flipscores test: Robust Inference in GLMs and Beyond.

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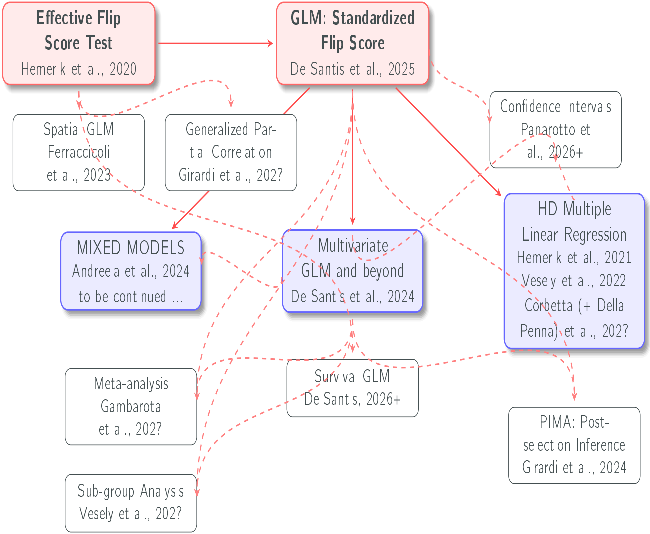
Outline

1. A very general approach
2. Motivation
3. Effective Flip score test
4. Standardized Flip Score Test

The big picture



Articles I

Outline

Permutation tests

Usually

- require less assumptions
- exact control of Type I Error, even for small sample size
- converge to parametric counterpart
  (i.e. asymptotically same power)
- multivariate (multiplicity correction): easy and powerful

BUT the assumption of exchangeability of the observations (under the null hypothesis)

- makes hard to deal with counfounders
- doesn't allow to deal the case of hereroscedasticity

Permutation tests on GLM WithOut Confounders

Example: Poisson model ($g() = log()$ link function)

$$log(E(y_i)) = g(\mu) = \eta = \gamma_0 + \beta x_i, \;\; i = 1, \ldots, n$$

Tested Hypothesis: $H_0: \;\; \beta = 0$
under H_0 the model reduces to

$$log(E(y_i)) = g(\mu) = \eta = \gamma_0, \;\; i = 1, \ldots, n$$

That is, observations are exchangeable, therefore

- Compute $S^{obs} = \hat{\beta}(y_i)$ (or any test stat)
- Permute y_i to get y_i^{*b} and
  compute $S^{*b} = \hat{\beta}(y_i^{*b})$
- repeat the step above (large) B times to the null distribution
- p-value $= \frac{\#(|S^{*b}| \geq |S^{obs}|)}{B+1}$

A major limitation: GLM with Confounders

Example: Poisson model ($g() = log()$ link function)

$$log(E(y_i)) = g(\mu_i) = \eta_i = \gamma_0 + \gamma_1 z_i + \beta x_i, \;\; i = 1, \ldots, n$$

$$H_0: \;\beta = 0 \;\; \forall\, \gamma = (\gamma_0, \gamma_1)$$

When $H_0: \;\beta = 0$ is true:

$$log(E(y_i)) = g(\mu_i) = \eta_i = \gamma_0 + \gamma_1 z_i, \;\; i = 1, \ldots, n$$

- Therefore observations are not exchangeable: $E(y_i) = e^{\gamma_0 + \gamma_1 z_i}$
- (outside the Linear Model) not only the mean, but even the variance is not equal among obs: e.g. $V(y_i) = e^{\gamma_0 + \gamma_1 z_i}$

Outline

The parametric score test

$$
\begin{aligned}
Score &= \left.\frac{\partial \ell(\beta|x,z,y)}{\partial \beta}\right|_{\beta=0} \\
&= \sum_{i=1}^{n} \frac{\partial}{\partial \beta} \log f_{\beta,\gamma,X_i}(Y_i)\Big|_{\beta=0,\gamma=\hat{\gamma}} = \\
&= \sum_{i=1}^{n} \nu_i \underset{H_0}{\dot{\sim}} N(0,\mathcal{I}) \quad \text{(asymptotically, under } H_0) \\
&\quad \mathcal{I}\text{: Fisher Information Matrix}
\end{aligned}
$$

$\nu_i \sim NOTnormal(0, var(\nu_i))$ + Centr.Lim.Thm =
Approximated Type I Error control, but very good in practice.

Effective Score

$$Effective\ Score = \sum_i^n (\nu_i - \hat{\mathcal{I}}'_{XZ}\hat{\mathcal{I}}^{-1}_{ZZ}\boldsymbol{\nu}^{(k-1)}_{\hat{\gamma},i})$$

with $\boldsymbol{\nu}^{(k-1)}_{\hat{\gamma},i} = \frac{\partial}{\partial\gamma} \log f_{\beta,\gamma,X_i}(Y_i)\Big|_{\beta=0,\gamma=\hat{\gamma}} \in \mathbb{R}^{k-1},\ 1 \leq i \leq n$

and $\hat{\mathcal{I}}$ the Observed Fisher Information under H_0:

$$\hat{\mathcal{I}} = \begin{bmatrix} \hat{\mathcal{I}}_{XX} & \hat{\mathcal{I}}'_{XZ} \\ \hat{\mathcal{I}}_{XZ} & \hat{\mathcal{I}}_{ZZ}. \end{bmatrix}$$

Since $\sum_i^n \hat{\mathcal{I}}'_{XZ}\hat{\mathcal{I}}^{-1}_{ZZ}\boldsymbol{\nu}^{(k-1)}_{\hat{\gamma},i} = 0 \ \Rightarrow\ Effective\ Score = Score$

(Also named Efficient Score in Cox and Hinkley, 1979)

Effective Score in GLM

In GLM the effective score takes the following form:

$$
\begin{aligned}
S &= \sum_{i}^{n} (\nu_i - \hat{\mathcal{I}}'_{XZ}\hat{\mathcal{I}}^{-1}_{ZZ}\boldsymbol{\nu}^{(k-1)}_{\hat{\gamma},i}) = \\
&= \sum_{i=1}^{n} \left(x_i - X^\top WZ(Z^\top WZ)^{-1} z_i\right) \frac{(y_i - \hat{\mu}_i)d_i}{v_i} = \\
&= X^T W^{1/2}(I - H)V^{-1/2}(y - \hat{\mu})
\end{aligned}
$$

where

$$
\begin{aligned}
H = W^{1/2}Z(Z^T WZ)^{-1}Z^T W^{1/2} \\
W = DV^{-1}D \\
D = \mathrm{diag}\left\{\frac{\partial \mu_i}{\partial \eta_i}\right\} \\
V = \mathrm{diag}\{\mathrm{Var}(y_i)\}.
\end{aligned}
$$

An intuition: Effective score as a Partial Correlation

In Linear Models, a special case of GLM:

$$Y = Z\gamma + X\beta + \varepsilon$$

the Effective Score is a Double Residualization
(dropping some constant, e.g. the common variance of errors ε):
hat matrix simplifies to $H = Z(Z^T Z)^{-1} Z^T$ and $\hat{\mu} = Hy$ so that:

$$\begin{aligned} S &= X^T (I - H)(y - \hat{\mu}) \\ &= X^T (I - H)(I - H)y \\ &= \sum_{i=1}^{n} (x_i - \hat{x}_i)\,(y_i - \hat{y}_i) \end{aligned}$$

the partial correlation can be written as

$$\frac{X^T (I - H)\,(I - H)y}{\|(I - H)X\| \|(I - H)y\|} = \frac{\sum_{i=1}^{n} (x_i - \hat{x}_i)\,(y_i - \hat{y}_i)}{\sqrt{\sum_{i=1}^{n} (x_i - \hat{x}_i)^2 \sum_{i=1}^{n} (y_i - \hat{y}_i)^2}}$$

Generalized Partial Correlation in GLM

$$\rho = \frac{X^T W^{1/2}(I - H)\, V^{-1/2}(y - \hat{\mu})}{\|(I - H) W^{1/2} X\| \|V^{-1/2}(y - \hat{\mu})\|}$$

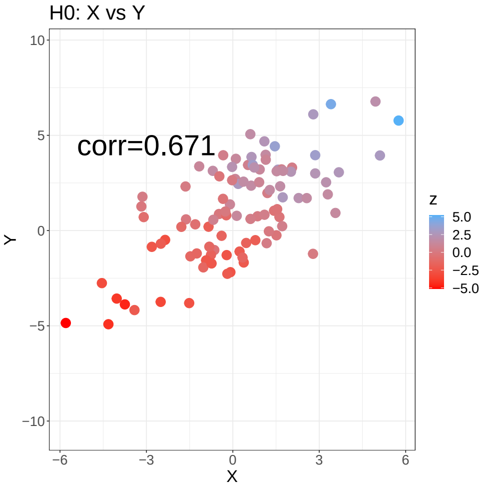
- It becomes the well known partial correlation coefficient in LM
- $-1 \leq \rho \leq 1$
- Easily extended to (Generalized) Determination Coefficient R^2 for multiple X.

Finos and Girardi, 2026+

A toy example, $\beta = 0$

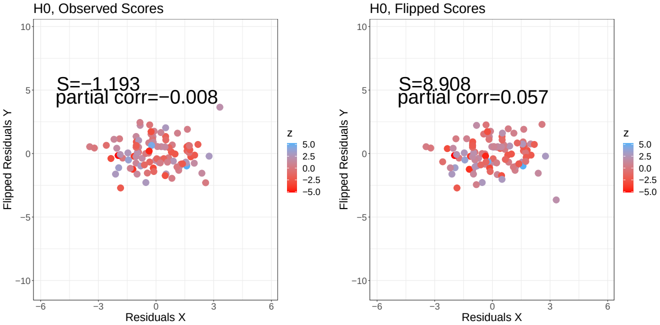
$$Y = Z\gamma + X\beta + \varepsilon$$

$$cor(X, Z) = 0.80,\ \ \gamma = 1,\ \beta = 0,\ \ \varepsilon \sim N(0, 1)$$



A toy example, $\beta = 0$

$$\sum_{i=1}^{n} (x_i - \hat{x}_i)(y_i - \hat{y}_i) \text{ Vs } \sum_{i=1}^{n} (x_i - \hat{x}_i) \pm (y_i - \hat{y}_i)$$



A toy example, $\beta \neq 0$

$$Y = Z\gamma + X\beta + \varepsilon$$

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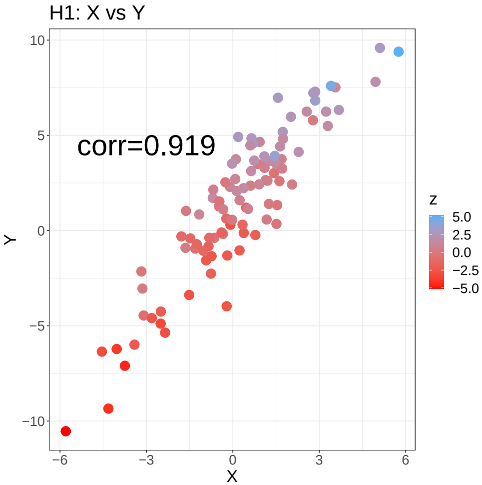
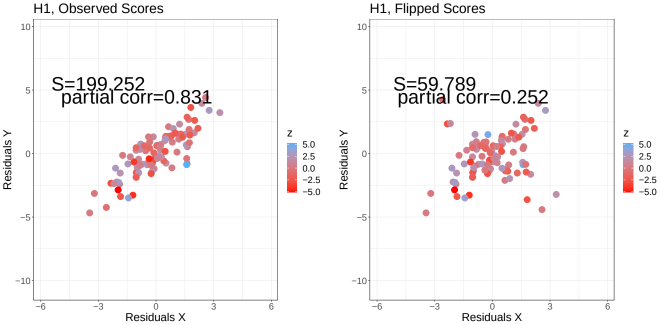


A toy example, $\beta \neq 0$

$$\sum_{i=1}^{n} \left(x_i - \hat{x}_i\right)\left(y_i - \hat{y}_i\right) \text{ Vs } \sum_{i=1}^{n} \left(x_i - \hat{x}_i\right) \pm \left(y_i - \hat{y}_i\right)$$



Effective Flip Score test

Hemerik, Goeman, Finos. *Robust testing in generalized linear models by sign-flipping score contributions*. JRSS-B
doi:10.1111/rssb.12369

$$S^* = \sum_{i=1}^{n} \pm(\nu_i - \hat{\mathcal{I}}'_{XZ}\hat{\mathcal{I}}^{-1}_{ZZ}\boldsymbol{\nu}^{(k-1)}_{\hat{\gamma},i})$$

Algorithm

- Compute $S^{obs} = S$
- Compute S^{*b}
- repeat the step above (large) B times to the null distribution.
- p-value $= \frac{\#|S^{*b}| \geq |S^{obs}|}{B+1}$

REMARK:

- $\sum_i^n +\hat{\mathcal{I}}'_{XZ}\hat{\mathcal{I}}^{-1}_{ZZ}\boldsymbol{\nu}^{(k-1)}_{\hat{\gamma},i} = 0$ BUT
- $\sum_i^n \pm\hat{\mathcal{I}}'_{XZ}\hat{\mathcal{I}}^{-1}_{ZZ}\boldsymbol{\nu}^{(k-1)}_{\hat{\gamma},i} \neq 0$ (in general)

  this is why we need Effective Score

Properties

Asymptotically Exact

- 0-mean: $E(\nu_i) = 0 \; AND \; E(\boldsymbol{\nu}_{\hat{\gamma},i}^{(k-1)}) = 0 \Rightarrow E(\pm\nu_i) = 0$
- $y_i \perp\!\!\!\perp y_j \;\; i,j = 1,\dots,n$
- constant variance (Asymptotically):
  $V(+(\nu_i - \hat{\mathcal{I}}'_{XZ}\hat{\mathcal{I}}^{-1}_{ZZ}\boldsymbol{\nu}_{\hat{\gamma},i}^{(k-1)})) = V(-(\nu_i - \hat{\mathcal{I}}'_{XZ}\hat{\mathcal{I}}^{-1}_{ZZ}\boldsymbol{\nu}_{\hat{\gamma},i}^{(k-1)})) \Rightarrow$
  $V(S^*) = V(S^{obs})$

Properties

It converges to parametric score test (i.e. asymptotically):

i. is normal $N(0, \mathcal{I})$
ii. is exact
iii. is locally most powerful (LMP)
iv. if the parametric S test is UMP (UMPU), S^* is asymptotically UMP (UMPU)

Effective Flip Score is Asymptotically Exact

- We need: $\nu_i \perp\!\!\!\perp \nu_{i'}$.
- However, when we plug $\hat{\gamma}$ into $S_{\hat{\gamma}}$, the $\nu_{\hat{\gamma},i}$ become dependent (e.g. in linear model the effective d.f. are $n - \mathrm{rank}(Z)$).
- The correlation disappears when $n \to \infty$

We get **asymptotically exact** test (with any variance estimates).

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We get **asymptotically exact** test (with any variance estimates).

We propose the **Standardized** Flip Score for small (and large) sample size!

Outline

Standardized Flip Scores

De Santis, Goeman, Hemerik, Finos (2025) Inference in generalized linear models with robustness to misspecified variances. JASA

It is easy to derive:

$$Var\{S(d(\pm 1))\} =$$
$$X^T W^{1/2}(I - H)d(\pm 1)(I - H)d(\pm 1)(I - H)W^{1/2}X + o_p(1)$$

(i.e. variance depends on sign-flips)

$$Standardized\ flipscores = S^*(d(\pm 1)) = S(d(\pm 1))/Var\{S(d(\pm 1))\}^{1/2}$$

Results: the anti-conservativeness disappears:

- we stabilize first and second moment (almost exact, see later)

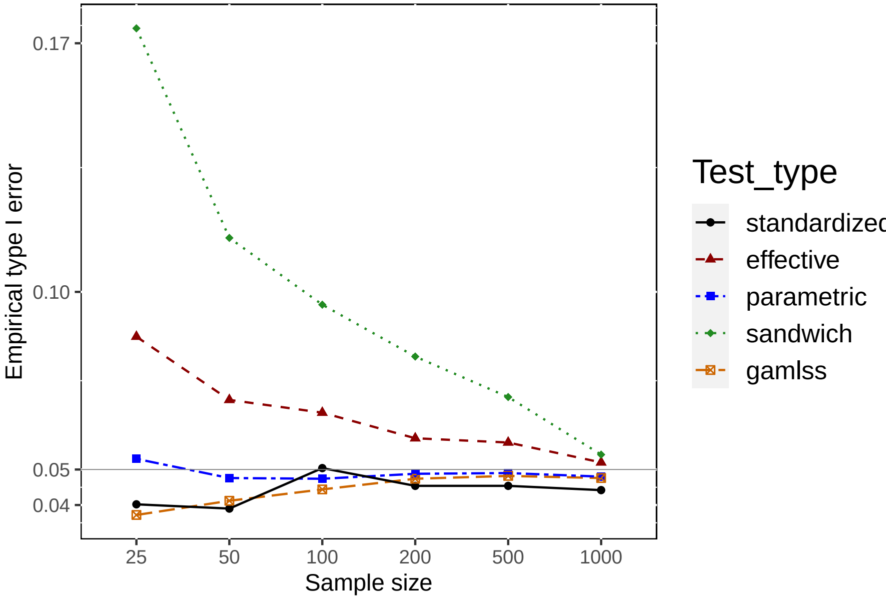
Simulation Study

GLM with 4 confounders (3 variables + intercept), which are correlated with X. The null hypothesis $H_0: \ \beta = 0$ against a two-sided alternative ($\alpha = 0.05$)
5 000 replications

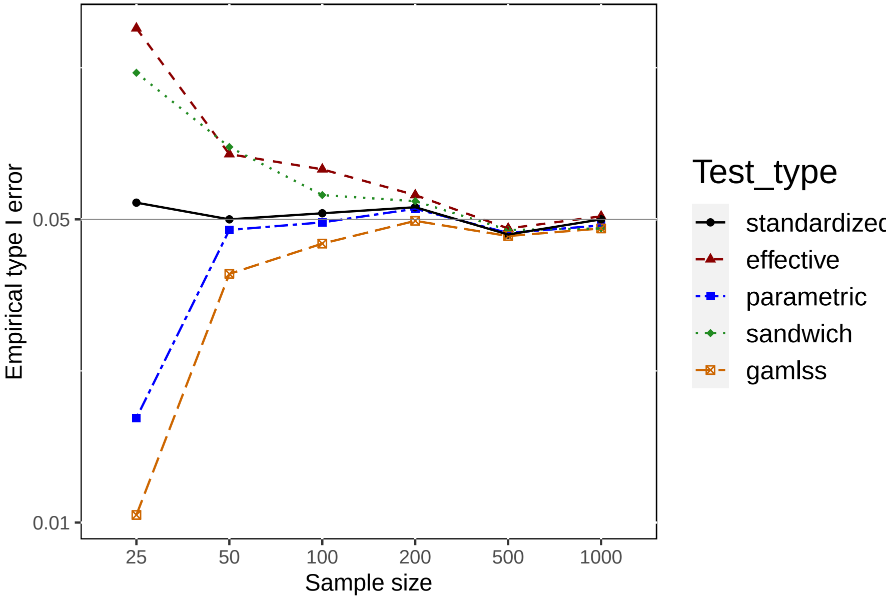
Comparison with:

- Wald test (paramtric)
- Wald test with sandwich (sandwich)
- Generalized Additive Models for Location, Scale and Shape (gamlss)

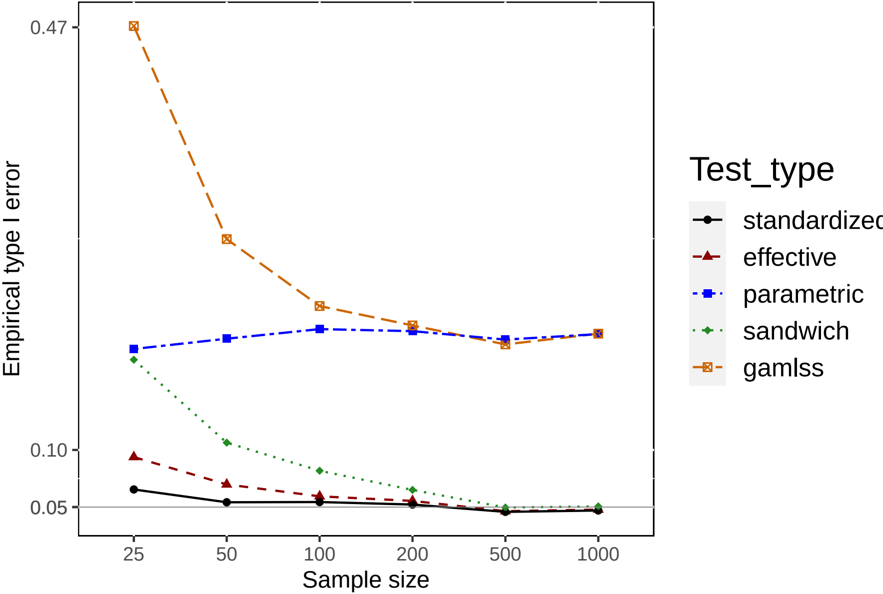
Simulation: Type I error control: Poisson model



Simulation: Type I error control: Logistic model

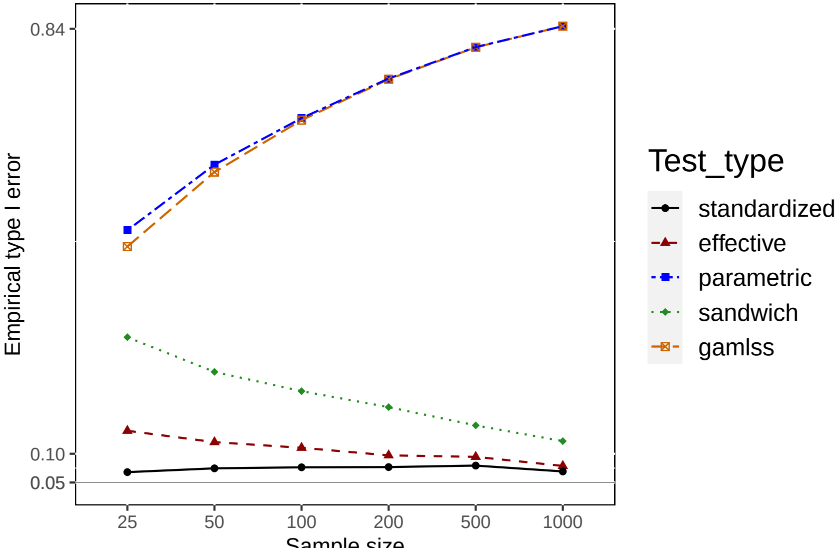


Simulation: Type I error control: Normal with heteroscedasticity ($var(y_i) = 4x_i^2$)

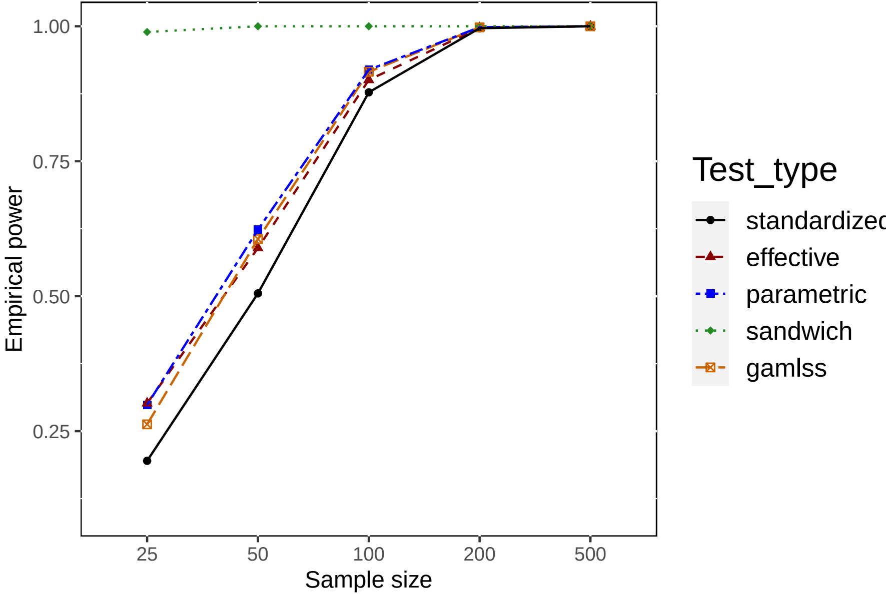


Simulation: Type I error control: Neg Binomial data, fitted Poisson Model

(i.e. not accounting for hetheroscedasticity)



Simulation: Power, Poisson model



R package: `flipscores`

Same syntax as `glm()`

An Example:

- Response: Binomial, logit link
- Predictors: x(3-groups) + z(continuous)+interaction

```
set.seed(1)
x=factor(rep(LETTERS[1:3],15))
D=data.frame(y=rbinom(45,1,.05+(x=="C")*.8),
             x=x,
             z=rnorm(45))
```

R package: flipscores

```
library(flipscores)
mod=flipscores(y~x*z,data=D,family = binomial, data = D)
summary(mod)
```

```
##
## Call:
## flipscores(formula = y ~ x * z, family = binomial, data = D)
##
## Coefficients:
##              Estimate      Score Std. Error z value Pr(>|z|)
## (Intercept) -2.057e+01 -7.211e+00  2.772e+00  -2.601    0.054 .
## xB          -6.564e-11 -5.673e-16  4.881e-16  -1.162    0.384
## xC           2.195e+01  5.861e+00  3.239e+00   1.810    0.020 *
## z           -4.722e-09 -3.166e-16  3.952e-16  -0.801    0.442
## xB:z         4.722e-09 -5.008e-16  4.076e-16  -1.229    0.278
## xC:z        -5.465e-03  2.433e-16  5.275e-09   0.000    1.000
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

R package: flipscores

```
anova(mod,type=3)

## Analysis of Deviance Table: Type III test
## Model: binomial, link: logit
## Inference is provided by FlipScores approach (5000 sign flips).
##
## Response: y
##      Score Df Pr(>Score)
## x   7.6516  2     0.0020 **
## z   0.5828  1     0.4484
## x:z 0.0001  2     0.9904
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Conclusion

Standardized Flip Score Test

- for GLM
- gooood control of the type I error

Effective Flip Score Test:

- general: any score statistics
- Asymtotically exact

Both

- As we will see: General Approach, many extensions
- assume the link function to be right ($E(\hat{\mu}) = \mu$)
- very **robust** (heteroscedasticity, overdispersion etc)
- quite **fast** to compute
- R package: `https://github.com/livioivil/flipscores`
- some relationship with solution of F. Pesarin (2001) to Behrens-Fisher problem