# Benchmarking SCEPTRE

Tim

2023-04-17

In this document I evaluate the results of SCEPTRE on the negative and positive control data. I apply four versions of SCEPTRE: exact vs. approximate, and Poisson vs. negative binomial (NB) regression. (The exact version of SCEPTRE uses the entire set of cells for the precomputation, while the approximate version of SCEPTRE uses the NT cells only.) In all cases I fit skew-normal to the resampling distribution to obtain a more accurate p-value. Note that this is the first time that we have evaluated SCEPTRE with the skew-normal module on all datasets.

Negative control results

For each dataset, I plot the results of each version of SCEPTRE on a transformed QQ-plot. I also print the number of Bonferroni rejections at level 0.1.

Frangieh Co-Culture

```
analyze_dataset(undercover_res = undercover_res,
                dataset = "frangieh/co_culture/gene")
```
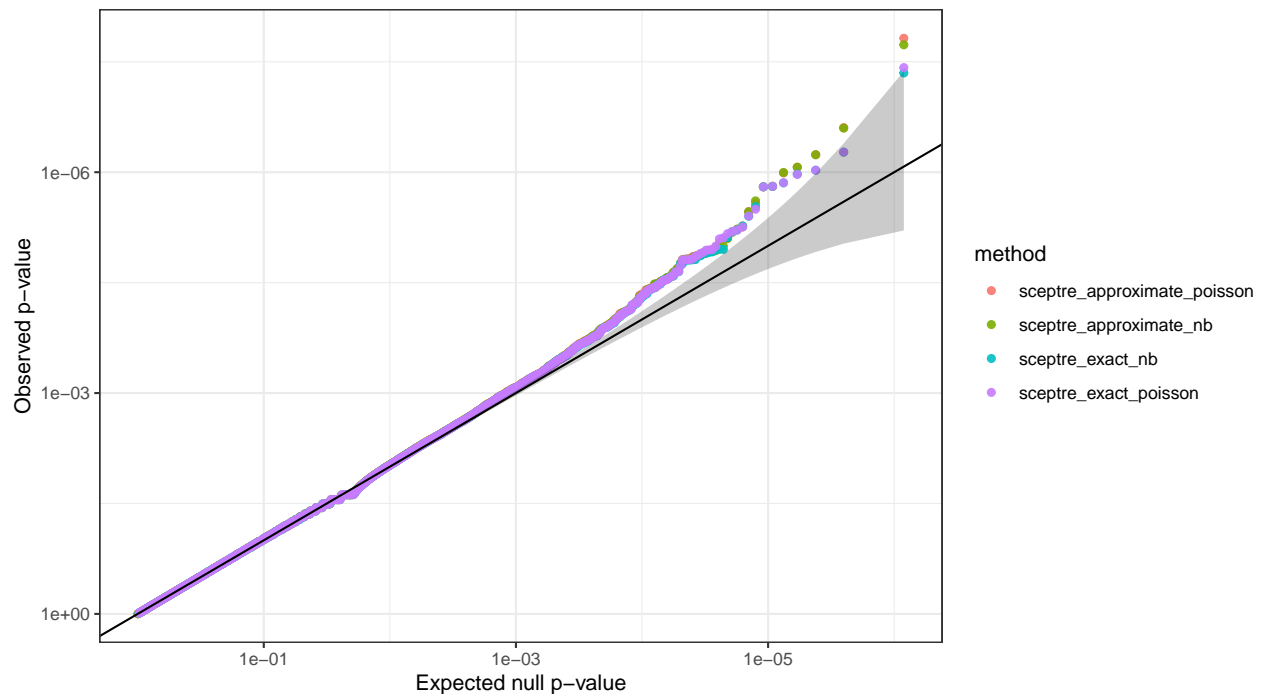


```
## # A tibble: 4 x 2
```
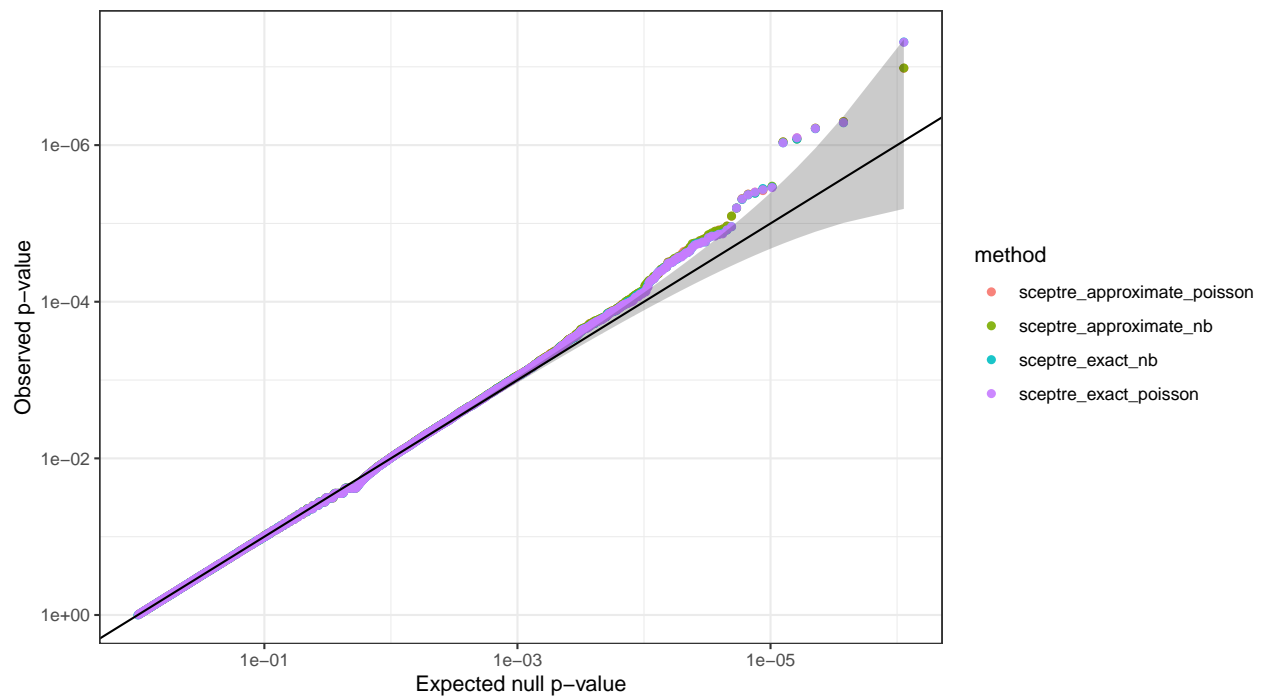
```
##    method                   n_reject
##    <fct>                       <int>
## 1 sceptre_approximate_poisson     1
## 2 sceptre_approximate_nb          1
## 3 sceptre_exact_nb                1
## 4 sceptre_exact_poisson           1
```

Frangieh IFN-gamma
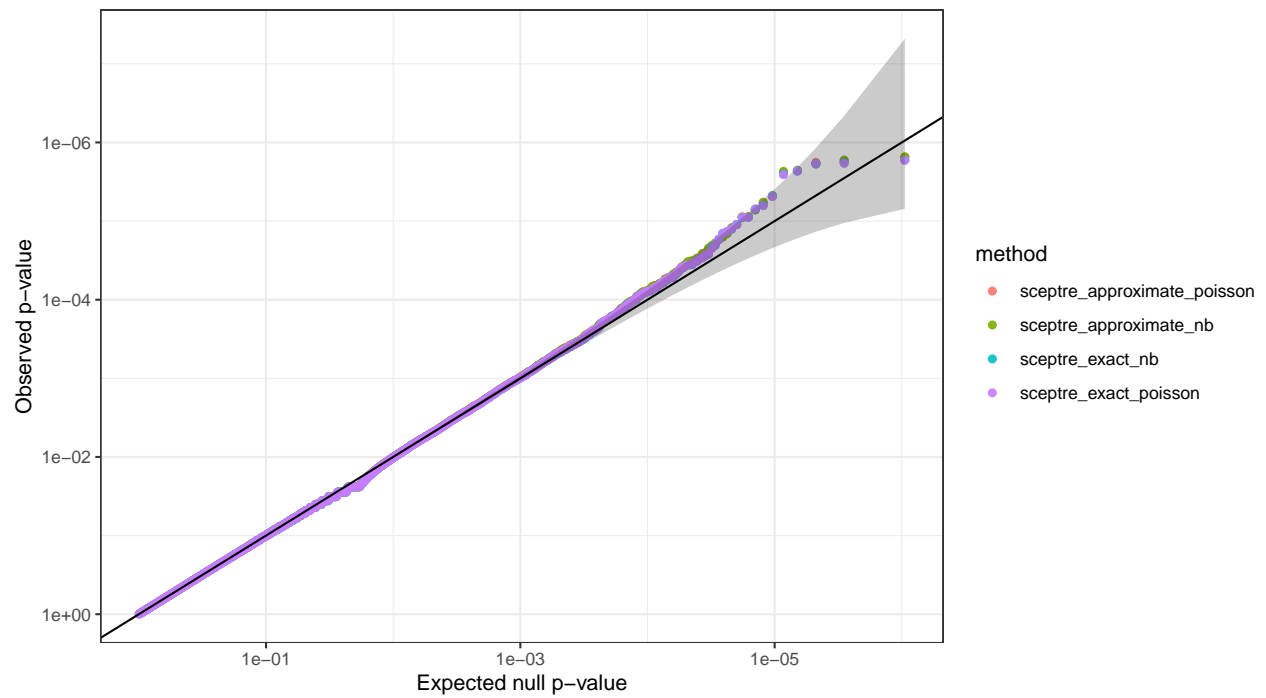
```
analyze_dataset(undercover_res = undercover_res,
                dataset = "frangieh/ifn_gamma/gene")
```



```
## # A tibble: 4 x 2
##    method                   n_reject
##    <fct>                       <int>
## 1 sceptre_approximate_poisson     1
## 2 sceptre_approximate_nb          1
## 3 sceptre_exact_nb                1
## 4 sceptre_exact_poisson           1
```

Frangieh Control

```
analyze_dataset(undercover_res = undercover_res,
                dataset = "frangieh/control/gene")
```
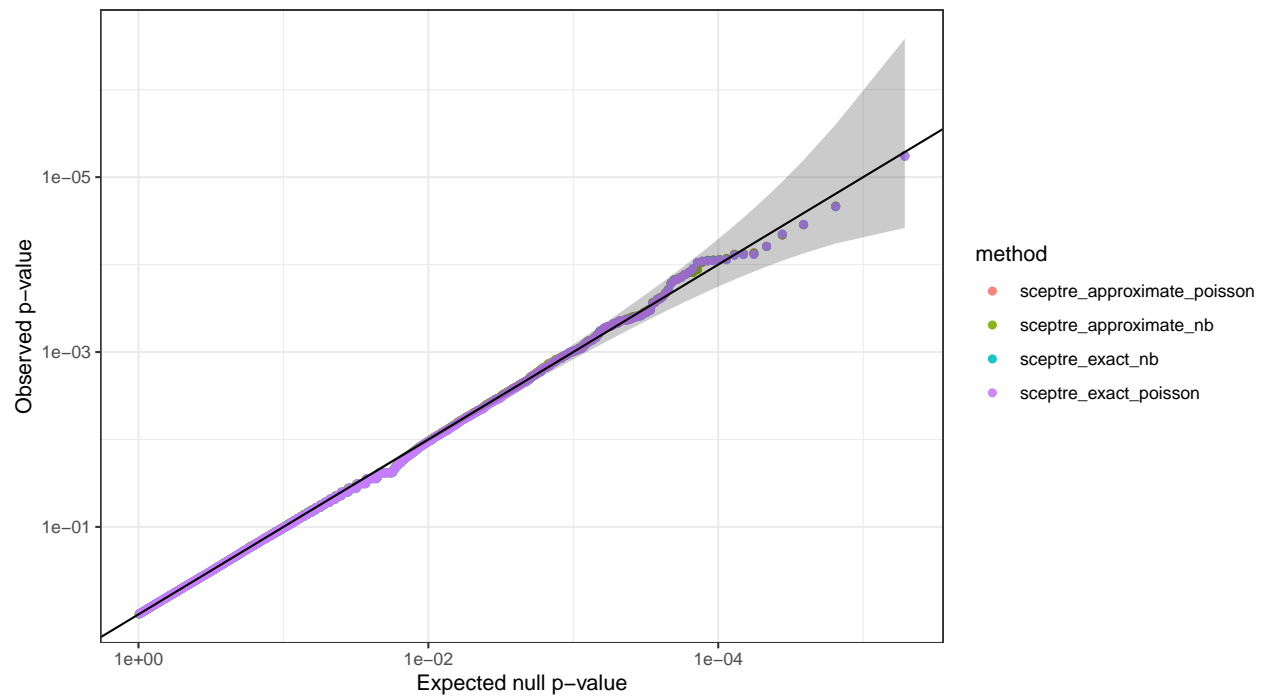
```
## # A tibble: 4 x 2
##   method                  n_reject
##   <fct>                      <int>
## 1 sceptre_approximate_poisson     0
## 2 sceptre_approximate_nb          0
## 3 sceptre_exact_nb                0
## 4 sceptre_exact_poisson           0
```

Simulated experiment
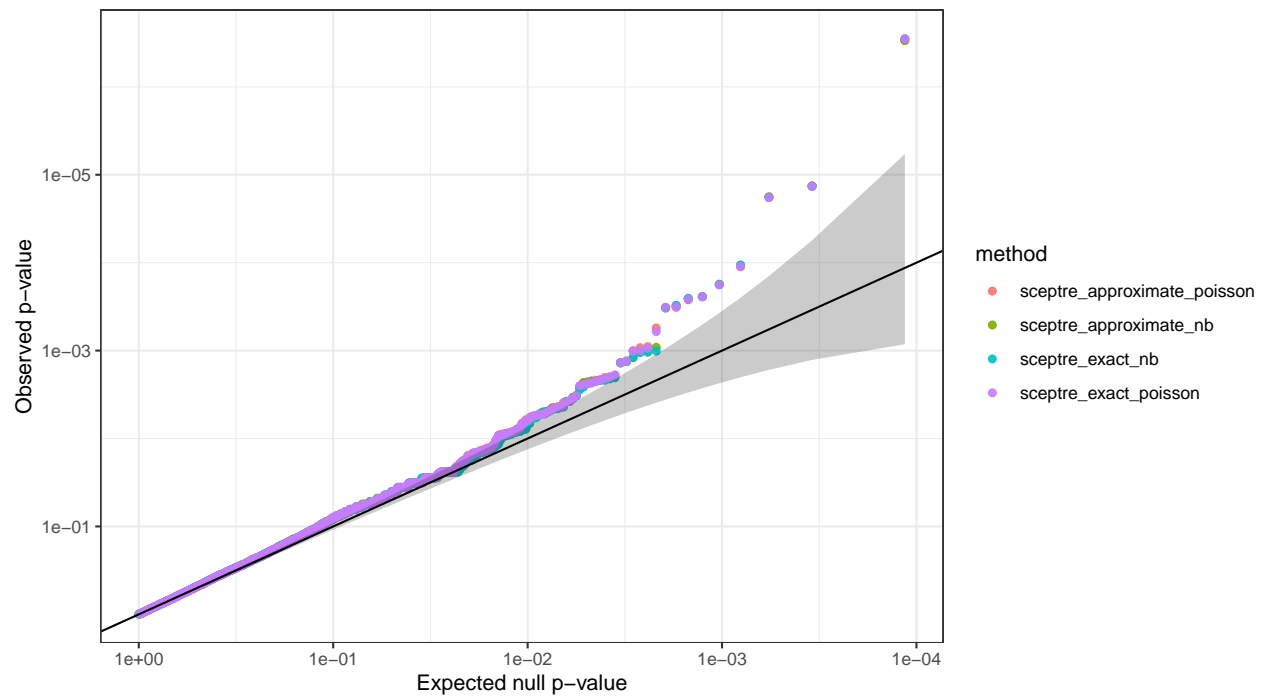
```
analyze_dataset(undercover_res = undercover_res,
                dataset = "simulated/experiment_1/gene")
```

```
## # A tibble: 4 x 2
##   method                 n_reject
##   <fct>                     <int>
## 1 sceptre_approximate_poisson      0
## 2 sceptre_approximate_nb           0
## 3 sceptre_exact_nb                 0
## 4 sceptre_exact_poisson            0
```

Schraivogel Enhancer

```
analyze_dataset(undercover_res = undercover_res,
                dataset = "schraivogel_enh")
```
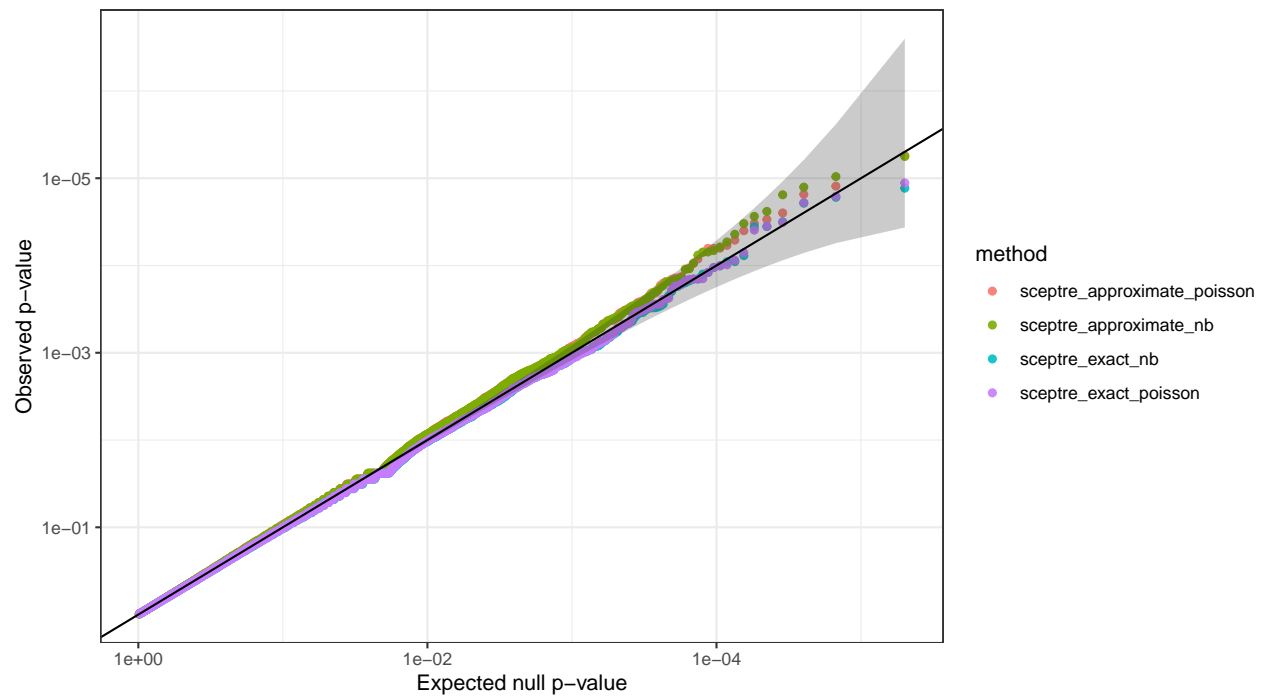
```
## # A tibble: 4 x 2
##   method                n_reject
##   <fct>                    <int>
## 1 sceptre_approximate_poisson    3
## 2 sceptre_approximate_nb         3
## 3 sceptre_exact_nb               3
## 4 sceptre_exact_poisson          3
```

Papalexi Gene

```
analyze_dataset(undercover_res = undercover_res,
                dataset = "papalexi/eccite_screen/gene")
```

```
## # A tibble: 4 x 2
##   method                  n_reject
##   <fct>                      <int>
## 1 sceptre_approximate_poisson       0
## 2 sceptre_approximate_nb            0
## 3 sceptre_exact_nb                  0
## 4 sceptre_exact_poisson             0
```
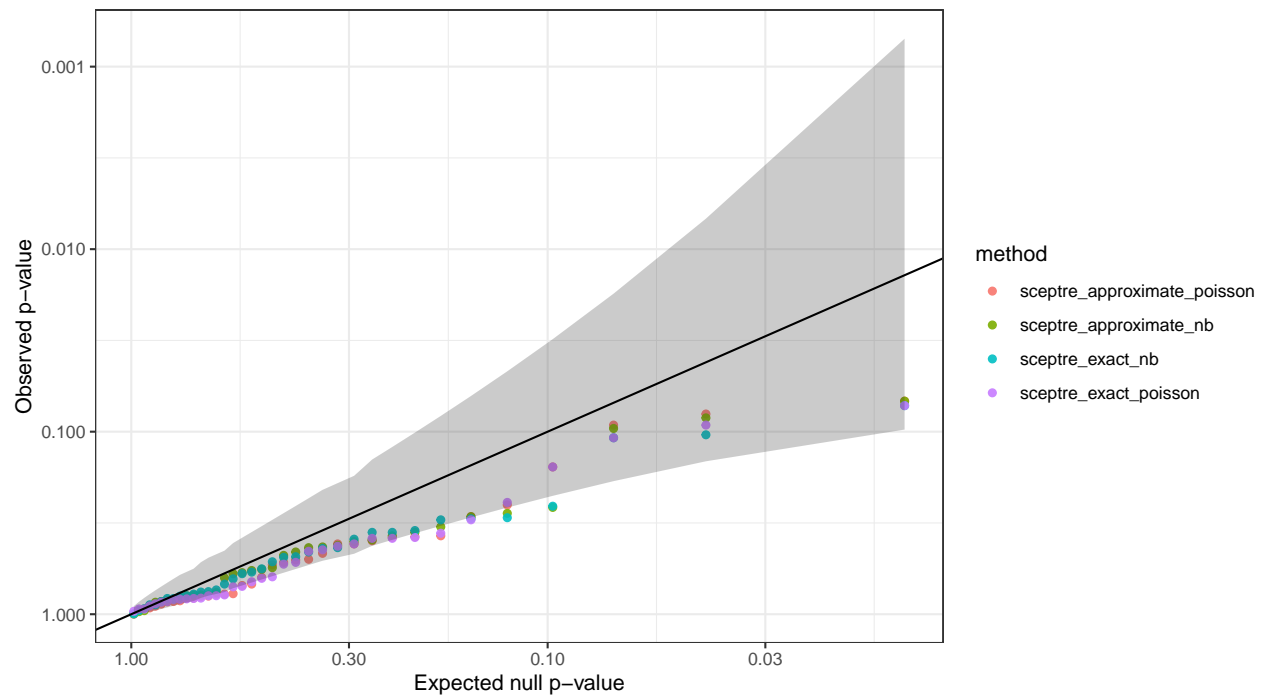
Papalexi Protein

```
analyze_dataset(undercover_res = undercover_res,
                dataset = "papalexi/eccite_screen/protein")
```

```
## # A tibble: 4 x 2
##   method                  n_reject
##   <fct>                      <int>
## 1 sceptre_approximate_poisson      0
## 2 sceptre_approximate_nb           0
## 3 sceptre_exact_nb                 0
## 4 sceptre_exact_poisson            0
```

Conclusions

The four (asymptotic) versions of SCEPTRE analyzed here are nearly identical.

Relative to the finite-sample version of SCEPTRE, the results do not change much. The calibration of SCEPTRE on the Frangieh data improves slightly, going from 1 to 0 false rejections. On the other hand, the calibration of SCEPTRE on the Schraivogel data degrades slightly, going from 2 to 3 false rejections.

Positive control results

The number of rejections that each version of SCEPTRE makes on the positive control data at level 1e-5 (the same as we currently use in the paper) is as follows.

```
pc_res <- readRDS(paste0(result_dir, "positive_control_analysis/sceptre_benchmark_0423.rds"))
pc_res |> na.omit() |>
    group_by(dataset, method) |>
    summarize(n_pc_reject = sum(p_value < 1e-5)) |>
  print(n = 40)
```

```
## `summarise()` has grouped output by 'dataset'. You can override using the
## `.groups` argument.
```

```
## # A tibble: 28 x 3
## # Groups:   dataset [7]
```

```
##    dataset                                 method                      n_pc_reject
##    <fct>                                   <fct>                              <int>
##  1 frangieh/co_culture/gene                sceptre_exact_poisson                103
##  2 frangieh/co_culture/gene                sceptre_approximate_nb               101
##  3 frangieh/co_culture/gene                sceptre_approximate_poiss~           102
##  4 frangieh/co_culture/gene                sceptre_exact_nb                     102
##  5 frangieh/ifn_gamma/gene                 sceptre_exact_poisson                 94
##  6 frangieh/ifn_gamma/gene                 sceptre_approximate_nb                95
##  7 frangieh/ifn_gamma/gene                 sceptre_approximate_poiss~            94
##  8 frangieh/ifn_gamma/gene                 sceptre_exact_nb                      95
##  9 papalexi/eccite_screen/gene             sceptre_exact_poisson                 13
## 10 papalexi/eccite_screen/gene             sceptre_approximate_nb                13
## 11 papalexi/eccite_screen/gene             sceptre_approximate_poiss~            13
## 12 papalexi/eccite_screen/gene             sceptre_exact_nb                      13
## 13 papalexi/eccite_screen/protein          sceptre_exact_poisson                  2
## 14 papalexi/eccite_screen/protein          sceptre_approximate_nb                 2
## 15 papalexi/eccite_screen/protein          sceptre_approximate_poiss~             2
## 16 papalexi/eccite_screen/protein          sceptre_exact_nb                       2
## 17 schraivogel/enhancer_screen_chr11/gene sceptre_exact_poisson                 10
## 18 schraivogel/enhancer_screen_chr11/gene sceptre_approximate_nb                10
## 19 schraivogel/enhancer_screen_chr11/gene sceptre_approximate_poiss~            10
## 20 schraivogel/enhancer_screen_chr11/gene sceptre_exact_nb                      10
## 21 schraivogel/enhancer_screen_chr8/gene  sceptre_exact_poisson                 12
## 22 schraivogel/enhancer_screen_chr8/gene  sceptre_approximate_nb                12
## 23 schraivogel/enhancer_screen_chr8/gene  sceptre_approximate_poiss~            12
## 24 schraivogel/enhancer_screen_chr8/gene  sceptre_exact_nb                      12
## 25 frangieh/control/gene                   sceptre_exact_poisson                 77
## 26 frangieh/control/gene                   sceptre_approximate_nb                77
## 27 frangieh/control/gene                   sceptre_approximate_poiss~            77
## 28 frangieh/control/gene                   sceptre_exact_nb                      77
```
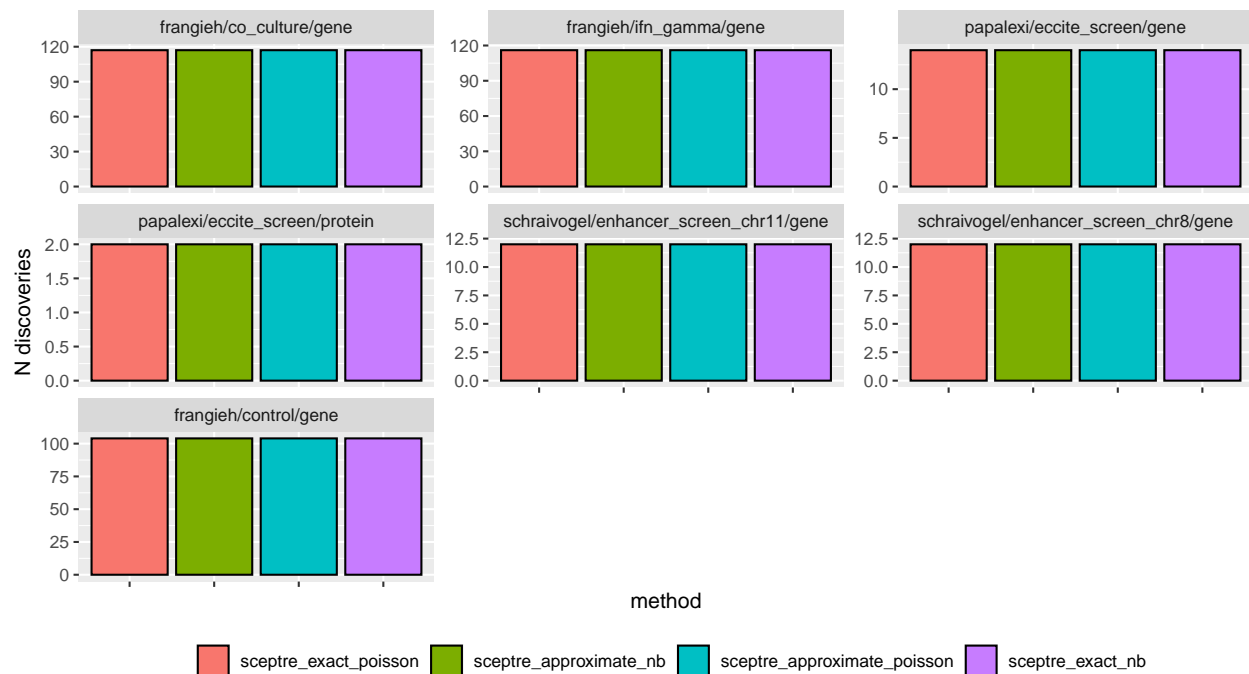
I plot the number of rejections that each method makes on the positive control pairs of each dataset, varying the rejection threshold over the set { 1e-3, 1e-4, 1e-5, 1e-6, 1e-7 }.

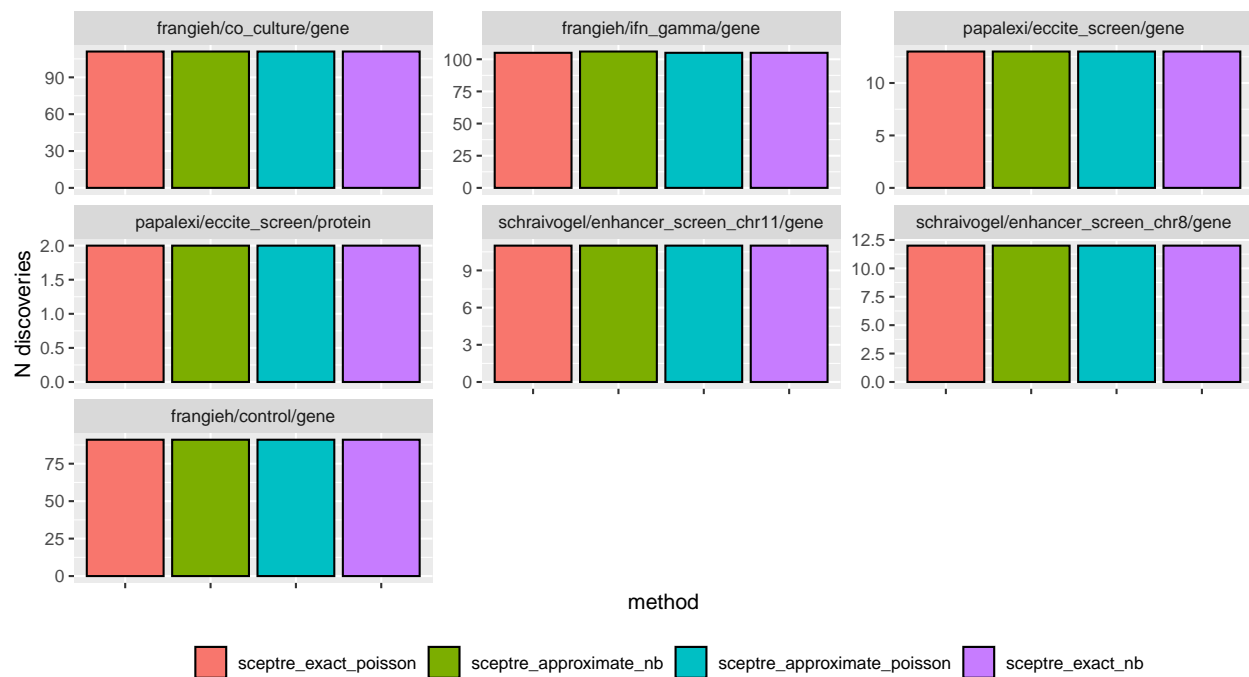First, let us see how many rejections that each method makes at a threshold of 1e-3.
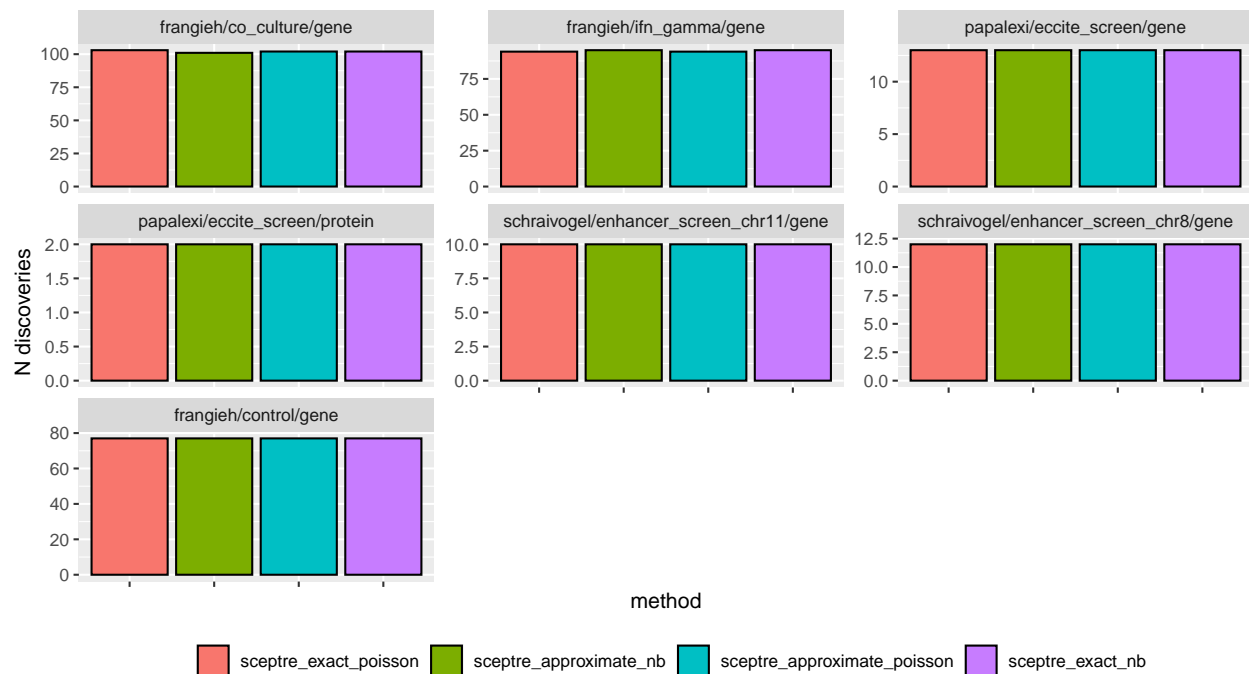
```
make_barplot(pc_res, 1e-3)
```

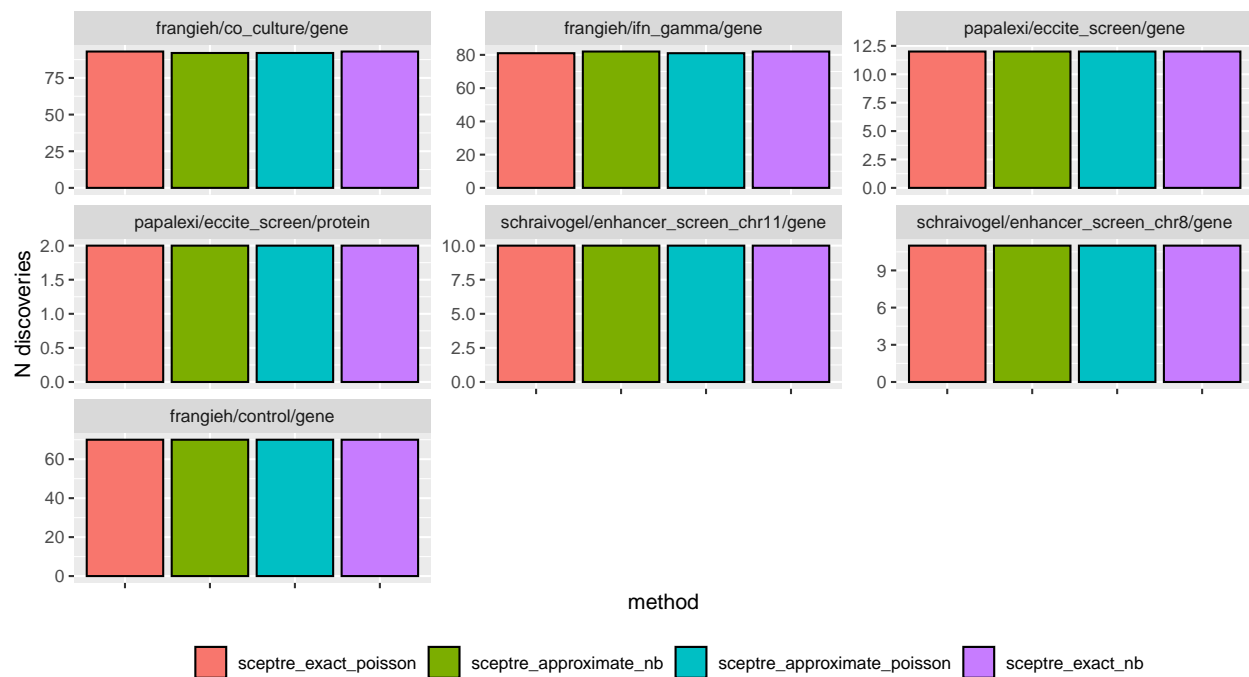Next, we use a threshold of 1e-4.

```
make_barplot(pc_res, 1e-4)
```
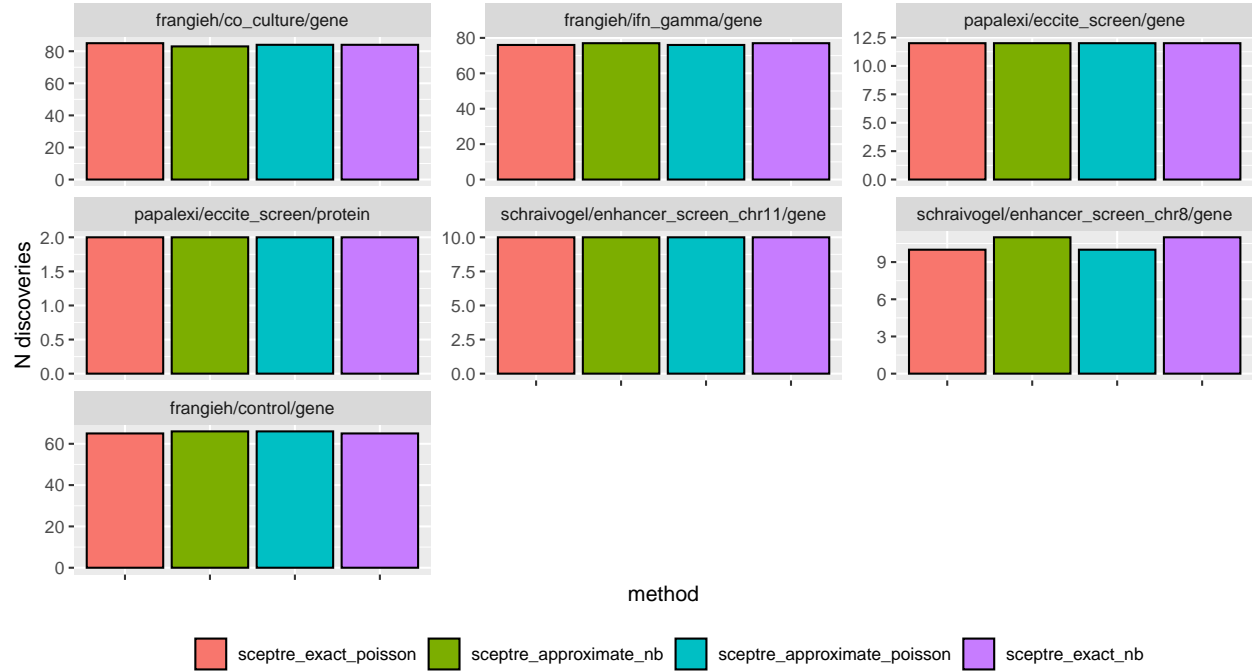

Now, 1e-5.

```
make_barplot(pc_res, 1e-5)
```

After this, 1e-6.

```
make_barplot(pc_res, 1e-6)
```


Finally, 1e-7.

```
make_barplot(pc_res, 1e-7)
```

Each version of SCEPTRE essentially makes the same number of rejections on each dataset using each threshold. The skew-normal versions of SCEPTRE are somewhat less powerful than the finite-sample version of SCEPTRE. However, the skew-normal versions of SCEPTRE are still more powerful than the competing methods.