October 5, 2006

Professor A. T. A. Wood School of Mathematical Sciences University of Nottingham University Park Nottingham NG7 2RD United Kingdom

Dear Professor Wood:

Please find enclosed our revision to (Please note the new title):

JRSSB submission B6215: "Alpha investing: A new multiple hypothesis testing procedure that controls mFDR." (with Foster)

We have substantially rewritten the entire paper to address the suggestions and comments. We have removed the EDC criterion which we introduced in the prior version and instead concentrate on an existing criterion, namely mFDR. This puts the focus on the new procedure, namely alpha investing. We have added several new theorems to help show how the new procedure differs from existing procedures.

On our own rereading, we agreed that the original version was too terse. Hopefully this version will be easier on the referees and more attractive to them.

We enclose a detailed response to all the comments we received, starting with your comments, the AE's, and then those of the two referees.

Sincerely,

Robert A. Stine stine@wharton.upenn.edu

## Wood's comments

Paragraph 1: We have deleted the EDC criterion which was introduced in the previous version and replaced it by a slight modification of the mFDR criterion.

We have rewritten the entire paper to simplify it and clarify the presentation.

Paragraph 2: Our first choice is still JRSS! Since so much of the original research of this nature was published there, we would prefer to have our paper in JRSS also. Hopefully this version is more deserving.

## AE's report

paragraph 1: We have taken to heart the criticism that introducing EDC was unnecessary and have removed it. In its stead, we use mFDR (or more accurately, a slight modification of mFDR). We have a section relating our version of mFDR to several of the other versions of FDR (cFDR, pFDR, eFDR).

We honestly don't see much of a connection to the tail probabilities of the false discovery proportions. But we made an effort to generate a result (without proof) that is similar in spirit to the tail probability results. (See statements 4 and 5 after theorem 3.) We left out the proof since it is standard for martingales.

paragraph 2: We don't need EDC to handle the sequential nature for evaluation. But we do need the new alpha investing rule that is presented in the paper. So this focus has been removed.

Response to referee #1 titled: "Report on B6215"

paragraph 1 & 2 & 3: Agreed!

paragraph 4: We now compare to a variety of existing criteria. We felt the dependent testing

was both difficult and not relevant for the ideas we discuss and have removed that section.

paragraph **The criterion.** We removed the concept of EDC and replaced it by a modification of mFDR. We show that controlling our stopped version of mFDR makes almost all FDR-like

definitions equivalent.

GW02, GW04 paragraph: Thanks for pointing out this connection. We have added a dis-

cussion of these papers in the "Relating mFDR to FDR" subsection.

Choice paragraph: We removed the EDC criterion and use mFDR. We have worked with that

criterion throughout. Interesting side light: Yoav Benjamini said that he actually considered

mFDR first and then switched his focus to FDR.

**Dependent tests.** The issue of dependent testing gets very difficult. We have removed

the extensive discussion of it since we didn't feel it was laid out clearly enough. We are

working on developing an algorithm that will generate  $\alpha_m$  hypothesis tests without having

to orthogonalize the tests. To make this precise, we need some new theorems about Gibbs

sampling of convex sets before we can claim to have a complete solution. (We need a slight

extension of the recent work of Santosh Vempala, "Sampling Integration and Optimization

of High-dimensional Log-concave Functions." We have been pushing Santosh to include

these extensions in a review paper he is writing. So we will wait until that is out before

tackling our application.) In our more applied research, we have tended to simply ignore the

dependence in the tests and cross our fingers. It empirically works well in data mining. We

hope to pursue that in yet a different paper.

Minor remarks.

a) New graphs, hopefully to your liking.

b) Fixed.

**References**: Both have been added.

## Response to referee #2 titled: "B6215-ref2"

Your opening paragraph: We apologize for being confusing in the first version. Hopefully this version will be easier to track and your initial enthusiasm will return.

- "(1)" The introduction has been significantly rewritten. Hopefully it is clearer now.
- "(2)" We have removed the EDC and replaced it by the slightly modified version of mFDR. This helps focus attention on the sequential aspect (which you correctly identified as our primary contribution) and the new algorithm, alpha investing. Though the ratio of expectations has some undesirable properties, we show that in our setting it is often close to the other more traditional criteria. The numerical equivalence of 5 different criteria is one of the new theorems in this version.
- "(3)" We have thought hard about the language to use here. We want to leverage the idea that our approach is a modification of alpha spending rules. The word "spending" correctly suggests that we are burning through alpha and never get any new alpha back. So we want a metaphor that suggests that we are spending alpha, but that we can earn new alpha to spend. So the "investment" language is best thought of as a metaphor, but we give it no more meaning than the spending analogy. So neither alpha spending nor alpha investing advocate that alpha-wealth is appropriate as a utility function.
- "(4)" We have tried to make it clear that an alpha investing rule is representative of a class of rules. Some of these rules might make multiple passes over the hypothesis, others won't. Some might only test further hypothesis when the primary endpoints have been proven (i.e. rejected). Others might save alpha for the future. All of these are design decisions that go into creating the testing rule. To help clarify this, we have added a new section called "designing alpha investing rules."

"In summary:" We have rewritten the entire paper. We have added several new theorems that will hopefully show what it is that we have accomplished. We have added a discussion of how to design rules.

**Detailed comments:** We have made all the changes you suggested.

## Changes made in new revision of B6215: Foster and Stine

A quick "diff" showed 1800 changes in the latex source file. So we will not provide a line by line list of changes. But major changes are listed below:

- $\mathbf{EDC} \to \mathbf{mFDR}$  The most visible change, is removing the new criteria of EDC. We have replaced it with mFDR. This allows a more direct comparison to other versions of FDR.
- Language Much of the language has been changed to better match standard usage.
- **Stopped testing** We have some new results concerning stopping the testing. In particular, the new theorem 1 converts our results to a "conditional" form of FDR. These ideas are further elaborated in the new section entitled "Universal mFDR."
- **Stopping time discussion** We discuss a situation where one can expect to be able to stop at a fixed number of rejections. This allows a very close connection between 5 versions of FDR.
- Figures New figures have been generated to match the use of mFDR.
- **Removed example** We removed the dependent testing example from the *Examples* section. We feel that to do it justice will take a paper in its own right. So we defer it to another day.
- **Designing alpha investing rules** A new section has been added to help understand issues that go into designing alpha investing rules. This will also help set up the rules that we discuss in the examples section.