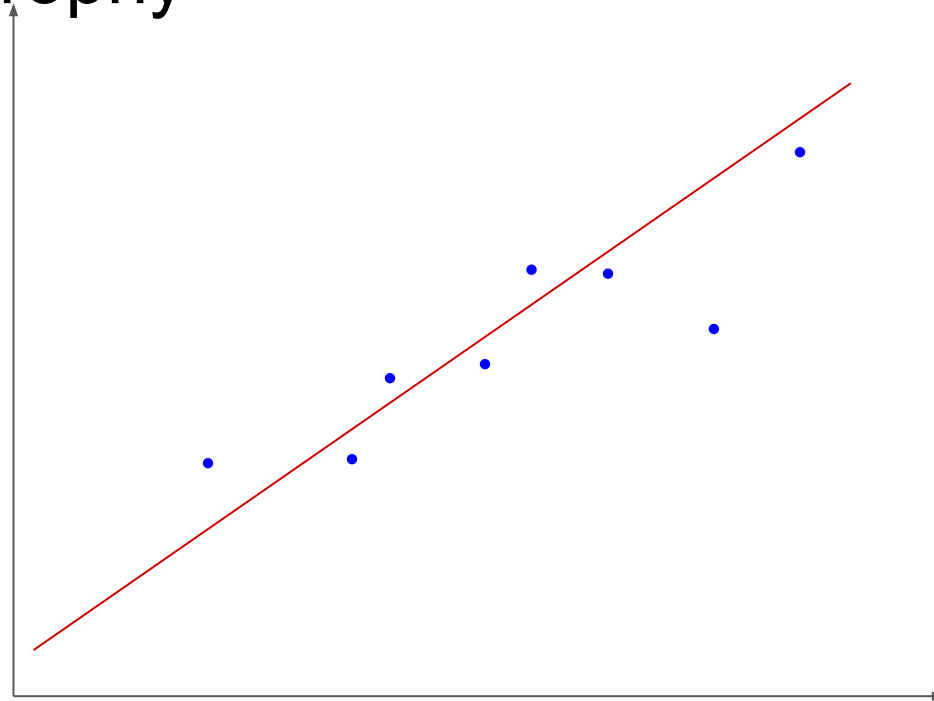


Fallacy of Case / Control Paradigm



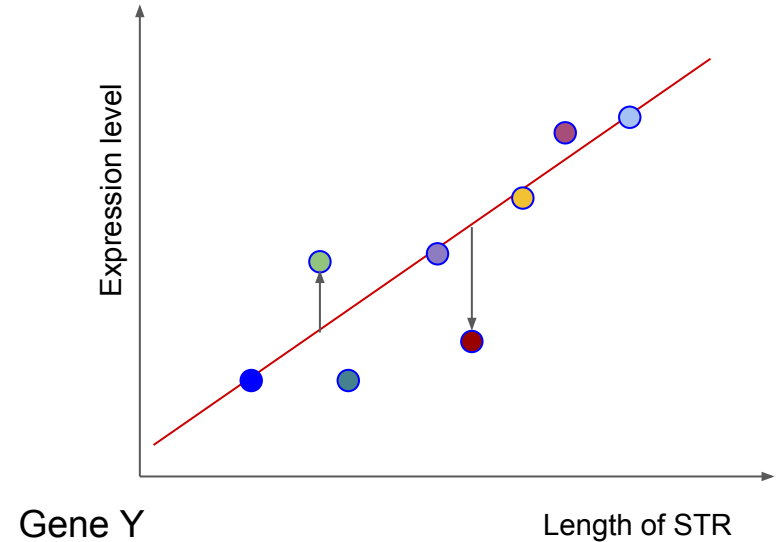
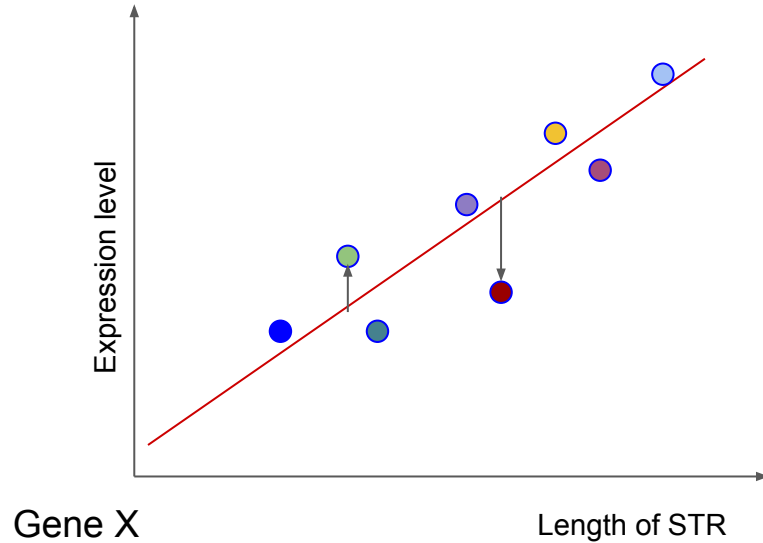
Genotype to molecular phenotype correlations in myotonic dystrophy

**Expression
of gene X**



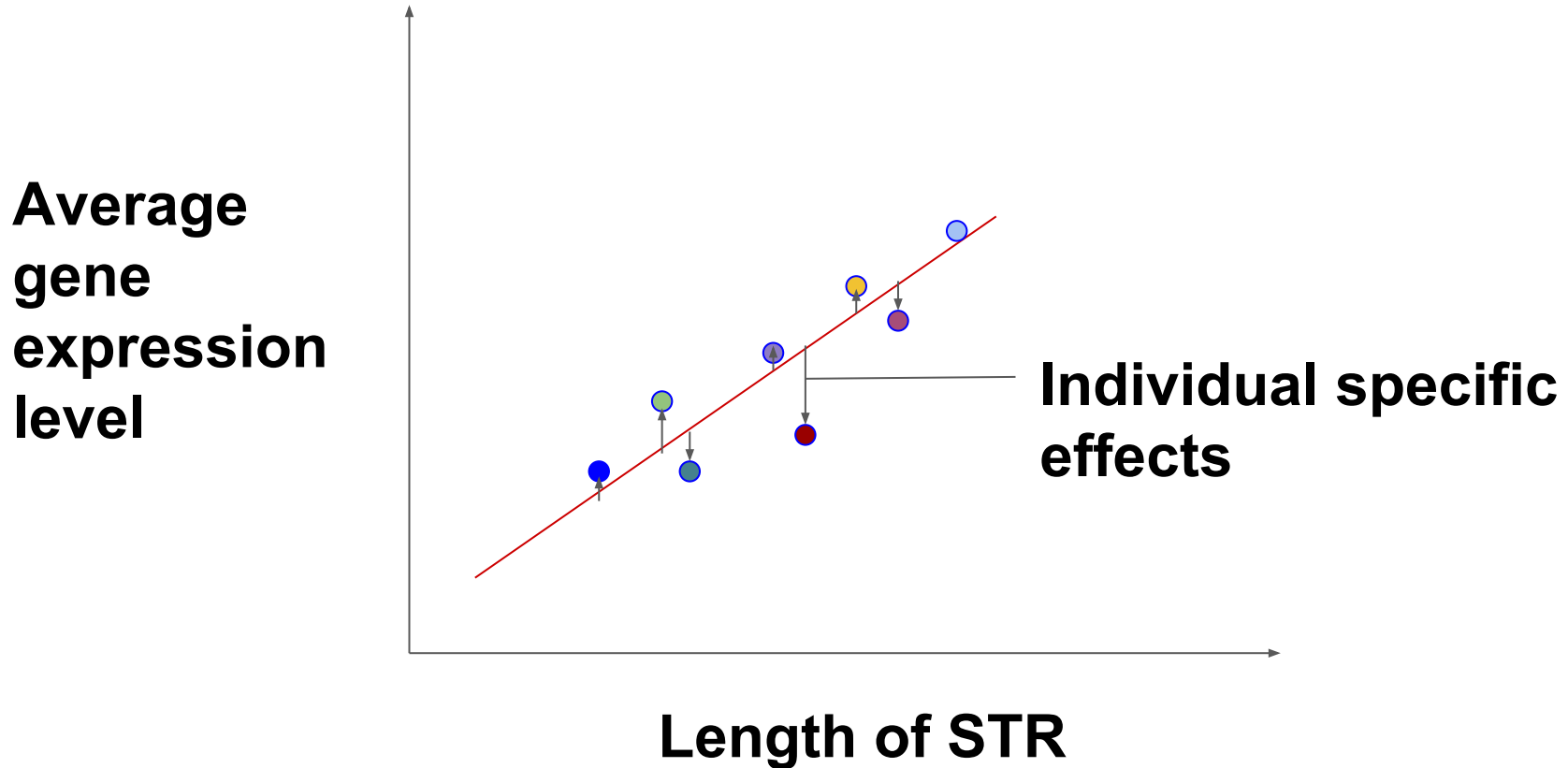
Length of STR

Evidence for novel individual specific effects



The pattern seems to work for many genes at a time
With highly significant deviations from expected for individuals

individual specific effects in myotonic dystrophy



individual specific effects in myotonic dystrophy

New questions for the PhD project

How can we use these effects to normalise the data and better identify disease relevant genes and pathways?

How do these molecular effects correlate to differences in disease severity?

What is the basis for these effects (variation in other genes?)

How can we apply this approach to other diseases?

(we have similar data for Huntington disease (same type of mutation) and lots of data for complex disease such as heart disease)

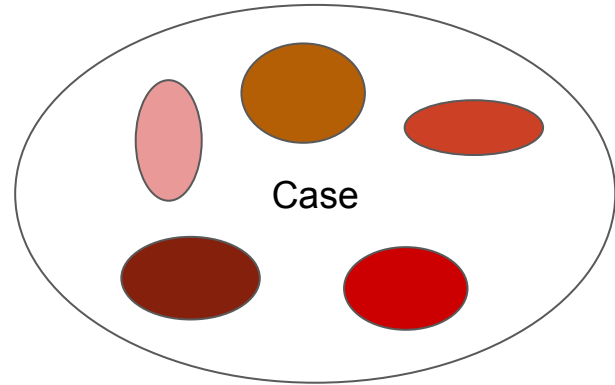
How can we apply this approach to other omics datasets (e.g. proteomics, metabolomics)

Challenges

Data multidimensionality



Individual Specificity



Why me?

First Class programmer – all programming courses at A5 or higher.

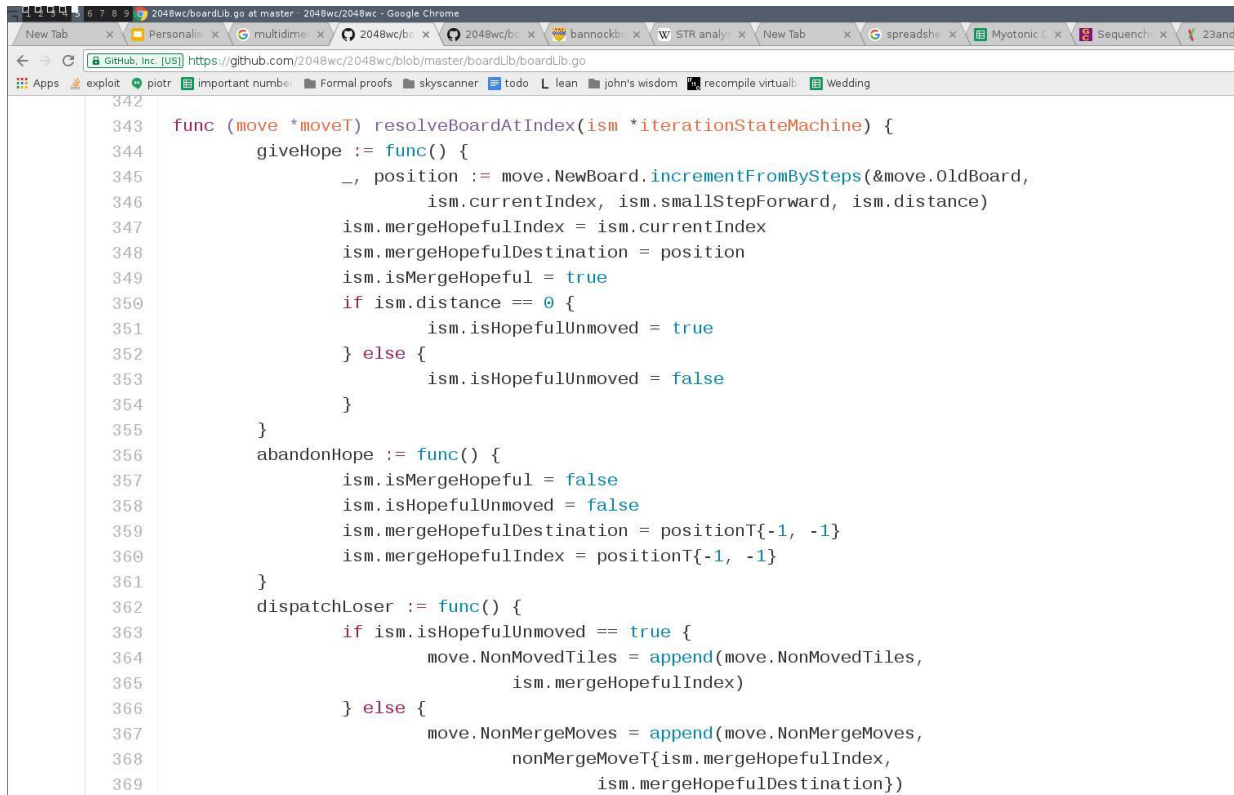
Python – A4 (UoG)

Java – A4 (UoG)

C – A5 (UoG)

SAS – 94% (SAS Ltd.)

Also Javascript, Go, Haskell

A screenshot of a web browser window displaying a GitHub repository. The address bar shows the URL 'https://github.com/2048wc/2048wc/blob/master/boardLib/boardLib.go'. The browser tabs include 'New Tab', 'Personal...', 'multitime...', '2048wc/...', 'bannock...', 'STR analy...', 'New Tab', 'spreadsh...', 'Myotonic', 'Sequenc...', and '23and...'. The code editor shows Go code for a board game, with line numbers 342 through 369 visible on the left. The code defines functions for resolving board states and dispatching losers.

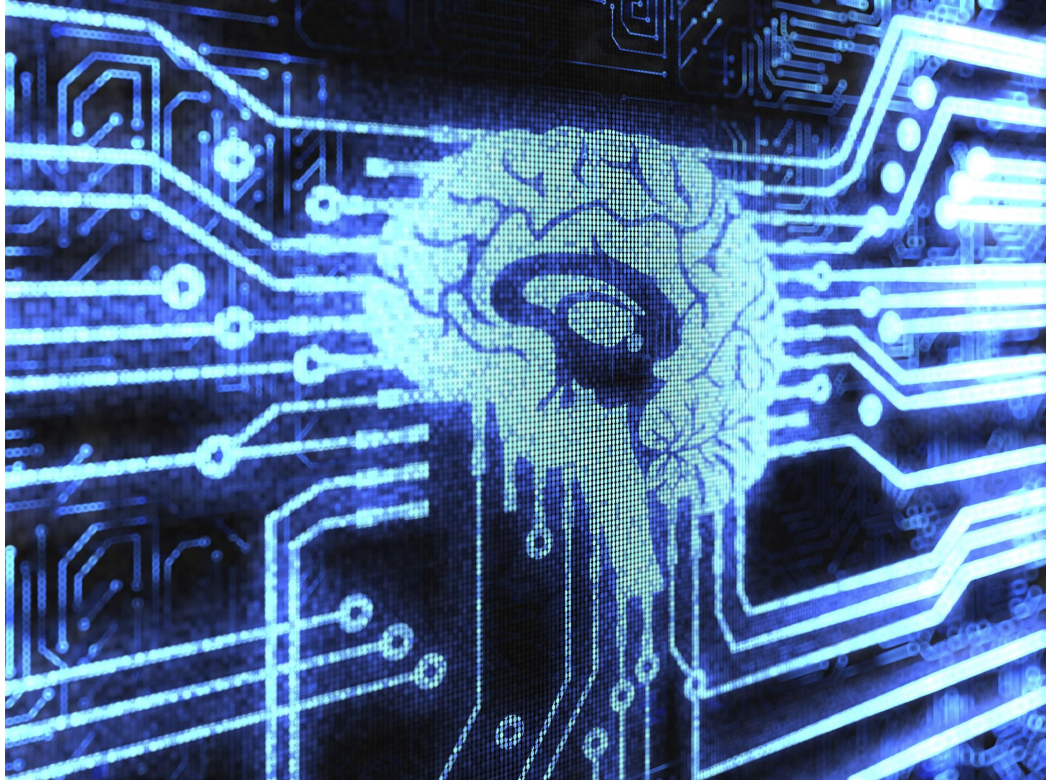
```
342  
343 func (move *moveT) resolveBoardAtIndex(ism *iterationStateMachine) {  
344     giveHope := func() {  
345         _, position := move.NewBoard.incrementFromBySteps(&move.OldBoard,  
346             ism.currentIndex, ism.smallStepForward, ism.distance)  
347         ism.mergeHopefulIndex = ism.currentIndex  
348         ism.mergeHopefulDestination = position  
349         ism.isMergeHopeful = true  
350         if ism.distance == 0 {  
351             ism.isHopefulUnmoved = true  
352         } else {  
353             ism.isHopefulUnmoved = false  
354         }  
355     }  
356     abandonHope := func() {  
357         ism.isMergeHopeful = false  
358         ism.isHopefulUnmoved = false  
359         ism.mergeHopefulDestination = positionT{-1, -1}  
360         ism.mergeHopefulIndex = positionT{-1, -1}  
361     }  
362     dispatchLoser := func() {  
363         if ism.isHopefulUnmoved == true {  
364             move.NonMovedTiles = append(move.NonMovedTiles,  
365                 ism.mergeHopefulIndex)  
366         } else {  
367             move.NonMergeMoves = append(move.NonMergeMoves,  
368                 nonMergeMoveT{ism.mergeHopefulIndex,  
369                     ism.mergeHopefulDestination})  
370         }  
371     }  
372 }
```

Machine Learning

Machine Learning often
programmed in Python or Java

Project co-supervised by a
Machine Learning specialist

First class result in Machine
Learning.



Real, sustained interest in Natural Science

A named author of an article on bacterial membrane composition published in Journal of Analytical Chemistry [1]

A dissertation on the effect of evolution on relatedness at University of Glasgow [2]. Dissertation graded 1st class.

1st and 2nd year Biology, 1st year Chemistry

1. Kurkiewicz S, Kurkiewicz A. Profiling of bacterial cellular fatty acids by pyrolytic derivatization to 3-pyridylcarbinol esters. *Journal of Analytical Chemistry*. 2015;70(10):1225-1228.
2. The effect of natural selection on relatedness in randomly mating population. <https://github.com/picrin/naturalSelection/blob/master/dissertation/l4proj.pdf>

Advanced understanding of maths and stats

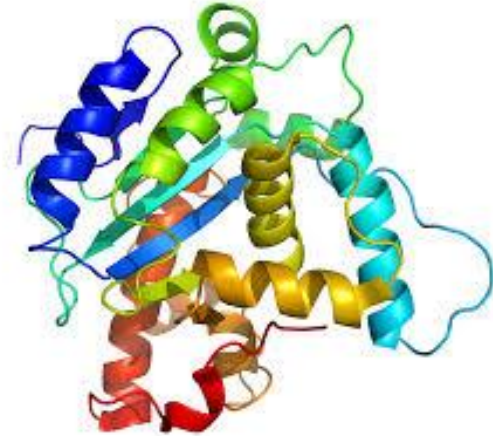
Joint Honours CS + Mathematics.

Courses in Algebra, Number Theory, Analysis, Topology, Galois Theory among others.

Data Scientist

Myotonic Dystrophy				
File Edit View Insert Format Data Tools Add-ons Help All changes saved in Drive				
fx % .0 .00 123 Arial 10 B I A				
	A	B	C	D
1	STR Length	SVC	PDS	UTV
2	16	79.30503154	53.66494735	99.39480806
3	2	27.60830944	49.5799717	95.54343672
4	6	39.05532438	58.25547738	71.37035929
5	75	79.71036365	29.36261104	48.92653332
6	8	51.31822568	61.10106565	74.75878487
7	56	96.25467951	61.91121989	1.472790237
8	56	35.49397726	2.659524191	80.56169642
9	86	53.92754623	59.69084768	15.64899263
10	27	61.52810613	85.95784659	41.01678275
11	11	1.138643908	37.37886323	84.13838703
12	34	44.07580252	24.64222558	42.90677395
13	47	13.27244813	56.86627767	58.34800339
14	98	0.3442644536	92.84082127	91.83154141
15	69	97.75043892	18.01711082	22.1369293
16	31	50.12865421	20.97989761	62.20895579
17	61	39.9197019	51.82645568	58.03116393
18	7	61.55727941	6.693946769	72.77012805
19	9	5.783592283	97.61782404	78.19065519
20	81	71.06162991	34.97044669	72.31466216
21	44	42.5900577	70.92045384	17.3941752
22	95	31.08689137	26.66984376	45.49154693
23	44	43.29324197	53.66714888	10.30762802
24	3	64.05856009	59.56142465	73.37129992
25	57	65.90402343	63.3533141	0.3014363331
26	64	26.12079261	31.01566545	8.574997453
27	22	62.3156615	62.3156615	62.3156615

Molecular Biologist






Me

Project Title: Individual Specific Effects in Omics Datasets

Applicant: Adam Kurkiewicz

Key Strengths: Programming, Science, Statistics, Mathematics.

Myotonic Dystrophy				
File Edit View Insert Format Data Tools Add-ons Help All changes saved in Drive				
Arial 10 B I A				
fx				
	A	B	C	D
1	STR Length	SVC	PDS	UTV
2				
3	74	69.79699327	77.46701588	4.412729493
4	48	37.87186459	38.99386395	45.38076955
5	52	90.46065936	44.31130363	1.847847681
6	27	48.60114054	97.92687912	51.20549062
7	84	95.32333851	58.84361652	38.61107999
8	48	92.83209813	25.8212163	41.81696974
9	17	9.415304917	41.53725979	4.53417832
10	76	47.05982892	82.82677861	68.61934607
11	66	5.776771441	81.22928954	75.70567254
12	23	81.28215322	35.74824568	14.85560364
13	71	68.94866087	38.02854155	64.39506314
14	96	38.8386664	29.0835935	13.29603345
15	33	54.14819832	46.25419573	50.30635407
16	85	28.53614663	99.25722126	77.48260907
17	83	56.5824286	34.98297138	38.86403732
18	98	6.013477299	12.12575391	54.73238259
19	33	30.35281934	8.783093891	17.23469883
20	57	46.29919127	28.83470147	34.10306957
21	6	21.40402448	56.21315882	3.787336983
22	10	34.51476418	30.1040506	67.52387407
23	49	3.96999211	78.66400335	11.69551067
24	34	26.67679744	54.02096248	87.29476021
25	71	34.97049505	57.12172969	72.3844848
26	14	57.5511758	27.41764311	28.15723574
27	56	65.81122554	99.42998672	89.52645357
28	48	97.51239133	95.91257261	87.13980548
29	58	76.04058696	35.62965668	19.28698063
30	0	85.36108237	82.69317378	79.38119212
31	66	18.31629922	53.95404642	97.52581141
32	92	89.0529725	31.11807009	73.13448816
...				
+ Sheet1				