Hi Kevin,

I've had a look through, it's an interesting paper.

I think reviewer 1 has gotten confused. The comment you highlighted is about the 7 concentrations of drugs used for the calibration curves, but then they seem to go on about the 7 repeats per bank note.

Anyway, I know what they want in that bit. R1 wants a test of statistical significance of R^2 to test whether the linear relationship in the sample data is strong enough. I can do this with the data. They are also suggesting that you do more concentrations of the standards to get the calibration. I'm going to guess that isn't too hard to do if you need more? I can do the tests they ask for anyway, and we can see how good the calibration is. (I think it's a bit of overkill, I've never seen that in a chemistry paper before, people normally just bung their fits into the SI so people can eyeball it). Anyway, send me the data and I'll do that bit.

I have attached an Excel file “Calibration curves Drugs on £B” which has all the calibration curves and data. I have had a look at this myself, and better R^2 values can be gained between 1 and 100 ng/mL than all the way to 1000 ng/mL. I cannot get back in the lab to do more work on this. At present, we will need to go with the data we have. If you could look into the tests on that, would be very helpful.

There are a few more things I could add, I think. They are asking for more banknotes, I can do a quick statistical power calculation to figure out how many more you would need to draw conclusions regarding the difference between the drugs and banknotes. I do think the effect that you have found is real, as I would bet that the average cocaine user is richer than the average ketamine user, and more likely to be showing off (and thus using a higher denomination note). It would be nice to prove it.

If you could some statistical analysis on this that would be great. I think that the data is not normally distributed. I have attached a second Excel spreadsheet with all the data. I hope this make sense.

Other things I would like to do.

1. plot the histogram for cocaine (or do all of them) to show that the distribution is made up of 2 normal distributions: 1 for notes in the wallet and 1 for notes used for snorting. I think you can see this in the cocaine data already, but more data would be useful (there are stats tests you can do to 'prove' this sort of thing).

This sounds great. The data would appear not to normally distributed, so this drug use and non-drug use would be good to investigate. I put some words on this in the conclusion section. I think that the levels of contamination of the £B notes was found to fit into three board groups. Those contaminated at low levels were believed to have originated from contamination from contact with other notes and represent a background level. A smaller set of medium level contaminated notes were believed to have resulted from the taking of drugs, in some point in the past. The third set with high contamination levels were thought to have resulted from their use in recent drug taking.

1. figure 2: I think that your study should have error bars, and it would be nice to have statistical significance tests between those mean values and your data, much as I did in the supplementary information of this paper: [https://arxiv.org/ftp/arxiv/papers/2002/2002.00940.pdf](https://eur01.safelinks.protection.outlook.com/?url=https%3A%2F%2Farxiv.org%2Fftp%2Farxiv%2Fpapers%2F2002%2F2002.00940.pdf&data=02%7C01%7CKevin.Honeychurch%40uwe.ac.uk%7C71ee40087acc40e4d4eb08d822ad4fca%7C07ef1208413c4b5e9cdd64ef305754f0%7C0%7C1%7C637297475055295634&sdata=60YePaJtYVuHi94W%2BY8XDmdvKnf0VELz1CX7rO41ovI%3D&reserved=0) I can do that as well for you, and then you could say which currencies were significantly different from the £B. It would be good to see how many repeats these studies had, as if they only had 28 or similar banknotes then you can tell the reviewers that! I think there is nothing wrong with 28 repeats for the overall mean values. I would also average the 3 £ studies to see if Bristol's cocaine use is higher than the country average (it looks like it is).

If you can form some error bars from the data that would be great. Regarding the means, I was not sure as to do as the data was not normally distributed. The three studies undertaken on the Pound Sterling, had only a small number of in their sample. It is difficult to do studies on the Pound Sterling as damaging the Queen’s image is against the law, but we could still average them.

figure 1. Again error bars would help (I can add them), could even do statistical significance between the datasets. It looks like the cocaine 20 £B result is statistically different from the rest. But, this would also benefit from more data.

I am not sure as to what can be done here as the plot is for individual £B notes.

Anyway.

Can you do any more repeats? I do think it would be a stronger paper with more banknotes, although that will involve going back into the lab. Are the UWE labs open atm? Bristol is, but with only a third occupancy of the labs allowed.

I have asked about going back into the labs, but we will not be able to use the LC/MS/MS as it is the teaching lab. They will not allow researcher into that lab, so I cannot use it.

If not, we could improve the stats of it at the moment, call it a preliminary study and add a note to the editor suggesting that further lab work could not be done within a decent time frame due to students being out the lab due to covid.

I think that the only way forward we have at present is to try and do something more with the data we have and see if we can answer the referees sufficiently well enough with that.

I also think you can reframe it a bit, suggest that the similarity to the other studies (with regards to cocaine) is good for verifying the technique, then point out that the measurement of such high levels of ketamine is an important finding that speaks to a change in Bristol's drug consumption (I think both reviewers missed that bit).

I agree, I have to try and cut it down as the referee #1 is asking for it to be a Technical Note.

Anyway, I'll do what I can if you send over the data for me to play with. And thanks for asking, as I need papers that demonstrate that I am able to add machine learning/stats to chemistry papers to try and persuade UoB to invest in me (!) and keep me on after this contract. At the moment I've been emailing people asking for data and taking on extra teaching.

Thank you, Ella, for going through all of this so deeply. I will properly have more in the future. If the ‘New Normal’ continues, I will properly have to think of research which is not lab based.

Hope the drilling isn't too annoying, and good to hear from you. And I'd be happy to get involved in doing stats and data science for any future studies you end up doing.

Regards

Ella

Dr. Ella Gale  
Research Associate and Machine Learning Subject Specialist,

Technology Enhanced Chemical Synthesis CDT, School of Chemistry, University of Bristol

Turing Data Study Groups Academic Lead, University of Bristol

School of Chemistry,

Cantock's Close

Bristol,

BS8 1TS

United Kingdom

email: [ella.gale@bristol.ac.uk](mailto:name.name@bristol.ac.uk)