Simulation Fixed Effect

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1 Motivation

Based on the previous simulation results, the interaction effect estimation is biased. One possible reason is that we consider the $\beta's$ as random effects, which will affect the covariance structure of the signals. More specifically, If β is fixed, then we have following

$$Var(X\beta) = \beta^T \Sigma_X \beta,$$

Where $\Sigma_X = Var(X)$. We can see that the X's covariance has an affect on the signal's variance.

However, if we consider β as an random effect, then $Var(X\beta)$ is not only related with X but also with $\beta's$ covariance. Therefore, in the following simulation the β is fixed and there is no average out summary across different values of β .

2 Simulation result

2.1 Setup

In the following simulation, I just randomly generated 3 different sets of values for β (main and interaction). Give each set of $\beta's$, the values of y is generated 100 times and thus 100 estimations of variance of main effects and interaction effects.

2.2 Full data

2.2.1 Averaged estimation

Table 1: null-full

| $\overline{	ext{true_main}}$ | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-------------------------------|------------------|-----------|------------------|------------|------------------|
| 3.2158113 | 49.40766 | 4.3544031 | 9.8020884 | 6.3131046 | 19.9637333 |
| 0.0000000 | 0.00000 | 1.7708630 | 0.3238356 | 1.3104548 | 0.5987790 |
| 1.4348505 | 13.20353 | 4.2029131 | 0.5565153 | 8.8826209 | 1.8856730 |
| 0.0000000 | 0.00000 | 0.7651304 | 0.0759305 | 0.7295852 | 0.2124003 |
| 0.8500824 | 29.33039 | 9.0731883 | 3.6950261 | 11.2518946 | 3.9226269 |
| 0.0000000 | 0.00000 | 1.3603169 | 0.2463424 | 1.1417417 | 0.2855682 |

Table 2: rank-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|------------|------------------|-----------|------------------|
| 2.6873762 | 4.291104 | 2.8521057 | 5.6127113 | 2.9875348 | 0.8293864 |
| 0.0000000 | 0.000000 | 0.5219216 | 0.9289016 | 0.4989542 | 0.4139479 |
| 1.5461695 | 1.903794 | 0.7875891 | 0.8296039 | 1.8003643 | 0.2571868 |
| 0.0000000 | 0.000000 | 0.2677982 | 0.2455065 | 0.3886742 | 0.2667834 |
| 0.4947499 | 5.449791 | -0.0100967 | 4.7920416 | 1.1578751 | 0.4965576 |
| 0.0000000 | 0.000000 | 0.0475158 | 0.6945106 | 0.2787832 | 0.2714290 |

Table 3: quantile-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|-----------|------------------|-----------|------------------|
| 2.808878 | 6.248359 | 4.2725694 | 7.1142656 | 5.1323716 | 2.7324792 |
| 0.000000 | 0.000000 | 0.6741903 | 0.8282731 | 0.6488152 | 0.5126386 |
| 1.493517 | 2.945494 | 1.3331202 | 0.8386872 | 2.5937373 | 0.6850581 |
| 0.000000 | 0.000000 | 0.3637601 | 0.2097083 | 0.4655614 | 0.3297226 |
| 0.577709 | 8.209279 | 0.1982071 | 4.9213341 | 2.5304851 | 1.5261274 |
| 0.000000 | 0.000000 | 0.2193605 | 0.6382106 | 0.4427720 | 0.3743509 |

Table 4: log-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|-----------|------------------|-----------|------------------|
| 2.6937805 | 6.107954 | 5.0208023 | 7.7236308 | 5.5848707 | 1.3456888 |
| 0.0000000 | 0.000000 | 0.7177300 | 0.9656956 | 0.6280478 | 0.3237447 |
| 1.6151267 | 2.360681 | 0.5707424 | 0.8223152 | 2.0697999 | 0.3163978 |
| 0.0000000 | 0.000000 | 0.2375397 | 0.2171377 | 0.3980136 | 0.2521233 |
| 0.5805219 | 6.281979 | 0.0926633 | 3.3529820 | 1.9173150 | 0.4860522 |
| 0.0000000 | 0.000000 | 0.1422832 | 0.5058683 | 0.3574811 | 0.2421702 |

Table 5: sqrt-full

| ${ m true_main}$ | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-------------------|------------------|-----------|------------------|------------|------------------|
| 2.8923511 | 16.154550 | 5.8498863 | 11.1069955 | 11.1032750 | 17.2475250 |
| 0.0000000 | 0.000000 | 1.0780650 | 0.6580931 | 0.9545424 | 1.0366619 |
| 1.3593689 | 4.740357 | 1.6579450 | 0.7002400 | 3.6527756 | 2.2664512 |
| 0.0000000 | 0.000000 | 0.4476342 | 0.1572187 | 0.5130434 | 0.5033004 |
| 0.6224476 | 11.267165 | 0.5178294 | 3.2208614 | 3.7014124 | 2.2444958 |
| 0.0000000 | 0.000000 | 0.4421995 | 0.3660503 | 0.5833727 | 0.2835238 |

Table 6: cat-10-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|------------|------------------|-----------|------------------|
| 2.6921130 | 4.090163 | 3.2023234 | 5.3127400 | 3.0219314 | 2.3507786 |
| 0.0000000 | 0.000000 | 0.5573301 | 0.9149534 | 0.4715617 | 0.6328867 |
| 1.4802190 | 2.017695 | 0.7938607 | 1.0346787 | 1.7375762 | 0.9872728 |
| 0.0000000 | 0.000000 | 0.2702883 | 0.2869367 | 0.3890169 | 0.4708470 |
| 0.5241891 | 5.244097 | -0.0565079 | 4.7258258 | 0.9887204 | 1.3254654 |
| 0.0000000 | 0.000000 | 0.0360078 | 0.6983307 | 0.2675379 | 0.4672848 |

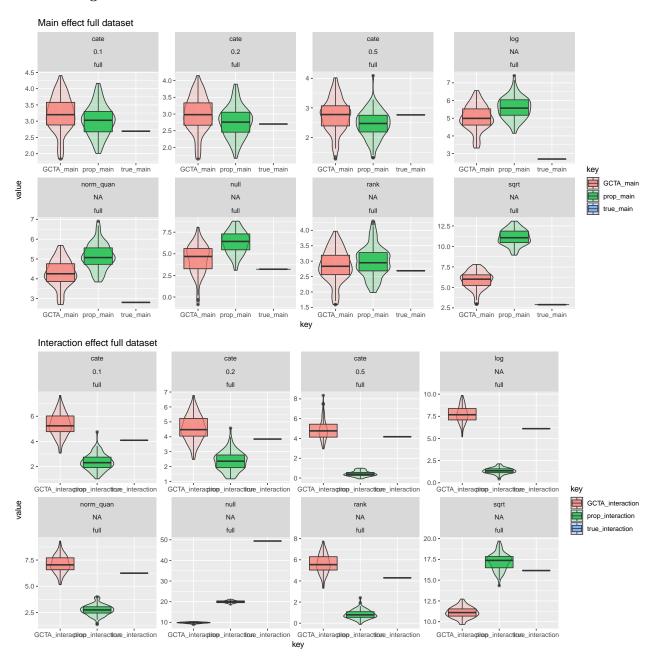
Table 7: cat-5-full

| ${ m true_main}$ | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-------------------|------------------|------------|------------------|-----------|------------------|
| 2.7000186 | 3.845413 | 2.9814892 | 4.5664152 | 2.7577871 | 2.3837907 |
| 0.0000000 | 0.000000 | 0.5389448 | 0.8707940 | 0.4572031 | 0.6435033 |
| 1.5233407 | 2.095205 | 0.6560493 | 1.1843935 | 1.6552562 | 1.4631640 |
| 0.0000000 | 0.000000 | 0.2460147 | 0.3280028 | 0.3682952 | 0.5492955 |
| 0.5844635 | 5.039599 | -0.0089763 | 4.9405562 | 0.9122658 | 1.7972413 |
| 0.0000000 | 0.000000 | 0.0597922 | 0.7460484 | 0.2607959 | 0.5506845 |

Table 8: cat-2-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|-----------|------------------|-----------|------------------|
| 2.7625360 | 4.174994 | 2.7357569 | 4.8980288 | 2.4478650 | 0.4305927 |
| 0.0000000 | 0.000000 | 0.5691043 | 1.0556699 | 0.4673456 | 0.2555173 |
| 2.0988911 | 2.415461 | 0.6686098 | 1.4511920 | 2.0919194 | 0.2109776 |
| 0.0000000 | 0.000000 | 0.2497561 | 0.4816661 | 0.4485330 | 0.1846766 |
| 0.8243926 | 4.359497 | 0.0476966 | 7.2911735 | 0.5193437 | 0.6674842 |
| 0.0000000 | 0.000000 | 0.0733865 | 1.3249693 | 0.2321657 | 0.2455678 |

2.2.2 Histgram of 100 iterations



2.3 Remove 7 subset data

2.3.1 Averaged estimation

Table 9: null-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|------------|------------------|------------|------------------|
| 2.326047 | 11.04140 | 2.9874170 | 1.1487788 | 8.6919450 | 1.4596337 |
| 0.000000 | 0.00000 | 0.8428856 | 0.1439049 | 0.7281087 | 0.1605680 |
| 1.201223 | 43.48742 | -0.7370419 | 7.7927874 | 14.1694376 | 5.0495201 |
| 0.000000 | 0.00000 | 1.4242304 | 0.3720183 | 1.0371484 | 0.2705839 |
| 1.012090 | 10.01595 | 1.2742855 | 1.4205766 | 5.6320471 | 1.8196181 |
| 0.000000 | 0.00000 | 0.6075589 | 0.1547535 | 0.7061331 | 0.1748635 |

Table 10: rank-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|-----------|------------------|-----------|------------------|
| 2.3586213 | 1.7099875 | 3.4010825 | 0.5564496 | 2.9142539 | 0.1923090 |
| 0.0000000 | 0.0000000 | 0.5509228 | 0.1968368 | 0.4829440 | 0.2634942 |
| 0.8726516 | 4.8404613 | 0.4423640 | 6.9471978 | 0.8599029 | 0.2515139 |
| 0.0000000 | 0.0000000 | 0.1999645 | 0.9871361 | 0.3064646 | 0.1832223 |
| 0.9815092 | 0.6539307 | 0.9953976 | 0.0356594 | 1.1013735 | -0.0422894 |
| 0.0000000 | 0.0000000 | 0.2466602 | 0.0546254 | 0.2439542 | 0.1668013 |

Table 11: quantile-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|------------|------------------|-----------|------------------|
| 2.3824357 | 2.1391474 | 3.8844804 | 0.6773023 | 3.4683656 | 0.2292941 |
| 0.0000000 | 0.0000000 | 0.5892784 | 0.2351244 | 0.5273831 | 0.2151068 |
| 0.9031948 | 8.2892384 | -0.1832356 | 8.8315811 | 2.2951339 | 1.0422520 |
| 0.0000000 | 0.0000000 | 0.1090191 | 0.9395930 | 0.4331523 | 0.3285844 |
| 0.9728945 | 0.9235943 | 1.0575944 | 0.0864704 | 1.2314344 | 0.0207744 |
| 0.0000000 | 0.0000000 | 0.2574253 | 0.1056672 | 0.2871658 | 0.1485006 |

Table 12: log-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|------------|------------------|-----------|------------------|
| 2.3753731 | 2.1161346 | 3.4175941 | 0.5725289 | 3.1828043 | -0.0139009 |
| 0.0000000 | 0.0000000 | 0.5604288 | 0.1949268 | 0.4740381 | 0.1380879 |
| 1.0225968 | 7.1152262 | -0.1619669 | 6.8799631 | 0.6129037 | 0.4824211 |
| 0.0000000 | 0.0000000 | 0.0915385 | 0.8938767 | 0.2883702 | 0.2353967 |
| 0.9626496 | 0.9838793 | 1.1858619 | 0.0188071 | 1.3573222 | -0.0626020 |
| 0.0000000 | 0.0000000 | 0.2710320 | 0.0669914 | 0.2651128 | 0.1017684 |

Table 13: sqrt-full

| ${\it true_main}$ | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|--------------------|------------------|------------|------------------|-----------|------------------|
| 2.3533282 | 4.161740 | 3.9640479 | 1.2051462 | 5.1160571 | 1.1605548 |
| 0.0000000 | 0.000000 | 0.6546046 | 0.2669356 | 0.5408662 | 0.1912425 |
| 1.0021315 | 17.942518 | -1.3056548 | 8.5014977 | 4.9446045 | 3.4550858 |
| 0.0000000 | 0.000000 | 0.6491687 | 0.6615934 | 0.5798050 | 0.3046042 |
| 0.9796173 | 1.796764 | 1.6992198 | 0.4067622 | 2.3081148 | 0.6194889 |
| 0.0000000 | 0.000000 | 0.3404351 | 0.1760265 | 0.3708196 | 0.1935866 |

Table 14: cat-10-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|-----------|------------------|-----------|------------------|
| 2.3457539 | 1.7426962 | 3.3972965 | 0.6514204 | 2.8515749 | 0.7056741 |
| 0.0000000 | 0.0000000 | 0.5548752 | 0.2188062 | 0.4614171 | 0.4096501 |
| 0.8910848 | 4.5900370 | 0.3960131 | 6.5894462 | 0.8452006 | 0.8720525 |
| 0.0000000 | 0.0000000 | 0.1896358 | 0.9805470 | 0.2703615 | 0.3231284 |
| 0.9856932 | 0.6969061 | 1.0796944 | 0.0418221 | 1.1523672 | 0.1498357 |
| 0.0000000 | 0.0000000 | 0.2573330 | 0.0588064 | 0.2616573 | 0.3030559 |

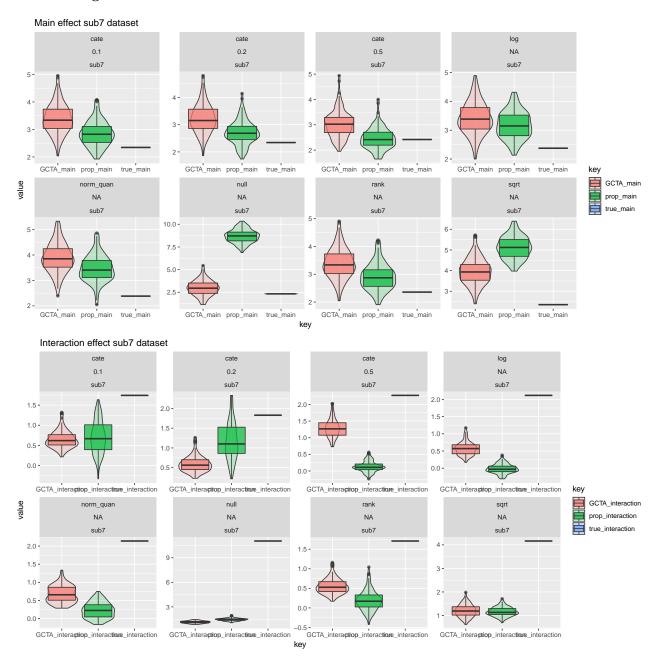
Table 15: cat-5-full

| ${ m true_main}$ | $true_interaction$ | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-------------------|---------------------|-----------|------------------|-----------|------------------|
| 2.3430307 | 1.8309328 | 3.2338604 | 0.5909319 | 2.7097974 | 1.1819612 |
| 0.0000000 | 0.0000000 | 0.5517777 | 0.2007778 | 0.4455850 | 0.4850347 |
| 0.9577299 | 4.1246182 | 0.4700609 | 6.0277129 | 0.7653511 | 1.4748726 |
| 0.0000000 | 0.0000000 | 0.2049841 | 0.9805762 | 0.2545628 | 0.4718127 |
| 0.9904863 | 0.7478858 | 1.0610726 | 0.0538243 | 1.0722304 | 0.3622345 |
| 0.0000000 | 0.0000000 | 0.2581064 | 0.0648982 | 0.2624449 | 0.3666438 |

Table 16: cat-2-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|-----------|------------------|-----------|------------------|
| 2.419468 | 2.271585 | 3.0376944 | 1.2854136 | 2.4576324 | 0.1298660 |
| 0.000000 | 0.000000 | 0.5485878 | 0.2819082 | 0.4326550 | 0.1626354 |
| 1.154539 | 2.698032 | 0.4646134 | 3.9490138 | 1.1831423 | 0.9354951 |
| 0.000000 | 0.000000 | 0.2102208 | 0.9285393 | 0.3262500 | 0.2752220 |
| 1.020003 | 1.312834 | 1.0350381 | 0.2530629 | 1.0065813 | 0.2144515 |
| 0.000000 | 0.000000 | 0.2848867 | 0.1596577 | 0.2784719 | 0.1572541 |

2.3.2 Histgram of 100 iterations



2.4 Remove 11 subset data

2.4.1 Averaged estimation

Table 17: null-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|-------------|------------------|-----------|------------------|
| 2.7276371 | 7.708914 | 4.4996190 | 0.4411341 | 5.8478080 | 0.3475610 |
| 0.0000000 | 0.000000 | 0.6803805 | 0.0948647 | 0.7255906 | 0.0896674 |
| 0.6782210 | 42.661785 | -12.8748992 | 7.1828950 | 6.7056205 | 6.4783280 |
| 0.0000000 | 0.000000 | 0.9794912 | 0.3166469 | 1.1283617 | 0.2888135 |
| 0.2546506 | 6.389698 | 0.7262481 | 0.3570885 | 1.4882557 | 0.4238215 |
| 0.0000000 | 0.000000 | 0.3645878 | 0.0613997 | 0.3866327 | 0.0865650 |

Table 18: rank-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|-----------|------------------|-----------|------------------|
| 2.7824456 | 4.265218 | 3.2448657 | 5.7896516 | 3.3443064 | 0.3522793 |
| 0.0000000 | 0.000000 | 0.4651041 | 0.8349188 | 0.4655195 | 0.3027861 |
| 0.5280393 | 7.799071 | 0.1915601 | 12.8500545 | 1.0191591 | 0.8875884 |
| 0.0000000 | 0.000000 | 0.1012524 | 1.3903298 | 0.3209896 | 0.2369106 |
| 0.2060431 | 2.062459 | 0.0258525 | 2.1557215 | 0.3198292 | 0.3661274 |
| 0.0000000 | 0.000000 | 0.0471755 | 0.4058309 | 0.2069629 | 0.1993032 |

Table 19: quantile-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|------------|------------------|-----------|------------------|
| 2.7681842 | 4.328651 | 3.4609212 | 3.1788078 | 3.7258411 | 0.3012130 |
| 0.0000000 | 0.000000 | 0.4966609 | 0.4563100 | 0.4782636 | 0.2437290 |
| 0.5720811 | 8.861475 | -0.0018297 | 7.9277357 | 1.7294550 | 1.0911548 |
| 0.0000000 | 0.000000 | 0.0888270 | 0.7577563 | 0.3681743 | 0.3112944 |
| 0.2102370 | 2.610060 | -0.0241759 | 1.7490392 | 0.5688029 | 0.3255822 |
| 0.0000000 | 0.000000 | 0.0369378 | 0.3481334 | 0.2419591 | 0.1781135 |

Table 20: log-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|------------|------------------|-----------|------------------|
| 2.8015527 | 4.236281 | 3.0436241 | 3.1225664 | 2.9212645 | -0.0994888 |
| 0.0000000 | 0.000000 | 0.4760496 | 0.4733557 | 0.4227479 | 0.1129165 |
| 0.6880008 | 9.662155 | -0.2681637 | 10.3492981 | 1.2794970 | 0.6664158 |
| 0.0000000 | 0.000000 | 0.1165141 | 0.9915211 | 0.3792009 | 0.2268278 |
| 0.2162960 | 2.792241 | 0.0495233 | 2.1310087 | 0.8529974 | 0.1647751 |
| 0.0000000 | 0.000000 | 0.0943554 | 0.4004703 | 0.3055376 | 0.1289602 |

Table 21: sqrt-full

| $true_main$ | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|--------------|------------------|------------|------------------|-----------|------------------|
| 2.7496796 | 4.991774 | 3.0698755 | 1.5439183 | 3.6669050 | 0.7706162 |
| 0.0000000 | 0.000000 | 0.5303200 | 0.2727694 | 0.5097033 | 0.2278629 |
| 0.5875359 | 16.125727 | -3.4030933 | 7.2550194 | 3.5858543 | 3.8049015 |
| 0.0000000 | 0.000000 | 0.4246016 | 0.5041032 | 0.6744699 | 0.4693367 |
| 0.2177059 | 4.100766 | 0.1425676 | 1.0639445 | 1.0052705 | 0.4198141 |
| 0.0000000 | 0.000000 | 0.2658448 | 0.1919450 | 0.2954893 | 0.1160203 |

Table 22: cat-10-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|-----------|------------------|-----------|------------------|
| 2.7746561 | 4.240363 | 3.2331377 | 6.0088024 | 3.1935942 | 1.3455091 |
| 0.0000000 | 0.000000 | 0.4643888 | 0.8805231 | 0.4701595 | 0.4992688 |
| 0.5420920 | 7.563943 | 0.2166931 | 13.1758133 | 0.8792574 | 2.4572655 |
| 0.0000000 | 0.000000 | 0.1080425 | 1.4595610 | 0.3151668 | 0.4405500 |
| 0.2080076 | 2.064543 | 0.0303424 | 2.2531848 | 0.2375642 | 0.9637317 |
| 0.0000000 | 0.000000 | 0.0489175 | 0.4187737 | 0.1802348 | 0.3818249 |

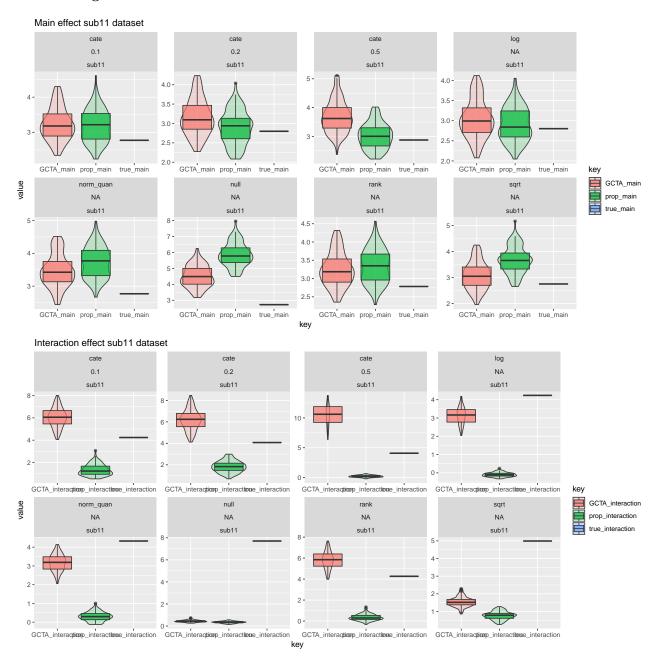
Table 23: cat-5-full

| ${ m true_main}$ | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-------------------|------------------|-----------|------------------|-----------|------------------|
| 2.7983825 | 4.074101 | 3.1560364 | 6.1755836 | 2.8901981 | 1.8244826 |
| 0.0000000 | 0.000000 | 0.4657834 | 0.9608235 | 0.4291065 | 0.5208825 |
| 0.5726266 | 7.321955 | 0.2078162 | 14.0873765 | 0.6228696 | 3.5184265 |
| 0.0000000 | 0.000000 | 0.1087906 | 1.6044594 | 0.2741144 | 0.5669474 |
| 0.2206165 | 2.011403 | 0.0396105 | 2.3074825 | 0.2352814 | 1.3355904 |
| 0.0000000 | 0.000000 | 0.0539100 | 0.4253049 | 0.1751183 | 0.4619231 |

Table 24: cat-2-full

| true_main | true_interaction | GCTA_main | GCTA_interaction | prop_main | prop_interaction |
|-----------|------------------|-----------|------------------|-----------|------------------|
| 2.8738907 | 4.081361 | 3.6856333 | 10.4923095 | 3.0103562 | 0.2178511 |
| 0.0000000 | 0.000000 | 0.5611821 | 1.7717503 | 0.4416661 | 0.1725719 |
| 0.7660228 | 6.637190 | 0.2339092 | 19.1607206 | 0.7280669 | 0.7893286 |
| 0.0000000 | 0.000000 | 0.1074537 | 2.4910043 | 0.2514666 | 0.1600060 |
| 0.2473301 | 1.650984 | 0.0654467 | 2.1605270 | 0.1597307 | 0.6293876 |
| 0.0000000 | 0.000000 | 0.0702851 | 0.6144138 | 0.1620340 | 0.2556775 |

2.4.2 Histgram of 100 iterations



3 Conclusion

4 Further work