**Supplementary Material**

**Table S1.** Predictive performance of ML models using NIR spectral data from first trimester serum samples (Full, 10500-4000 cm-1).

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Model number** | **Dataset** | **Detail** | **Pretreatment** | **Width** | **Sp (Av)** | **Sp (StD)** | **Se (Av)** | **Se (StD)** | **NER (Av)** | **NER (StD)** |
| 1 | NIR1T | Full | MC |  | 0.6185 | 0.0459 | 0.3253 | 0.1091 | 0.4719 | 0.0592 |
| 2 |  |  | N+MC |  | 0.6490 | 0.0445 | 0.4347 | 0.0886 | 0.5418 | 0.0496 |
| 3 |  |  | WLS+MC |  | 0.7143 | 0.0372 | 0.3013 | 0.0906 | 0.5078 | 0.0490 |
| 4 |  |  | WLS+N+MC |  | 0.6970 | 0.0314 | 0.3093 | 0.0891 | 0.5032 | 0.0472 |
| 5 |  |  | SNV + MC |  | 0.6749 | 0.0396 | 0.3493 | 0.0948 | 0.5121 | 0.0514 |
| 6 |  |  | SNV + WLS + MC |  | 0.7000 | 0.0433 | 0.1627 | 0.0810 | 0.4313 | 0.0459 |
| 7 |  |  | SNV + N + MC |  | 0.6803 | 0.0448 | 0.3333 | 0.0808 | 0.5068 | 0.0462 |
| 8 |  |  | SNV + WLS + N + MC |  | 0.6970 | 0.0314 | 0.3093 | 0.0891 | 0.5032 | 0.0472 |
| 9 |  |  | 1D + MC | 3 | 0.8212 | 0.0262 | 0.0827 | 0.0370 | 0.4519 | 0.0227 |
| 10 |  |  |  | 7 | 0.8140 | 0.0222 | 0.1080 | 0.0444 | 0.4610 | 0.0248 |
| 11 |  |  |  | 11 | 0.8006 | 0.0326 | 0.1213 | 0.0440 | 0.4610 | 0.0274 |
| 12 |  |  |  | 15 | 0.7266 | 0.0317 | 0.1760 | 0.0657 | 0.4513 | 0.0364 |
| 13 |  |  |  | 19 | 0.7036 | 0.0471 | 0.1787 | 0.0767 | 0.4411 | 0.0450 |
| 14 |  |  |  | 23 | 0.6519 | 0.0528 | 0.2133 | 0.0738 | 0.4326 | 0.0454 |
| 15 |  |  | 1D + N + MC | 3 | 0.8239 | 0.0268 | 0.0720 | 0.0183 | 0.4479 | 0.0162 |
| 16 |  |  |  | 7 | 0.8236 | 0.0287 | 0.1120 | 0.0475 | 0.4678 | 0.0278 |
| 17 |  |  |  | 11 | 0.7824 | 0.0333 | 0.1027 | 0.0430 | 0.4425 | 0.0272 |
| 18 |  |  |  | 15 | 0.7481 | 0.0310 | 0.1640 | 0.0649 | 0.4560 | 0.0360 |
| 19 |  |  |  | 19 | 0.7296 | 0.0404 | 0.1680 | 0.0777 | 0.4488 | 0.0438 |
| 20 |  |  |  | 23 | 0.6782 | 0.0529 | 0.1960 | 0.0743 | 0.4371 | 0.0456 |
| 21 |  |  | 2D + MC | 3 | 0.7854 | 0.0263 | 0.1147 | 0.0405 | 0.4500 | 0.0241 |
| 22 |  |  |  | 7 | 0.7821 | 0.0252 | 0.0400 | 0.0426 | 0.4110 | 0.0248 |
| 23 |  |  |  | 11 | 0.8027 | 0.0277 | 0.1000 | 0.0431 | 0.4513 | 0.0256 |
| 24 |  |  |  | 15 | 0.8131 | 0.0294 | 0.1440 | 0.0492 | 0.4786 | 0.0287 |
| 25 |  |  |  | 19 | 0.7463 | 0.0321 | 0.1347 | 0.0436 | 0.4405 | 0.0271 |
| 26 |  |  |  | 23 | 0.7579 | 0.0291 | 0.1213 | 0.0613 | 0.4396 | 0.0339 |
| 27 |  |  | 2D + N + MC | 3 | 0.7860 | 0.0296 | 0.1040 | 0.0385 | 0.4450 | 0.0243 |
| 28 |  |  |  | 7 | 0.7737 | 0.0352 | 0.0333 | 0.0387 | 0.4035 | 0.0262 |
| 29 |  |  |  | 11 | 0.8227 | 0.0290 | 0.1160 | 0.0568 | 0.4693 | 0.0319 |
| 30 |  |  |  | 15 | 0.8224 | 0.0194 | 0.1560 | 0.0439 | 0.4892 | 0.0240 |
| 31 |  |  |  | 19 | 0.7484 | 0.0302 | 0.1293 | 0.0283 | 0.4388 | 0.0207 |
| 32 |  |  |  | 23 | 0.7582 | 0.0316 | 0.1307 | 0.0485 | 0.4444 | 0.0289 |
| 33 |  |  | SM + MC | 3 | 0.6158 | 0.0449 | 0.3267 | 0.0964 | 0.4712 | 0.0532 |
| 34 |  |  |  | 7 | 0.6143 | 0.0430 | 0.3400 | 0.0992 | 0.4772 | 0.0541 |
| 35 |  |  |  | 11 | 0.6131 | 0.0462 | 0.3360 | 0.1017 | 0.4746 | 0.0558 |
| 36 |  |  |  | 15 | 0.6322 | 0.0448 | 0.2880 | 0.1154 | 0.4601 | 0.0619 |
| 37 |  |  |  | 19 | 0.6278 | 0.0454 | 0.2960 | 0.0925 | 0.4619 | 0.0515 |
| 38 |  |  |  | 23 | 0.6239 | 0.0522 | 0.3000 | 0.0955 | 0.4619 | 0.0544 |
| 39 |  |  | SM + SNV + MC | 3 | 0.6934 | 0.0454 | 0.3453 | 0.0669 | 0.5194 | 0.0404 |
| 40 |  |  |  | 7 | 0.6946 | 0.0503 | 0.3187 | 0.0789 | 0.5066 | 0.0468 |
| 41 |  |  |  | 11 | 0.6964 | 0.0404 | 0.3320 | 0.0731 | 0.5142 | 0.0418 |
| 42 |  |  |  | 15 | 0.7179 | 0.0477 | 0.3373 | 0.0692 | 0.5276 | 0.0420 |
| 43 |  |  |  | 19 | 0.7197 | 0.0504 | 0.3480 | 0.0811 | 0.5339 | 0.0478 |
| 44 |  |  |  | 23 | 0.7072 | 0.0529 | 0.3387 | 0.0784 | 0.5229 | 0.0473 |
| 45 |  |  | SM + SNV + WLS + MC | 3 | 0.7012 | 0.0554 | 0.1667 | 0.0635 | 0.4339 | 0.0421 |
| 46 |  |  |  | 7 | 0.7322 | 0.0435 | 0.2000 | 0.0700 | 0.4661 | 0.0412 |
| 47 |  |  |  | 11 | 0.7439 | 0.0485 | 0.1947 | 0.0806 | 0.4693 | 0.0470 |
| 48 |  |  |  | 15 | 0.7528 | 0.0411 | 0.2453 | 0.0824 | 0.4991 | 0.0461 |
| 49 |  |  |  | 19 | 0.7540 | 0.0409 | 0.2373 | 0.0605 | 0.4957 | 0.0365 |
| 50 |  |  |  | 23 | 0.7645 | 0.0421 | 0.2227 | 0.0733 | 0.4936 | 0.0423 |
| 51 |  |  | SM + SNV + N + MC | 3 | 0.6815 | 0.0458 | 0.3307 | 0.0785 | 0.5061 | 0.0454 |
| 52 |  |  |  | 7 | 0.7060 | 0.0551 | 0.3387 | 0.0748 | 0.5223 | 0.0465 |
| 53 |  |  |  | 11 | 0.7051 | 0.0524 | 0.3293 | 0.0779 | 0.5172 | 0.0469 |
| 54 |  |  |  | 15 | 0.7030 | 0.0461 | 0.3480 | 0.0865 | 0.5255 | 0.0490 |
| 55 |  |  |  | 19 | 0.7101 | 0.0507 | 0.3520 | 0.0700 | 0.5311 | 0.0432 |
| 56 |  |  |  | 23 | 0.7248 | 0.0468 | 0.3400 | 0.0777 | 0.5324 | 0.0453 |
| 57 |  |  | SM + SNV + WLS + N + MC | 3 | 0.6934 | 0.0386 | 0.2973 | 0.0906 | 0.4954 | 0.0492 |
| 58 |  |  |  | 7 | 0.6958 | 0.0382 | 0.3027 | 0.1001 | 0.4992 | 0.0536 |
| 59 |  |  |  | 11 | 0.6964 | 0.0385 | 0.2853 | 0.0884 | 0.4909 | 0.0482 |
| 60 |  |  |  | 15 | 0.7099 | 0.0422 | 0.2573 | 0.0863 | 0.4836 | 0.0480 |
| 61 |  |  |  | 19 | 0.7152 | 0.0420 | 0.2600 | 0.0945 | 0.4876 | 0.0517 |
| 62 |  |  |  | 23 | 0.7119 | 0.0416 | 0.2760 | 0.0863 | 0.4940 | 0.0479 |
| 63 |  |  | SM + WLS + MC | 3 | 0.7131 | 0.0391 | 0.3200 | 0.0774 | 0.5166 | 0.0433 |
| 64 |  |  |  | 7 | 0.7200 | 0.0347 | 0.2947 | 0.0904 | 0.5073 | 0.0484 |
| 65 |  |  |  | 11 | 0.7164 | 0.0378 | 0.2853 | 0.0894 | 0.5009 | 0.0485 |
| 66 |  |  |  | 15 | 0.7182 | 0.0433 | 0.2533 | 0.0893 | 0.4858 | 0.0497 |
| 67 |  |  |  | 19 | 0.7322 | 0.0491 | 0.2493 | 0.0979 | 0.4908 | 0.0548 |
| 68 |  |  |  | 23 | 0.7278 | 0.0445 | 0.2573 | 0.0785 | 0.4925 | 0.0451 |
| 69 |  |  | SM + WLS + N + MC | 3 | 0.6976 | 0.0408 | 0.3227 | 0.1038 | 0.5101 | 0.0557 |
| 70 |  |  |  | 7 | 0.6875 | 0.0439 | 0.3093 | 0.0997 | 0.4984 | 0.0545 |
| 71 |  |  |  | 11 | 0.6967 | 0.0343 | 0.3160 | 0.0795 | 0.5064 | 0.0433 |
| 72 |  |  |  | 15 | 0.7122 | 0.0421 | 0.2680 | 0.0791 | 0.4901 | 0.0448 |
| 73 |  |  |  | 19 | 0.7158 | 0.0432 | 0.2733 | 0.0875 | 0.4946 | 0.0488 |
| 74 |  |  |  | 23 | 0.7045 | 0.0412 | 0.2773 | 0.0705 | 0.4909 | 0.0408 |
| 75 |  |  | SM + N + MC | 3 | 0.6451 | 0.0408 | 0.4440 | 0.0826 | 0.5445 | 0.0461 |
| 76 |  |  |  | 7 | 0.6681 | 0.0488 | 0.4333 | 0.0875 | 0.5507 | 0.0501 |
| 77 |  |  |  | 11 | 0.6824 | 0.0443 | 0.4427 | 0.0747 | 0.5625 | 0.0434 |
| 78 |  |  |  | 15 | 0.6687 | 0.0559 | 0.4347 | 0.0765 | 0.5517 | 0.0474 |
| 79 |  |  |  | 19 | 0.6955 | 0.0461 | 0.4440 | 0.0733 | 0.5698 | 0.0433 |
| 80 |  |  |  | 23 | 0.6946 | 0.0456 | 0.4507 | 0.0681 | 0.5726 | 0.0410 |

*NIR: near-infrared; 1T: first trimester; Sp: specificity; Se: sensitivity; NER: non-error rate; Av: average; StD: standard deviation; MC: mean centering; N: normalization; WLS: weighted least squares; SNV: standard normal variate; 1D: first derivative; 2D: second derivative; SM: smoothing.*

**Table S2.** Predictive performance of ML models using NIR spectral data from first trimester serum samples (range 1, 10500-7600 cm-1).

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Model number** | **Dataset** | **Detail** | **Pretreatment** | **Width** | **Sp (Av)** | **Sp (StD)** | **Se (Av)** | **Se (StD)** | **NER (Av)** | **NER (StD)** |
| 1 | NIR1T | R1 | MC |  | 0.6245 | 0.0328 | 0.4320 | 0.1010 | 0.5282 | 0.0531 |
| 2 |  |  | N+MC |  | 0.6722 | 0.0361 | 0.5920 | 0.0910 | 0.6321 | 0.0489 |
| 3 |  |  | WLS+MC |  | 0.7373 | 0.0549 | 0.1480 | 0.0753 | 0.4427 | 0.0466 |
| 4 |  |  | WLS+N+MC |  | 0.7499 | 0.0395 | 0.3067 | 0.0883 | 0.5283 | 0.0484 |
| 5 |  |  | SNV + MC |  | 0.6800 | 0.0406 | 0.4133 | 0.0738 | 0.5467 | 0.0421 |
| 6 |  |  | SNV + WLS + MC |  | 0.7579 | 0.0458 | 0.1320 | 0.0768 | 0.4450 | 0.0447 |
| 7 |  |  | SNV + N + MC |  | 0.6764 | 0.0346 | 0.4120 | 0.0793 | 0.5442 | 0.0433 |
| 8 |  |  | SNV + WLS + N + MC |  | 0.7433 | 0.0325 | 0.3840 | 0.0732 | 0.5636 | 0.0401 |
| 9 |  |  | 1D + MC | 3 | 0.8146 | 0.0272 | 0.0987 | 0.0387 | 0.4566 | 0.0236 |
| 10 |  |  |  | 7 | 0.8239 | 0.0289 | 0.1147 | 0.0382 | 0.4693 | 0.0240 |
| 11 |  |  |  | 11 | 0.7857 | 0.0306 | 0.1240 | 0.0426 | 0.4548 | 0.0262 |
| 12 |  |  |  | 15 | 0.7203 | 0.0274 | 0.1987 | 0.0579 | 0.4595 | 0.0320 |
| 13 |  |  |  | 19 | 0.7110 | 0.0437 | 0.2120 | 0.0816 | 0.4615 | 0.0463 |
| 14 |  |  |  | 23 | 0.6555 | 0.0543 | 0.2227 | 0.0837 | 0.4391 | 0.0499 |
| 15 |  |  | 1D + N + MC | 3 | 0.8358 | 0.0273 | 0.0907 | 0.0399 | 0.4632 | 0.0242 |
| 16 |  |  |  | 7 | 0.8352 | 0.0226 | 0.1160 | 0.0400 | 0.4756 | 0.0230 |
| 17 |  |  |  | 11 | 0.7839 | 0.0282 | 0.1267 | 0.0387 | 0.4553 | 0.0239 |
| 18 |  |  |  | 15 | 0.7439 | 0.0355 | 0.2093 | 0.0646 | 0.4766 | 0.0369 |
| 19 |  |  |  | 19 | 0.7269 | 0.0372 | 0.2067 | 0.0765 | 0.4668 | 0.0425 |
| 20 |  |  |  | 23 | 0.6493 | 0.0518 | 0.2253 | 0.0736 | 0.4373 | 0.0450 |
| 21 |  |  | 2D + MC | 3 | 0.7985 | 0.0214 | 0.1173 | 0.0394 | 0.4579 | 0.0224 |
| 22 |  |  |  | 7 | 0.7761 | 0.0305 | 0.0653 | 0.0369 | 0.4207 | 0.0239 |
| 23 |  |  |  | 11 | 0.8030 | 0.0250 | 0.1120 | 0.0546 | 0.4575 | 0.0300 |
| 24 |  |  |  | 15 | 0.8158 | 0.0274 | 0.1520 | 0.0357 | 0.4839 | 0.0225 |
| 25 |  |  |  | 19 | 0.7403 | 0.0362 | 0.1427 | 0.0426 | 0.4415 | 0.0280 |
| 26 |  |  |  | 23 | 0.7612 | 0.0342 | 0.1600 | 0.0602 | 0.4606 | 0.0346 |
| 27 |  |  | 2D + N + MC | 3 | 0.7872 | 0.0252 | 0.1000 | 0.0387 | 0.4436 | 0.0231 |
| 28 |  |  |  | 7 | 0.7872 | 0.0300 | 0.0453 | 0.0367 | 0.4162 | 0.0237 |
| 29 |  |  |  | 11 | 0.8257 | 0.0236 | 0.1120 | 0.0475 | 0.4688 | 0.0265 |
| 30 |  |  |  | 15 | 0.8278 | 0.0270 | 0.1600 | 0.0467 | 0.4939 | 0.0270 |
| 31 |  |  |  | 19 | 0.7460 | 0.0299 | 0.1333 | 0.0269 | 0.4397 | 0.0201 |
| 32 |  |  |  | 23 | 0.7627 | 0.0306 | 0.1387 | 0.0536 | 0.4507 | 0.0309 |
| 33 |  |  | SM + MC | 3 | 0.6260 | 0.0423 | 0.3933 | 0.0936 | 0.5097 | 0.0513 |
| 34 |  |  |  | 7 | 0.6164 | 0.0384 | 0.4147 | 0.1153 | 0.5155 | 0.0608 |
| 35 |  |  |  | 11 | 0.6301 | 0.0381 | 0.3920 | 0.1132 | 0.5111 | 0.0597 |
| 36 |  |  |  | 15 | 0.6251 | 0.0314 | 0.4067 | 0.0983 | 0.5159 | 0.0516 |
| 37 |  |  |  | 19 | 0.6257 | 0.0326 | 0.4213 | 0.1047 | 0.5235 | 0.0548 |
| 38 |  |  |  | 23 | 0.6218 | 0.0395 | 0.3747 | 0.1142 | 0.4982 | 0.0604 |
| 39 |  |  | SM + SNV + MC | 3 | 0.6943 | 0.0343 | 0.4253 | 0.0736 | 0.5598 | 0.0406 |
| 40 |  |  |  | 7 | 0.6851 | 0.0356 | 0.4253 | 0.0818 | 0.5552 | 0.0446 |
| 41 |  |  |  | 11 | 0.6797 | 0.0388 | 0.4027 | 0.0785 | 0.5412 | 0.0438 |
| 42 |  |  |  | 15 | 0.6946 | 0.0507 | 0.3653 | 0.0822 | 0.5300 | 0.0483 |
| 43 |  |  |  | 19 | 0.7000 | 0.0495 | 0.3613 | 0.0842 | 0.5307 | 0.0488 |
| 44 |  |  |  | 23 | 0.7099 | 0.0460 | 0.3453 | 0.0920 | 0.5276 | 0.0515 |
| 45 |  |  | SM + SNV + WLS + MC | 3 | 0.7522 | 0.0577 | 0.1347 | 0.0966 | 0.4435 | 0.0563 |
| 46 |  |  |  | 7 | 0.7609 | 0.0442 | 0.1640 | 0.0788 | 0.4624 | 0.0452 |
| 47 |  |  |  | 11 | 0.7779 | 0.0403 | 0.1627 | 0.0740 | 0.4703 | 0.0421 |
| 48 |  |  |  | 15 | 0.7872 | 0.0405 | 0.1760 | 0.0722 | 0.4816 | 0.0414 |
| 49 |  |  |  | 19 | 0.7961 | 0.0426 | 0.1893 | 0.0651 | 0.4927 | 0.0389 |
| 50 |  |  |  | 23 | 0.7878 | 0.0382 | 0.2147 | 0.0811 | 0.5012 | 0.0448 |
| 51 |  |  | SM + SNV + N + MC | 3 | 0.6872 | 0.0395 | 0.4173 | 0.0891 | 0.5522 | 0.0488 |
| 52 |  |  |  | 7 | 0.6839 | 0.0399 | 0.4160 | 0.0814 | 0.5499 | 0.0453 |
| 53 |  |  |  | 11 | 0.6890 | 0.0423 | 0.3987 | 0.0731 | 0.5438 | 0.0422 |
| 54 |  |  |  | 15 | 0.7045 | 0.0426 | 0.3507 | 0.0912 | 0.5276 | 0.0503 |
| 55 |  |  |  | 19 | 0.7152 | 0.0474 | 0.3427 | 0.0713 | 0.5289 | 0.0428 |
| 56 |  |  |  | 23 | 0.7087 | 0.0542 | 0.3693 | 0.0764 | 0.5390 | 0.0469 |
| 57 |  |  | SM + SNV + WLS + N + MC | 3 | 0.7543 | 0.0371 | 0.3613 | 0.0751 | 0.5578 | 0.0419 |
| 58 |  |  |  | 7 | 0.7469 | 0.0344 | 0.3453 | 0.0870 | 0.5461 | 0.0468 |
| 59 |  |  |  | 11 | 0.7597 | 0.0405 | 0.3520 | 0.1008 | 0.5559 | 0.0543 |
| 60 |  |  |  | 15 | 0.7481 | 0.0402 | 0.3253 | 0.0968 | 0.5367 | 0.0524 |
| 61 |  |  |  | 19 | 0.7522 | 0.0445 | 0.2800 | 0.0873 | 0.5161 | 0.0490 |
| 62 |  |  |  | 23 | 0.7549 | 0.0385 | 0.2507 | 0.0889 | 0.5028 | 0.0484 |
| 63 |  |  | SM + WLS + MC | 3 | 0.7475 | 0.0633 | 0.1320 | 0.0731 | 0.4397 | 0.0484 |
| 64 |  |  |  | 7 | 0.7349 | 0.0725 | 0.1360 | 0.0785 | 0.4355 | 0.0534 |
| 65 |  |  |  | 11 | 0.7699 | 0.0533 | 0.1347 | 0.0731 | 0.4523 | 0.0452 |
| 66 |  |  |  | 15 | 0.7678 | 0.0579 | 0.1613 | 0.0809 | 0.4645 | 0.0497 |
| 67 |  |  |  | 19 | 0.8000 | 0.0431 | 0.1867 | 0.0725 | 0.4933 | 0.0422 |
| 68 |  |  |  | 23 | 0.7979 | 0.0505 | 0.1747 | 0.0818 | 0.4863 | 0.0481 |
| 69 |  |  | SM + WLS + N + MC | 3 | 0.7522 | 0.0295 | 0.3653 | 0.0606 | 0.5588 | 0.0337 |
| 70 |  |  |  | 7 | 0.7433 | 0.0361 | 0.3453 | 0.0920 | 0.5443 | 0.0494 |
| 71 |  |  |  | 11 | 0.7501 | 0.0374 | 0.3387 | 0.0902 | 0.5444 | 0.0488 |
| 72 |  |  |  | 15 | 0.7561 | 0.0361 | 0.3093 | 0.0911 | 0.5327 | 0.0490 |
| 73 |  |  |  | 19 | 0.7499 | 0.0410 | 0.2840 | 0.0941 | 0.5169 | 0.0513 |
| 74 |  |  |  | 23 | 0.7460 | 0.0414 | 0.2813 | 0.0822 | 0.5137 | 0.0460 |
| 75 |  |  | SM + N + MC | 3 | 0.6752 | 0.0341 | 0.5653 | 0.1176 | 0.6203 | 0.0612 |
| 76 |  |  |  | 7 | 0.6663 | 0.0382 | 0.5840 | 0.1048 | 0.6251 | 0.0558 |
| 77 |  |  |  | 11 | 0.6746 | 0.0415 | 0.5293 | 0.0937 | 0.6020 | 0.0512 |
| 78 |  |  |  | 15 | 0.6761 | 0.0375 | 0.5480 | 0.1019 | 0.6121 | 0.0543 |
| 79 |  |  |  | 19 | 0.6842 | 0.0431 | 0.5040 | 0.0935 | 0.5941 | 0.0515 |
| 80 |  |  |  | 23 | 0.6988 | 0.0455 | 0.4987 | 0.0854 | 0.5987 | 0.0484 |

*NIR: near-infrared; 1T: first trimester; R1: range 1; Sp: specificity; Se: sensitivity; NER: non-error rate; Av: average; StD: standard deviation; MC: mean centering; N: normalization; WLS: weighted least squares; SNV: standard normal variate; 1D: first derivative; 2D: second derivative; SM: smoothing.*

**Table S3.** Predictive performance of ML models using NIR spectral data from first trimester serum samples (range 2, 7600-5100 cm-1).

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Model number** | **Dataset** | **Detail** | **Pretreatment** | **Width** | **Sp (Av)** | **Sp (StD)** | **Se (Av)** | **Se (StD)** | **NER (Av)** | **NER (StD)** |
| 1 | NIR1T | R2 | MC |  | 0.6063 | 0.0364 | 0.5240 | 0.0819 | 0.5651 | 0.0448 |
| 2 |  |  | N+MC |  | 0.5725 | 0.0312 | 0.6120 | 0.1083 | 0.5923 | 0.0564 |
| 3 |  |  | WLS+MC |  | 0.6872 | 0.0402 | 0.3213 | 0.0770 | 0.5042 | 0.0434 |
| 4 |  |  | WLS+N+MC |  | 0.6675 | 0.0638 | 0.1493 | 0.0780 | 0.4084 | 0.0504 |
| 5 |  |  | SNV + MC |  | 0.7313 | 0.0280 | 0.4187 | 0.0674 | 0.5750 | 0.0365 |
| 6 |  |  | SNV + WLS + MC |  | 0.6812 | 0.0424 | 0.3213 | 0.0880 | 0.5013 | 0.0488 |
| 7 |  |  | SNV + N + MC |  | 0.7293 | 0.0353 | 0.4293 | 0.0752 | 0.5793 | 0.0415 |
| 8 |  |  | SNV + WLS + N + MC |  | 0.7015 | 0.0439 | 0.3320 | 0.0994 | 0.5167 | 0.0543 |
| 9 |  |  | 1D + MC | 3 | 0.6027 | 0.0403 | 0.2800 | 0.1387 | 0.4413 | 0.0722 |
| 10 |  |  |  | 7 | 0.7069 | 0.0507 | 0.0920 | 0.0630 | 0.3994 | 0.0404 |
| 11 |  |  |  | 11 | 0.6666 | 0.0479 | 0.1227 | 0.0651 | 0.3946 | 0.0404 |
| 12 |  |  |  | 15 | 0.6791 | 0.0377 | 0.1680 | 0.0765 | 0.4236 | 0.0426 |
| 13 |  |  |  | 19 | 0.6776 | 0.0429 | 0.1800 | 0.0716 | 0.4288 | 0.0417 |
| 14 |  |  |  | 23 | 0.6812 | 0.0435 | 0.1893 | 0.0801 | 0.4353 | 0.0456 |
| 15 |  |  | 1D + N + MC | 3 | 0.6188 | 0.0354 | 0.3573 | 0.1304 | 0.4881 | 0.0676 |
| 16 |  |  |  | 7 | 0.6107 | 0.0650 | 0.1893 | 0.0917 | 0.4000 | 0.0562 |
| 17 |  |  |  | 11 | 0.6460 | 0.0566 | 0.1387 | 0.0748 | 0.3923 | 0.0469 |
| 18 |  |  |  | 15 | 0.6430 | 0.0613 | 0.1413 | 0.0682 | 0.3922 | 0.0458 |
| 19 |  |  |  | 19 | 0.6301 | 0.0456 | 0.1480 | 0.0822 | 0.3891 | 0.0470 |
| 20 |  |  |  | 23 | 0.6460 | 0.0612 | 0.1853 | 0.0592 | 0.4157 | 0.0426 |
| 21 |  |  | 2D + MC | 3 | 0.5331 | 0.0186 | 0.6507 | 0.0825 | 0.5919 | 0.0423 |
| 22 |  |  |  | 7 | 0.6767 | 0.0597 | 0.1573 | 0.0911 | 0.4170 | 0.0545 |
| 23 |  |  |  | 11 | 0.7185 | 0.0650 | 0.1093 | 0.0599 | 0.4139 | 0.0442 |
| 24 |  |  |  | 15 | 0.5722 | 0.0758 | 0.1013 | 0.0833 | 0.3368 | 0.0563 |
| 25 |  |  |  | 19 | 0.6272 | 0.0664 | 0.0693 | 0.0659 | 0.3482 | 0.0468 |
| 26 |  |  |  | 23 | 0.6463 | 0.0615 | 0.1093 | 0.0817 | 0.3778 | 0.0511 |
| 27 |  |  | 2D + N + MC | 3 | 0.7433 | 0.0394 | 0.1840 | 0.1074 | 0.4636 | 0.0572 |
| 28 |  |  |  | 7 | 0.7006 | 0.0649 | 0.1107 | 0.0654 | 0.4056 | 0.0461 |
| 29 |  |  |  | 11 | 0.6797 | 0.0552 | 0.1427 | 0.0797 | 0.4112 | 0.0485 |
| 30 |  |  |  | 15 | 0.6209 | 0.0346 | 0.3027 | 0.0982 | 0.4618 | 0.0521 |
| 31 |  |  |  | 19 | 0.6391 | 0.0434 | 0.2147 | 0.0974 | 0.4269 | 0.0533 |
| 32 |  |  |  | 23 | 0.6200 | 0.0659 | 0.0893 | 0.0837 | 0.3547 | 0.0533 |
| 33 |  |  | SM + MC | 3 | 0.6242 | 0.0317 | 0.5253 | 0.0746 | 0.5748 | 0.0405 |
| 34 |  |  |  | 7 | 0.6134 | 0.0268 | 0.5267 | 0.0854 | 0.5700 | 0.0448 |
| 35 |  |  |  | 11 | 0.6236 | 0.0277 | 0.5040 | 0.0832 | 0.5638 | 0.0438 |
| 36 |  |  |  | 15 | 0.6209 | 0.0426 | 0.5333 | 0.0913 | 0.5771 | 0.0504 |
| 37 |  |  |  | 19 | 0.6191 | 0.0361 | 0.5347 | 0.0878 | 0.5769 | 0.0475 |
| 38 |  |  |  | 23 | 0.6146 | 0.0310 | 0.5267 | 0.0800 | 0.5706 | 0.0429 |
| 39 |  |  | SM + SNV + MC | 3 | 0.7218 | 0.0306 | 0.4293 | 0.0689 | 0.5756 | 0.0377 |
| 40 |  |  |  | 7 | 0.7352 | 0.0327 | 0.4480 | 0.0603 | 0.5916 | 0.0343 |
| 41 |  |  |  | 11 | 0.7296 | 0.0279 | 0.4440 | 0.0640 | 0.5868 | 0.0349 |
| 42 |  |  |  | 15 | 0.7158 | 0.0374 | 0.4293 | 0.0787 | 0.5726 | 0.0436 |
| 43 |  |  |  | 19 | 0.7352 | 0.0283 | 0.4493 | 0.0657 | 0.5923 | 0.0358 |
| 44 |  |  |  | 23 | 0.7263 | 0.0339 | 0.4533 | 0.0673 | 0.5898 | 0.0377 |
| 45 |  |  | SM + SNV + WLS + MC | 3 | 0.6818 | 0.0384 | 0.3440 | 0.0730 | 0.5129 | 0.0412 |
| 46 |  |  |  | 7 | 0.6731 | 0.0461 | 0.2853 | 0.0831 | 0.4792 | 0.0475 |
| 47 |  |  |  | 11 | 0.6779 | 0.0485 | 0.3080 | 0.0872 | 0.4930 | 0.0499 |
| 48 |  |  |  | 15 | 0.6848 | 0.0447 | 0.2880 | 0.0947 | 0.4864 | 0.0524 |
| 49 |  |  |  | 19 | 0.6854 | 0.0460 | 0.3067 | 0.0893 | 0.4960 | 0.0502 |
| 50 |  |  |  | 23 | 0.6851 | 0.0488 | 0.2720 | 0.0658 | 0.4785 | 0.0410 |
| 51 |  |  | SM + SNV + N + MC | 3 | 0.7310 | 0.0323 | 0.4213 | 0.0743 | 0.5762 | 0.0405 |
| 52 |  |  |  | 7 | 0.7310 | 0.0325 | 0.4360 | 0.0663 | 0.5835 | 0.0369 |
| 53 |  |  |  | 11 | 0.7301 | 0.0313 | 0.4413 | 0.0570 | 0.5857 | 0.0325 |
| 54 |  |  |  | 15 | 0.7197 | 0.0277 | 0.4440 | 0.0781 | 0.5819 | 0.0414 |
| 55 |  |  |  | 19 | 0.7230 | 0.0384 | 0.4373 | 0.0648 | 0.5802 | 0.0377 |
| 56 |  |  |  | 23 | 0.7191 | 0.0337 | 0.4360 | 0.0728 | 0.5776 | 0.0401 |
| 57 |  |  | SM + SNV + WLS + N + MC | 3 | 0.6937 | 0.0420 | 0.3160 | 0.0931 | 0.5049 | 0.0511 |
| 58 |  |  |  | 7 | 0.6958 | 0.0395 | 0.3373 | 0.0947 | 0.5166 | 0.0513 |
| 59 |  |  |  | 11 | 0.6943 | 0.0410 | 0.3133 | 0.0777 | 0.5038 | 0.0439 |
| 60 |  |  |  | 15 | 0.6949 | 0.0424 | 0.3467 | 0.0883 | 0.5208 | 0.0490 |
| 61 |  |  |  | 19 | 0.6922 | 0.0387 | 0.3427 | 0.0883 | 0.5175 | 0.0482 |
| 62 |  |  |  | 23 | 0.6890 | 0.0310 | 0.3827 | 0.0969 | 0.5358 | 0.0509 |
| 63 |  |  | SM + WLS + MC | 3 | 0.6967 | 0.0331 | 0.3347 | 0.0836 | 0.5157 | 0.0449 |
| 64 |  |  |  | 7 | 0.6815 | 0.0383 | 0.3373 | 0.0730 | 0.5094 | 0.0412 |
| 65 |  |  |  | 11 | 0.6878 | 0.0436 | 0.3053 | 0.0884 | 0.4965 | 0.0493 |
| 66 |  |  |  | 15 | 0.6985 | 0.0402 | 0.3187 | 0.0906 | 0.5086 | 0.0496 |
| 67 |  |  |  | 19 | 0.6910 | 0.0473 | 0.3160 | 0.0902 | 0.5035 | 0.0509 |
| 68 |  |  |  | 23 | 0.6928 | 0.0400 | 0.3347 | 0.0857 | 0.5138 | 0.0473 |
| 69 |  |  | SM + WLS + N + MC | 3 | 0.7015 | 0.0399 | 0.3373 | 0.0743 | 0.5194 | 0.0422 |
| 70 |  |  |  | 7 | 0.7012 | 0.0375 | 0.3227 | 0.0927 | 0.5119 | 0.0500 |
| 71 |  |  |  | 11 | 0.6982 | 0.0495 | 0.3147 | 0.0797 | 0.5064 | 0.0469 |
| 72 |  |  |  | 15 | 0.6991 | 0.0361 | 0.3373 | 0.0743 | 0.5182 | 0.0413 |
| 73 |  |  |  | 19 | 0.6940 | 0.0348 | 0.3387 | 0.0784 | 0.5163 | 0.0429 |
| 74 |  |  |  | 23 | 0.6913 | 0.0412 | 0.3627 | 0.1079 | 0.5270 | 0.0577 |
| 75 |  |  | SM + N + MC | 3 | 0.5678 | 0.0322 | 0.6480 | 0.1035 | 0.6079 | 0.0542 |
| 76 |  |  |  | 7 | 0.5621 | 0.0406 | 0.6213 | 0.0985 | 0.5917 | 0.0533 |
| 77 |  |  |  | 11 | 0.5675 | 0.0269 | 0.6320 | 0.1028 | 0.5997 | 0.0531 |
| 78 |  |  |  | 15 | 0.5612 | 0.0273 | 0.6333 | 0.1071 | 0.5973 | 0.0553 |
| 79 |  |  |  | 19 | 0.5728 | 0.0330 | 0.6293 | 0.0991 | 0.6011 | 0.0522 |
| 80 |  |  |  | 23 | 0.5633 | 0.0322 | 0.6373 | 0.1045 | 0.6003 | 0.0547 |

*NIR: near-infrared; 1T: first trimester; R2: range 2; Sp: specificity; Se: sensitivity; NER: non-error rate; Av: average; StD: standard deviation; MC: mean centering; N: normalization; WLS: weighted least squares; SNV: standard normal variate; 1D: first derivative; 2D: second derivative; SM: smoothing.*

**Table S4.** Predictive performance of ML models using NIR spectral data from first trimester serum samples (range 3, 5100-4000 cm-1).

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Model number** | **Dataset** | **Detail** | **Pretreatment** | **Width** | **Sp (Av)** | **Sp (StD)** | **Se (Av)** | **Se (StD)** | **NER (Av)** | **NER (StD)** |
| 1 | NIR1T | R3 | MC |  | 0.5961 | 0.0295 | 0.4907 | 0.0870 | 0.5434 | 0.0459 |
| 2 |  |  | N+MC |  | 0.6167 | 0.0565 | 0.1387 | 0.0671 | 0.3777 | 0.0439 |
| 3 |  |  | WLS+MC |  | 0.6051 | 0.0452 | 0.1627 | 0.0727 | 0.3839 | 0.0428 |
| 4 |  |  | WLS+N+MC |  | 0.6606 | 0.0307 | 0.2733 | 0.0896 | 0.4670 | 0.0474 |
| 5 |  |  | SNV + MC |  | 0.6278 | 0.0351 | 0.1400 | 0.0844 | 0.3839 | 0.0457 |
| 6 |  |  | SNV + WLS + MC |  | 0.6140 | 0.0417 | 0.1200 | 0.0883 | 0.3670 | 0.0488 |
| 7 |  |  | SNV + N + MC |  | 0.6260 | 0.0407 | 0.1307 | 0.0749 | 0.3783 | 0.0426 |
| 8 |  |  | SNV + WLS + N + MC |  | 0.6081 | 0.0519 | 0.1787 | 0.0888 | 0.3934 | 0.0514 |
| 9 |  |  | 1D + MC | 3 | 0.7137 | 0.0375 | 0.1147 | 0.0539 | 0.4142 | 0.0328 |
| 10 |  |  |  | 7 | 0.6394 | 0.0467 | 0.1333 | 0.0797 | 0.3864 | 0.0462 |
| 11 |  |  |  | 11 | 0.6340 | 0.0407 | 0.1200 | 0.0660 | 0.3770 | 0.0388 |
| 12 |  |  |  | 15 | 0.6185 | 0.0348 | 0.1240 | 0.0841 | 0.3713 | 0.0455 |
| 13 |  |  |  | 19 | 0.6310 | 0.0374 | 0.1520 | 0.0884 | 0.3915 | 0.0480 |
| 14 |  |  |  | 23 | 0.6391 | 0.0401 | 0.1893 | 0.0717 | 0.4142 | 0.0411 |
| 15 |  |  | 1D + N + MC | 3 | 0.7188 | 0.0339 | 0.1333 | 0.0673 | 0.4261 | 0.0377 |
| 16 |  |  |  | 7 | 0.6588 | 0.0363 | 0.1400 | 0.0777 | 0.3994 | 0.0429 |
| 17 |  |  |  | 11 | 0.6439 | 0.0334 | 0.1333 | 0.0785 | 0.3886 | 0.0427 |
| 18 |  |  |  | 15 | 0.6484 | 0.0413 | 0.1093 | 0.0931 | 0.3788 | 0.0509 |
| 19 |  |  |  | 19 | 0.6472 | 0.0386 | 0.1747 | 0.0807 | 0.4109 | 0.0447 |
| 20 |  |  |  | 23 | 0.6337 | 0.0434 | 0.1573 | 0.0828 | 0.3955 | 0.0467 |
| 21 |  |  | 2D + MC | 3 | 0.7493 | 0.0261 | 0.0533 | 0.0426 | 0.4013 | 0.0250 |
| 22 |  |  |  | 7 | 0.7388 | 0.0309 | 0.1240 | 0.0660 | 0.4314 | 0.0364 |
| 23 |  |  |  | 11 | 0.7445 | 0.0321 | 0.1440 | 0.0412 | 0.4442 | 0.0261 |
| 24 |  |  |  | 15 | 0.7272 | 0.0353 | 0.1947 | 0.0585 | 0.4609 | 0.0341 |
| 25 |  |  |  | 19 | 0.6734 | 0.0320 | 0.1600 | 0.0750 | 0.4167 | 0.0408 |
| 26 |  |  |  | 23 | 0.6672 | 0.0451 | 0.1947 | 0.0658 | 0.4309 | 0.0399 |
| 27 |  |  | 2D + N + MC | 3 | 0.7591 | 0.0292 | 0.0467 | 0.0431 | 0.4029 | 0.0260 |
| 28 |  |  |  | 7 | 0.7436 | 0.0264 | 0.1040 | 0.0489 | 0.4238 | 0.0278 |
| 29 |  |  |  | 11 | 0.7385 | 0.0251 | 0.1453 | 0.0480 | 0.4419 | 0.0271 |
| 30 |  |  |  | 15 | 0.7104 | 0.0350 | 0.1853 | 0.0729 | 0.4479 | 0.0404 |
| 31 |  |  |  | 19 | 0.6857 | 0.0320 | 0.2187 | 0.0762 | 0.4522 | 0.0413 |
| 32 |  |  |  | 23 | 0.6743 | 0.0399 | 0.1947 | 0.0772 | 0.4345 | 0.0434 |
| 33 |  |  | SM + MC | 3 | 0.6018 | 0.0331 | 0.4987 | 0.0677 | 0.5502 | 0.0377 |
| 34 |  |  |  | 7 | 0.5878 | 0.0340 | 0.4813 | 0.0886 | 0.5345 | 0.0475 |
| 35 |  |  |  | 11 | 0.5791 | 0.0411 | 0.4773 | 0.1105 | 0.5282 | 0.0590 |
| 36 |  |  |  | 15 | 0.5866 | 0.0357 | 0.5147 | 0.0809 | 0.5506 | 0.0442 |
| 37 |  |  |  | 19 | 0.5955 | 0.0358 | 0.4973 | 0.0788 | 0.5464 | 0.0433 |
| 38 |  |  |  | 23 | 0.5931 | 0.0346 | 0.5133 | 0.0811 | 0.5532 | 0.0441 |
| 39 |  |  | SM + SNV + MC | 3 | 0.6242 | 0.0356 | 0.1573 | 0.0697 | 0.3908 | 0.0391 |
| 40 |  |  |  | 7 | 0.6272 | 0.0362 | 0.1600 | 0.0797 | 0.3936 | 0.0438 |
| 41 |  |  |  | 11 | 0.6272 | 0.0317 | 0.1173 | 0.0720 | 0.3722 | 0.0393 |
| 42 |  |  |  | 15 | 0.6254 | 0.0377 | 0.1413 | 0.0826 | 0.3834 | 0.0454 |
| 43 |  |  |  | 19 | 0.6230 | 0.0395 | 0.1347 | 0.0802 | 0.3788 | 0.0447 |
| 44 |  |  |  | 23 | 0.6251 | 0.0451 | 0.1467 | 0.0841 | 0.3859 | 0.0477 |
| 45 |  |  | SM + SNV + WLS + MC | 3 | 0.6233 | 0.0356 | 0.1627 | 0.0854 | 0.3930 | 0.0462 |
| 46 |  |  |  | 7 | 0.6173 | 0.0441 | 0.1467 | 0.0713 | 0.3820 | 0.0419 |
| 47 |  |  |  | 11 | 0.6084 | 0.0445 | 0.1627 | 0.0821 | 0.3855 | 0.0467 |
| 48 |  |  |  | 15 | 0.6242 | 0.0399 | 0.1387 | 0.0671 | 0.3814 | 0.0390 |
| 49 |  |  |  | 19 | 0.6266 | 0.0437 | 0.1693 | 0.0885 | 0.3980 | 0.0494 |
| 50 |  |  |  | 23 | 0.6128 | 0.0456 | 0.1893 | 0.0834 | 0.4011 | 0.0475 |
| 51 |  |  | SM + SNV + N + MC | 3 | 0.6322 | 0.0388 | 0.1573 | 0.0722 | 0.3948 | 0.0410 |
| 52 |  |  |  | 7 | 0.6101 | 0.0462 | 0.1360 | 0.0712 | 0.3731 | 0.0424 |
| 53 |  |  |  | 11 | 0.6310 | 0.0371 | 0.1427 | 0.0738 | 0.3869 | 0.0413 |
| 54 |  |  |  | 15 | 0.6072 | 0.0410 | 0.1427 | 0.0725 | 0.3749 | 0.0417 |
| 55 |  |  |  | 19 | 0.6221 | 0.0447 | 0.1587 | 0.0761 | 0.3904 | 0.0441 |
| 56 |  |  |  | 23 | 0.6119 | 0.0407 | 0.1440 | 0.0665 | 0.3780 | 0.0390 |
| 57 |  |  | SM + SNV + WLS + N + MC | 3 | 0.6173 | 0.0453 | 0.1760 | 0.0828 | 0.3967 | 0.0472 |
| 58 |  |  |  | 7 | 0.6152 | 0.0487 | 0.1853 | 0.0916 | 0.4003 | 0.0519 |
| 59 |  |  |  | 11 | 0.6051 | 0.0386 | 0.1800 | 0.0677 | 0.3925 | 0.0390 |
| 60 |  |  |  | 15 | 0.6063 | 0.0422 | 0.2093 | 0.0852 | 0.4078 | 0.0475 |
| 61 |  |  |  | 19 | 0.6203 | 0.0401 | 0.1827 | 0.0735 | 0.4015 | 0.0419 |
| 62 |  |  |  | 23 | 0.6164 | 0.0442 | 0.1813 | 0.0884 | 0.3989 | 0.0494 |
| 63 |  |  | SM + WLS + MC | 3 | 0.5848 | 0.0552 | 0.1493 | 0.0640 | 0.3671 | 0.0422 |
| 64 |  |  |  | 7 | 0.5958 | 0.0569 | 0.1653 | 0.0788 | 0.3806 | 0.0486 |
| 65 |  |  |  | 11 | 0.6036 | 0.0414 | 0.1867 | 0.0738 | 0.3951 | 0.0423 |
| 66 |  |  |  | 15 | 0.6039 | 0.0447 | 0.1880 | 0.0849 | 0.3959 | 0.0480 |
| 67 |  |  |  | 19 | 0.6131 | 0.0360 | 0.1933 | 0.0777 | 0.4032 | 0.0428 |
| 68 |  |  |  | 23 | 0.5961 | 0.0405 | 0.2000 | 0.0913 | 0.3981 | 0.0500 |
| 69 |  |  | SM + WLS + N + MC | 3 | 0.6191 | 0.0383 | 0.1600 | 0.0862 | 0.3896 | 0.0472 |
| 70 |  |  |  | 7 | 0.6176 | 0.0444 | 0.1853 | 0.0833 | 0.4015 | 0.0472 |
| 71 |  |  |  | 11 | 0.6075 | 0.0436 | 0.1973 | 0.0737 | 0.4024 | 0.0428 |
| 72 |  |  |  | 15 | 0.6167 | 0.0476 | 0.1920 | 0.0890 | 0.4044 | 0.0505 |
| 73 |  |  |  | 19 | 0.6182 | 0.0357 | 0.1880 | 0.0900 | 0.4031 | 0.0484 |
| 74 |  |  |  | 23 | 0.6221 | 0.0301 | 0.2013 | 0.0928 | 0.4117 | 0.0488 |
| 75 |  |  | SM + N + MC | 3 | 0.6179 | 0.0464 | 0.1493 | 0.0757 | 0.3836 | 0.0444 |
| 76 |  |  |  | 7 | 0.6152 | 0.0482 | 0.1560 | 0.0733 | 0.3856 | 0.0439 |
| 77 |  |  |  | 11 | 0.6134 | 0.0657 | 0.1760 | 0.0860 | 0.3947 | 0.0541 |
| 78 |  |  |  | 15 | 0.6093 | 0.0540 | 0.1733 | 0.0830 | 0.3913 | 0.0495 |
| 79 |  |  |  | 19 | 0.6245 | 0.0436 | 0.1440 | 0.0897 | 0.3842 | 0.0499 |
| 80 |  |  |  | 23 | 0.6078 | 0.0417 | 0.1947 | 0.0970 | 0.4012 | 0.0528 |

*NIR: near-infrared; 1T: first trimester; R3: range 3; Sp: specificity; Se: sensitivity; NER: non-error rate; Av: average; StD: standard deviation; MC: mean centering; N: normalization; WLS: weighted least squares; SNV: standard normal variate; 1D: first derivative; 2D: second derivative; SM: smoothing.*

**Table S5.** Predictive performance of ML models combining NIR spectral data of first trimester sera with medical parameters.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **NIR 1T range a** | **Plus** | **Block order b** | **Sp (Av)** | **Sp (StD)** | **Se (Av)** | **Se (StD)** | **NER (Av)** | **NER (StD)** |
| Full |  |  | 0.6946 | 0.0456 | 0.4507 | 0.0681 | 0.5726 | 0.0410 |
| Full | Medical | 1-2 | 0.7355 | 0.0479 | 0.3147 | 0.0863 | 0.5251 | 0.0493 |
|  |  | 2-1 | 0.7773 | 0.0432 | 0.3360 | 0.0883 | 0.5567 | 0.0491 |
| Full simp c | Medical simp c | 1-2 | 0.7525 | 0.0564 | 0.4227 | 0.1171 | 0.5876 | 0.0650 |
|  |  | 2-1 | 0.7728 | 0.0702 | 0.4453 | 0.0947 | 0.6091 | 0.0589 |
| R1 |  |  | 0.6722 | 0.0361 | 0.5920 | 0.0910 | 0.6321 | 0.0489 |
| R1 | Medical | 1-2 | 0.7048 | 0.0425 | 0.3827 | 0.1059 | 0.5437 | 0.0570 |
|  |  | 2-1 | 0.7227 | 0.0483 | 0.3827 | 0.0931 | 0.5527 | 0.0525 |
| R1 simp c | Medical simp c | 1-2 | 0.7328 | 0.0682 | 0.5027 | 0.1251 | 0.6178 | 0.0712 |
|  |  | 2-1 | 0.7513 | 0.0560 | 0.5013 | 0.1080 | 0.6263 d | 0.0608 d |

a Full: 10500-4000 cm-1; R1: 10500-7600 cm-1.

b NIR blocks were pretreated using the conditions identified as best in single-block analysis. Medical blocks were pretreated by autoscaling.

c Data obtained after variable selection, using the variable importance information from the original equivalent multi-block model.

d Best multi-block model. The NIR block consists of 41% of the original R1 variables (591 wavenumbers out of 1450). The medical block consists of 5 variables, history of GDM in a prior pregnancy, family history of DM, BMI, family history of hyperthyroidism and first period age. Its DCV-AUROC is 0.5219 ± 0.0922.

*NIR: near-infrared; 1T: first trimester; R1: range 1; Sp: specificity; Se: sensitivity; NER: non-error rate; Av: average; StD: standard deviation.*

**Table S6.** Predictive performance of ML models using NIR spectral data from second trimester serum samples (Full, 10500-4000 cm-1).

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Model number** | **Dataset** | **Detail** | **Pretreatment** | **Width** | **Sp (Av)** | **Sp (StD)** | **Se (Av)** | **Se (StD)** | **NER (Av)** | **NER (StD)** |
| 1 | NIR2T | Full | MC |  | 0.6528 | 0.1013 | 0.0425 | 0.0598 | 0.3477 | 0.0588 |
| 2 |  |  | N+MC |  | 0.6590 | 0.0645 | 0.0475 | 0.0709 | 0.3532 | 0.0480 |
| 3 |  |  | WLS+MC |  | 0.5769 | 0.0498 | 0.1625 | 0.1018 | 0.3697 | 0.0567 |
| 4 |  |  | WLS+N+MC |  | 0.5210 | 0.0927 | 0.1000 | 0.1211 | 0.3105 | 0.0763 |
| 5 |  |  | SNV + MC |  | 0.5738 | 0.0538 | 0.2150 | 0.1337 | 0.3944 | 0.0721 |
| 6 |  |  | SNV + WLS + MC |  | 0.5067 | 0.0868 | 0.0775 | 0.1007 | 0.2921 | 0.0665 |
| 7 |  |  | SNV + N + MC |  | 0.5728 | 0.0557 | 0.1900 | 0.1191 | 0.3814 | 0.0657 |
| 8 |  |  | SNV + WLS + N + MC |  | 0.5210 | 0.0776 | 0.0600 | 0.0808 | 0.2905 | 0.0560 |
| 9 |  |  | 1D + MC | 3 | 0.7908 | 0.0317 | 0.0000 | 0.0000 | 0.3954 | 0.0158 |
| 10 |  |  |  | 7 | 0.7436 | 0.0377 | 0.0400 | 0.0589 | 0.3918 | 0.0350 |
| 11 |  |  |  | 11 | 0.7651 | 0.0312 | 0.0525 | 0.0623 | 0.4088 | 0.0349 |
| 12 |  |  |  | 15 | 0.7615 | 0.0329 | 0.0600 | 0.0631 | 0.4108 | 0.0356 |
| 13 |  |  |  | 19 | 0.7815 | 0.0360 | 0.0675 | 0.0629 | 0.4245 | 0.0362 |
| 14 |  |  |  | 23 | 0.8149 | 0.0389 | 0.0800 | 0.0606 | 0.4474 | 0.0360 |
| 15 |  |  | 1D + N + MC | 3 | 0.7974 | 0.0285 | 0.0000 | 0.0000 | 0.3987 | 0.0142 |
| 16 |  |  |  | 7 | 0.7728 | 0.0284 | 0.0725 | 0.0623 | 0.4227 | 0.0342 |
| 17 |  |  |  | 11 | 0.7733 | 0.0333 | 0.0900 | 0.0567 | 0.4317 | 0.0329 |
| 18 |  |  |  | 15 | 0.7708 | 0.0368 | 0.0525 | 0.0623 | 0.4116 | 0.0362 |
| 19 |  |  |  | 19 | 0.7559 | 0.0388 | 0.0100 | 0.0343 | 0.3829 | 0.0259 |
| 20 |  |  |  | 23 | 0.7826 | 0.0422 | 0.0450 | 0.0606 | 0.4138 | 0.0369 |
| 21 |  |  | 2D + MC | 3 | 0.8677 | 0.0321 | 0.0050 | 0.0247 | 0.4363 | 0.0203 |
| 22 |  |  |  | 7 | 0.7487 | 0.0284 | 0.0000 | 0.0000 | 0.3744 | 0.0142 |
| 23 |  |  |  | 11 | 0.7267 | 0.0330 | 0.0000 | 0.0000 | 0.3633 | 0.0165 |
| 24 |  |  |  | 15 | 0.8036 | 0.0386 | 0.0700 | 0.0676 | 0.4368 | 0.0389 |
| 25 |  |  |  | 19 | 0.7836 | 0.0328 | 0.0750 | 0.0619 | 0.4293 | 0.0350 |
| 26 |  |  |  | 23 | 0.7687 | 0.0338 | 0.0425 | 0.0598 | 0.4056 | 0.0343 |
| 27 |  |  | 2D + N + MC | 3 | 0.8815 | 0.0219 | 0.0000 | 0.0000 | 0.4408 | 0.0110 |
| 28 |  |  |  | 7 | 0.7559 | 0.0333 | 0.0000 | 0.0000 | 0.3779 | 0.0166 |
| 29 |  |  |  | 11 | 0.7333 | 0.0332 | 0.0000 | 0.0000 | 0.3667 | 0.0166 |
| 30 |  |  |  | 15 | 0.8133 | 0.0324 | 0.1150 | 0.0556 | 0.4642 | 0.0321 |
| 31 |  |  |  | 19 | 0.7887 | 0.0361 | 0.0800 | 0.0606 | 0.4344 | 0.0353 |
| 32 |  |  |  | 23 | 0.7600 | 0.0376 | 0.0325 | 0.0554 | 0.3963 | 0.0335 |
| 33 |  |  | SM + MC | 3 | 0.6390 | 0.0766 | 0.0425 | 0.0649 | 0.3407 | 0.0502 |
| 34 |  |  |  | 7 | 0.6415 | 0.0831 | 0.0325 | 0.0554 | 0.3370 | 0.0499 |
| 35 |  |  |  | 11 | 0.6641 | 0.0694 | 0.0300 | 0.0595 | 0.3471 | 0.0457 |
| 36 |  |  |  | 15 | 0.6708 | 0.0642 | 0.0450 | 0.0657 | 0.3579 | 0.0459 |
| 37 |  |  |  | 19 | 0.6846 | 0.0798 | 0.0650 | 0.0808 | 0.3748 | 0.0568 |
| 38 |  |  |  | 23 | 0.6764 | 0.0667 | 0.0550 | 0.0805 | 0.3657 | 0.0523 |
| 39 |  |  | SM + SNV + MC | 3 | 0.5718 | 0.0668 | 0.2100 | 0.1055 | 0.3909 | 0.0624 |
| 40 |  |  |  | 7 | 0.5718 | 0.0467 | 0.1825 | 0.1190 | 0.3771 | 0.0639 |
| 41 |  |  |  | 11 | 0.5872 | 0.0554 | 0.1475 | 0.1000 | 0.3673 | 0.0572 |
| 42 |  |  |  | 15 | 0.6000 | 0.0515 | 0.1250 | 0.1101 | 0.3625 | 0.0608 |
| 43 |  |  |  | 19 | 0.6190 | 0.0720 | 0.1100 | 0.1175 | 0.3645 | 0.0689 |
| 44 |  |  |  | 23 | 0.6123 | 0.0694 | 0.1500 | 0.1237 | 0.3812 | 0.0709 |
| 45 |  |  | SM + SNV + WLS + MC | 3 | 0.5015 | 0.0905 | 0.0700 | 0.0881 | 0.2858 | 0.0631 |
| 46 |  |  |  | 7 | 0.4903 | 0.0926 | 0.0825 | 0.0897 | 0.2864 | 0.0645 |
| 47 |  |  |  | 11 | 0.5374 | 0.0804 | 0.0525 | 0.0841 | 0.2950 | 0.0582 |
| 48 |  |  |  | 15 | 0.5246 | 0.0762 | 0.0675 | 0.0918 | 0.2961 | 0.0596 |
| 49 |  |  |  | 19 | 0.5472 | 0.0812 | 0.0550 | 0.0721 | 0.3011 | 0.0543 |
| 50 |  |  |  | 23 | 0.5308 | 0.0887 | 0.0425 | 0.0598 | 0.2866 | 0.0535 |
| 51 |  |  | SM + SNV + N + MC | 3 | 0.5728 | 0.0557 | 0.1900 | 0.1191 | 0.3814 | 0.0657 |
| 52 |  |  |  | 7 | 0.5713 | 0.0486 | 0.1725 | 0.1208 | 0.3719 | 0.0651 |
| 53 |  |  |  | 11 | 0.5821 | 0.0513 | 0.1450 | 0.1140 | 0.3635 | 0.0625 |
| 54 |  |  |  | 15 | 0.6103 | 0.0695 | 0.1300 | 0.1100 | 0.3701 | 0.0650 |
| 55 |  |  |  | 19 | 0.6164 | 0.0604 | 0.1100 | 0.1119 | 0.3632 | 0.0636 |
| 56 |  |  |  | 23 | 0.6318 | 0.0706 | 0.0950 | 0.0781 | 0.3634 | 0.0526 |
| 57 |  |  | SM + SNV + WLS + N + MC | 3 | 0.4995 | 0.0848 | 0.0800 | 0.1003 | 0.2897 | 0.0657 |
| 58 |  |  |  | 7 | 0.5149 | 0.0766 | 0.0750 | 0.0875 | 0.2949 | 0.0581 |
| 59 |  |  |  | 11 | 0.5410 | 0.1073 | 0.0550 | 0.0844 | 0.2980 | 0.0683 |
| 60 |  |  |  | 15 | 0.5072 | 0.0953 | 0.0725 | 0.0841 | 0.2898 | 0.0635 |
| 61 |  |  |  | 19 | 0.5200 | 0.0770 | 0.0675 | 0.0766 | 0.2938 | 0.0543 |
| 62 |  |  |  | 23 | 0.5267 | 0.0875 | 0.0850 | 0.0960 | 0.3058 | 0.0649 |
| 63 |  |  | SM + WLS + MC | 3 | 0.5846 | 0.0647 | 0.1500 | 0.1071 | 0.3673 | 0.0626 |
| 64 |  |  |  | 7 | 0.5687 | 0.0673 | 0.1575 | 0.0938 | 0.3631 | 0.0577 |
| 65 |  |  |  | 11 | 0.5959 | 0.0537 | 0.1750 | 0.1101 | 0.3854 | 0.0612 |
| 66 |  |  |  | 15 | 0.5692 | 0.0667 | 0.1550 | 0.0996 | 0.3621 | 0.0600 |
| 67 |  |  |  | 19 | 0.5759 | 0.0616 | 0.1400 | 0.0933 | 0.3579 | 0.0559 |
| 68 |  |  |  | 23 | 0.5769 | 0.0458 | 0.1450 | 0.0923 | 0.3610 | 0.0515 |
| 69 |  |  | SM + WLS + N + MC | 3 | 0.5087 | 0.0820 | 0.1025 | 0.0968 | 0.3056 | 0.0634 |
| 70 |  |  |  | 7 | 0.5267 | 0.1044 | 0.0925 | 0.0972 | 0.3096 | 0.0713 |
| 71 |  |  |  | 11 | 0.5359 | 0.1001 | 0.0650 | 0.0919 | 0.3004 | 0.0679 |
| 72 |  |  |  | 15 | 0.5159 | 0.0860 | 0.0775 | 0.0833 | 0.2967 | 0.0599 |
| 73 |  |  |  | 19 | 0.5344 | 0.0810 | 0.0850 | 0.0926 | 0.3097 | 0.0615 |
| 74 |  |  |  | 23 | 0.5190 | 0.0978 | 0.0775 | 0.0974 | 0.2982 | 0.0690 |
| 75 |  |  | SM + N + MC | 3 | 0.6508 | 0.0729 | 0.0925 | 0.1066 | 0.3716 | 0.0646 |
| 76 |  |  |  | 7 | 0.6605 | 0.0808 | 0.0800 | 0.0866 | 0.3703 | 0.0592 |
| 77 |  |  |  | 11 | 0.6764 | 0.0752 | 0.0750 | 0.0911 | 0.3757 | 0.0591 |
| 78 |  |  |  | 15 | 0.6974 | 0.0705 | 0.0925 | 0.0904 | 0.3950 | 0.0573 |
| 79 |  |  |  | 19 | 0.7236 | 0.0744 | 0.1125 | 0.0809 | 0.4180 | 0.0549 |
| 80 |  |  |  | 23 | 0.7456 | 0.0655 | 0.1125 | 0.1079 | 0.4291 | 0.0631 |

*NIR: near-infrared; 2T: second trimester; Sp: specificity; Se: sensitivity; NER: non-error rate; Av: average; StD: standard deviation; MC: mean centering; N: normalization; WLS: weighted least squares; SNV: standard normal variate; 1D: first derivative; 2D: second derivative; SM: smoothing.*

**Table S7.** Predictive performance of ML models using NIR spectral data from second trimester serum samples (range 1, 10500-7600 cm-1).

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Model number** | **Dataset** | **Detail** | **Pretreatment** | **Width** | **Sp (Av)** | **Sp (StD)** | **Se (Av)** | **Se (StD)** | **NER (Av)** | **NER (StD)** |
| 1 | NIR2T | R1 | MC |  | 0.6682 | 0.0916 | 0.0325 | 0.0609 | 0.3504 | 0.0550 |
| 2 |  |  | N+MC |  | 0.6267 | 0.0714 | 0.0250 | 0.0505 | 0.3258 | 0.0437 |
| 3 |  |  | WLS+MC |  | 0.7918 | 0.0451 | 0.0200 | 0.0527 | 0.4059 | 0.0347 |
| 4 |  |  | WLS+N+MC |  | 0.8754 | 0.0414 | 0.1625 | 0.1218 | 0.5189 | 0.0643 |
| 5 |  |  | SNV + MC |  | 0.6805 | 0.0965 | 0.0475 | 0.0663 | 0.3640 | 0.0585 |
| 6 |  |  | SNV + WLS + MC |  | 0.6021 | 0.0711 | 0.1350 | 0.1180 | 0.3685 | 0.0689 |
| 7 |  |  | SNV + N + MC |  | 0.6503 | 0.1085 | 0.0300 | 0.0539 | 0.3401 | 0.0606 |
| 8 |  |  | SNV + WLS + N + MC |  | 0.6862 | 0.0656 | 0.1000 | 0.1071 | 0.3931 | 0.0628 |
| 9 |  |  | 1D + MC | 3 | 0.7785 | 0.0365 | 0.0000 | 0.0000 | 0.3892 | 0.0183 |
| 10 |  |  |  | 7 | 0.7559 | 0.0360 | 0.0375 | 0.0631 | 0.3967 | 0.0363 |
| 11 |  |  |  | 11 | 0.7646 | 0.0376 | 0.0625 | 0.0631 | 0.4136 | 0.0367 |
| 12 |  |  |  | 15 | 0.7508 | 0.0324 | 0.0400 | 0.0589 | 0.3954 | 0.0336 |
| 13 |  |  |  | 19 | 0.7656 | 0.0284 | 0.0675 | 0.0629 | 0.4166 | 0.0345 |
| 14 |  |  |  | 23 | 0.7795 | 0.0449 | 0.0525 | 0.0623 | 0.4160 | 0.0384 |
| 15 |  |  | 1D + N + MC | 3 | 0.7928 | 0.0319 | 0.0000 | 0.0000 | 0.3964 | 0.0159 |
| 16 |  |  |  | 7 | 0.7703 | 0.0362 | 0.0650 | 0.0631 | 0.4176 | 0.0364 |
| 17 |  |  |  | 11 | 0.7749 | 0.0367 | 0.0900 | 0.0567 | 0.4324 | 0.0338 |
| 18 |  |  |  | 15 | 0.7533 | 0.0366 | 0.0425 | 0.0598 | 0.3979 | 0.0351 |
| 19 |  |  |  | 19 | 0.7354 | 0.0465 | 0.0100 | 0.0343 | 0.3727 | 0.0289 |
| 20 |  |  |  | 23 | 0.7492 | 0.0452 | 0.0300 | 0.0539 | 0.3896 | 0.0352 |
| 21 |  |  | 2D + MC | 3 | 0.8103 | 0.0351 | 0.0000 | 0.0000 | 0.4051 | 0.0176 |
| 22 |  |  |  | 7 | 0.7472 | 0.0302 | 0.0000 | 0.0000 | 0.3736 | 0.0151 |
| 23 |  |  |  | 11 | 0.7359 | 0.0371 | 0.0025 | 0.0177 | 0.3692 | 0.0205 |
| 24 |  |  |  | 15 | 0.8236 | 0.0372 | 0.0725 | 0.0672 | 0.4480 | 0.0384 |
| 25 |  |  |  | 19 | 0.7867 | 0.0295 | 0.0500 | 0.0619 | 0.4183 | 0.0343 |
| 26 |  |  |  | 23 | 0.7646 | 0.0365 | 0.0625 | 0.0631 | 0.4136 | 0.0365 |
| 27 |  |  | 2D + N + MC | 3 | 0.8492 | 0.0305 | 0.0000 | 0.0000 | 0.4246 | 0.0152 |
| 28 |  |  |  | 7 | 0.7533 | 0.0323 | 0.0000 | 0.0000 | 0.3767 | 0.0162 |
| 29 |  |  |  | 11 | 0.7400 | 0.0384 | 0.0125 | 0.0379 | 0.3763 | 0.0270 |
| 30 |  |  |  | 15 | 0.8154 | 0.0366 | 0.1125 | 0.0725 | 0.4639 | 0.0406 |
| 31 |  |  |  | 19 | 0.7867 | 0.0321 | 0.0625 | 0.0680 | 0.4246 | 0.0376 |
| 32 |  |  |  | 23 | 0.7621 | 0.0298 | 0.0350 | 0.0567 | 0.3985 | 0.0320 |
| 33 |  |  | SM + MC | 3 | 0.6795 | 0.0972 | 0.0150 | 0.0482 | 0.3472 | 0.0543 |
| 34 |  |  |  | 7 | 0.6821 | 0.0881 | 0.0325 | 0.0554 | 0.3573 | 0.0520 |
| 35 |  |  |  | 11 | 0.6872 | 0.0777 | 0.0225 | 0.0485 | 0.3548 | 0.0458 |
| 36 |  |  |  | 15 | 0.6349 | 0.0866 | 0.0225 | 0.0485 | 0.3287 | 0.0496 |
| 37 |  |  |  | 19 | 0.6395 | 0.0892 | 0.0225 | 0.0485 | 0.3310 | 0.0508 |
| 38 |  |  |  | 23 | 0.6046 | 0.0902 | 0.0150 | 0.0410 | 0.3098 | 0.0495 |
| 39 |  |  | SM + SNV + MC | 3 | 0.6744 | 0.1102 | 0.0425 | 0.0598 | 0.3584 | 0.0627 |
| 40 |  |  |  | 7 | 0.6600 | 0.1153 | 0.0325 | 0.0554 | 0.3463 | 0.0640 |
| 41 |  |  |  | 11 | 0.6400 | 0.0915 | 0.0300 | 0.0595 | 0.3350 | 0.0546 |
| 42 |  |  |  | 15 | 0.5985 | 0.1008 | 0.0450 | 0.0747 | 0.3217 | 0.0627 |
| 43 |  |  |  | 19 | 0.5487 | 0.1031 | 0.0325 | 0.0554 | 0.2906 | 0.0585 |
| 44 |  |  |  | 23 | 0.5385 | 0.1105 | 0.0150 | 0.0410 | 0.2767 | 0.0589 |
| 45 |  |  | SM + SNV + WLS + MC | 3 | 0.6021 | 0.0821 | 0.1250 | 0.0911 | 0.3635 | 0.0613 |
| 46 |  |  |  | 7 | 0.6087 | 0.0829 | 0.1150 | 0.1207 | 0.3619 | 0.0732 |
| 47 |  |  |  | 11 | 0.5687 | 0.0764 | 0.1300 | 0.1335 | 0.3494 | 0.0769 |
| 48 |  |  |  | 15 | 0.5877 | 0.0695 | 0.1775 | 0.1290 | 0.3826 | 0.0733 |
| 49 |  |  |  | 19 | 0.5836 | 0.0679 | 0.2075 | 0.1303 | 0.3955 | 0.0734 |
| 50 |  |  |  | 23 | 0.5877 | 0.0647 | 0.2000 | 0.1312 | 0.3938 | 0.0731 |
| 51 |  |  | SM + SNV + N + MC | 3 | 0.6810 | 0.1007 | 0.0400 | 0.0589 | 0.3605 | 0.0583 |
| 52 |  |  |  | 7 | 0.6595 | 0.1011 | 0.0325 | 0.0609 | 0.3460 | 0.0590 |
| 53 |  |  |  | 11 | 0.6436 | 0.1146 | 0.0450 | 0.0657 | 0.3443 | 0.0660 |
| 54 |  |  |  | 15 | 0.5938 | 0.1052 | 0.0400 | 0.0641 | 0.3169 | 0.0616 |
| 55 |  |  |  | 19 | 0.5595 | 0.1257 | 0.0325 | 0.0609 | 0.2960 | 0.0698 |
| 56 |  |  |  | 23 | 0.5195 | 0.1116 | 0.0225 | 0.0547 | 0.2710 | 0.0621 |
| 57 |  |  | SM + SNV + WLS + N + MC | 3 | 0.6764 | 0.0691 | 0.1050 | 0.1082 | 0.3907 | 0.0642 |
| 58 |  |  |  | 7 | 0.6646 | 0.0669 | 0.1125 | 0.1079 | 0.3886 | 0.0635 |
| 59 |  |  |  | 11 | 0.6513 | 0.0639 | 0.1550 | 0.1117 | 0.4031 | 0.0643 |
| 60 |  |  |  | 15 | 0.6169 | 0.0666 | 0.1400 | 0.1303 | 0.3785 | 0.0732 |
| 61 |  |  |  | 19 | 0.6262 | 0.0521 | 0.2000 | 0.1406 | 0.4131 | 0.0750 |
| 62 |  |  |  | 23 | 0.6118 | 0.0505 | 0.2725 | 0.1280 | 0.4421 | 0.0688 |
| 63 |  |  | SM + WLS + MC | 3 | 0.8000 | 0.0541 | 0.0225 | 0.0547 | 0.4113 | 0.0385 |
| 64 |  |  |  | 7 | 0.7841 | 0.0602 | 0.0250 | 0.0505 | 0.4046 | 0.0393 |
| 65 |  |  |  | 11 | 0.7785 | 0.0423 | 0.0275 | 0.0523 | 0.4030 | 0.0336 |
| 66 |  |  |  | 15 | 0.7477 | 0.0664 | 0.0275 | 0.0581 | 0.3876 | 0.0441 |
| 67 |  |  |  | 19 | 0.7010 | 0.0644 | 0.0250 | 0.0505 | 0.3630 | 0.0409 |
| 68 |  |  |  | 23 | 0.6472 | 0.0858 | 0.0325 | 0.0706 | 0.3398 | 0.0556 |
| 69 |  |  | SM + WLS + N + MC | 3 | 0.6969 | 0.0659 | 0.1050 | 0.1082 | 0.4010 | 0.0633 |
| 70 |  |  |  | 7 | 0.6723 | 0.0594 | 0.1000 | 0.1101 | 0.3862 | 0.0625 |
| 71 |  |  |  | 11 | 0.6349 | 0.0619 | 0.1450 | 0.1021 | 0.3899 | 0.0597 |
| 72 |  |  |  | 15 | 0.6328 | 0.0585 | 0.1475 | 0.0968 | 0.3902 | 0.0565 |
| 73 |  |  |  | 19 | 0.6087 | 0.0540 | 0.1925 | 0.1455 | 0.4006 | 0.0776 |
| 74 |  |  |  | 23 | 0.6067 | 0.0482 | 0.1875 | 0.1218 | 0.3971 | 0.0655 |
| 75 |  |  | SM + N + MC | 3 | 0.6123 | 0.0769 | 0.0250 | 0.0505 | 0.3187 | 0.0460 |
| 76 |  |  |  | 7 | 0.6092 | 0.0933 | 0.0200 | 0.0527 | 0.3146 | 0.0536 |
| 77 |  |  |  | 11 | 0.6133 | 0.0830 | 0.0450 | 0.0657 | 0.3292 | 0.0529 |
| 78 |  |  |  | 15 | 0.6108 | 0.0702 | 0.0125 | 0.0379 | 0.3116 | 0.0399 |
| 79 |  |  |  | 19 | 0.5800 | 0.0910 | 0.0250 | 0.0505 | 0.3025 | 0.0521 |
| 80 |  |  |  | 23 | 0.5708 | 0.0833 | 0.0250 | 0.0565 | 0.2979 | 0.0503 |

*NIR: near-infrared; 2T: second trimester; R1: range 1; Sp: specificity; Se: sensitivity; NER: non-error rate; Av: average; StD: standard deviation; MC: mean centering; N: normalization; WLS: weighted least squares; SNV: standard normal variate; 1D: first derivative; 2D: second derivative; SM: smoothing.*

**Table S8.** Predictive performance of ML models using NIR spectral data from second trimester serum samples (range 2, 7600-5100 cm-1).

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Model number** | **Dataset** | **Detail** | **Pretreatment** | **Width** | **Sp (Av)** | **Sp (StD)** | **Se (Av)** | **Se (StD)** | **NER (Av)** | **NER (StD)** |
| 1 | NIR2T | R2 | MC |  | 0.6692 | 0.0602 | 0.2550 | 0.1183 | 0.4621 | 0.0664 |
| 2 |  |  | N+MC |  | 0.5974 | 0.0758 | 0.2900 | 0.1503 | 0.4437 | 0.0842 |
| 3 |  |  | WLS+MC |  | 0.7605 | 0.0410 | 0.1325 | 0.1084 | 0.4465 | 0.0579 |
| 4 |  |  | WLS+N+MC |  | 0.8267 | 0.0426 | 0.2200 | 0.0930 | 0.5233 | 0.0511 |
| 5 |  |  | SNV + MC |  | 0.6200 | 0.0540 | 0.2825 | 0.1308 | 0.4513 | 0.0707 |
| 6 |  |  | SNV + WLS + MC |  | 0.6554 | 0.0600 | 0.1550 | 0.0930 | 0.4052 | 0.0553 |
| 7 |  |  | SNV + N + MC |  | 0.6241 | 0.0527 | 0.2750 | 0.1360 | 0.4496 | 0.0729 |
| 8 |  |  | SNV + WLS + N + MC |  | 0.7656 | 0.0577 | 0.1850 | 0.0919 | 0.4753 | 0.0542 |
| 9 |  |  | 1D + MC | 3 | 0.5190 | 0.0638 | 0.3175 | 0.1365 | 0.4182 | 0.0753 |
| 10 |  |  |  | 7 | 0.7477 | 0.0519 | 0.1525 | 0.1109 | 0.4501 | 0.0612 |
| 11 |  |  |  | 11 | 0.7985 | 0.0466 | 0.1550 | 0.1088 | 0.4767 | 0.0592 |
| 12 |  |  |  | 15 | 0.7615 | 0.0425 | 0.1650 | 0.1169 | 0.4633 | 0.0622 |
| 13 |  |  |  | 19 | 0.7574 | 0.0452 | 0.1875 | 0.1049 | 0.4725 | 0.0571 |
| 14 |  |  |  | 23 | 0.7626 | 0.0528 | 0.2200 | 0.1145 | 0.4913 | 0.0630 |
| 15 |  |  | 1D + N + MC | 3 | 0.6364 | 0.0592 | 0.1975 | 0.1132 | 0.4170 | 0.0639 |
| 16 |  |  |  | 7 | 0.7662 | 0.0386 | 0.1550 | 0.1028 | 0.4606 | 0.0549 |
| 17 |  |  |  | 11 | 0.7892 | 0.0431 | 0.2225 | 0.1080 | 0.5059 | 0.0581 |
| 18 |  |  |  | 15 | 0.7769 | 0.0352 | 0.2600 | 0.1125 | 0.5185 | 0.0589 |
| 19 |  |  |  | 19 | 0.7697 | 0.0438 | 0.2550 | 0.1128 | 0.5124 | 0.0605 |
| 20 |  |  |  | 23 | 0.7595 | 0.0543 | 0.2400 | 0.0869 | 0.4997 | 0.0512 |
| 21 |  |  | 2D + MC | 3 | 0.5159 | 0.0314 | 0.5400 | 0.1113 | 0.5279 | 0.0578 |
| 22 |  |  |  | 7 | 0.4944 | 0.0740 | 0.1975 | 0.1290 | 0.3459 | 0.0744 |
| 23 |  |  |  | 11 | 0.6605 | 0.0642 | 0.1125 | 0.1108 | 0.3865 | 0.0640 |
| 24 |  |  |  | 15 | 0.6610 | 0.0688 | 0.1875 | 0.1018 | 0.4243 | 0.0614 |
| 25 |  |  |  | 19 | 0.7538 | 0.0683 | 0.1400 | 0.0999 | 0.4469 | 0.0605 |
| 26 |  |  |  | 23 | 0.7595 | 0.0538 | 0.1250 | 0.0911 | 0.4422 | 0.0529 |
| 27 |  |  | 2D + N + MC | 3 | 0.6821 | 0.0288 | 0.3875 | 0.1191 | 0.5348 | 0.0613 |
| 28 |  |  |  | 7 | 0.7282 | 0.0489 | 0.1025 | 0.0968 | 0.4154 | 0.0542 |
| 29 |  |  |  | 11 | 0.7595 | 0.0523 | 0.2050 | 0.0937 | 0.4822 | 0.0536 |
| 30 |  |  |  | 15 | 0.7282 | 0.0494 | 0.1800 | 0.0950 | 0.4541 | 0.0536 |
| 31 |  |  |  | 19 | 0.7995 | 0.0442 | 0.1825 | 0.0952 | 0.4910 | 0.0525 |
| 32 |  |  |  | 23 | 0.8246 | 0.0356 | 0.2025 | 0.0941 | 0.5136 | 0.0503 |
| 33 |  |  | SM + MC | 3 | 0.6554 | 0.0577 | 0.1950 | 0.1105 | 0.4252 | 0.0624 |
| 34 |  |  |  | 7 | 0.6610 | 0.0519 | 0.2175 | 0.1124 | 0.4393 | 0.0619 |
| 35 |  |  |  | 11 | 0.6518 | 0.0510 | 0.2450 | 0.1100 | 0.4484 | 0.0606 |
| 36 |  |  |  | 15 | 0.6349 | 0.0686 | 0.2275 | 0.1000 | 0.4312 | 0.0607 |
| 37 |  |  |  | 19 | 0.6262 | 0.0536 | 0.2250 | 0.1010 | 0.4256 | 0.0572 |
| 38 |  |  |  | 23 | 0.6415 | 0.0537 | 0.2275 | 0.1121 | 0.4345 | 0.0621 |
| 39 |  |  | SM + SNV + MC | 3 | 0.6221 | 0.0581 | 0.2700 | 0.1523 | 0.4460 | 0.0815 |
| 40 |  |  |  | 7 | 0.6303 | 0.0572 | 0.2750 | 0.1406 | 0.4526 | 0.0759 |
| 41 |  |  |  | 11 | 0.6359 | 0.0543 | 0.2525 | 0.1394 | 0.4442 | 0.0748 |
| 42 |  |  |  | 15 | 0.6185 | 0.0550 | 0.2925 | 0.1327 | 0.4555 | 0.0718 |
| 43 |  |  |  | 19 | 0.6287 | 0.0575 | 0.2775 | 0.1219 | 0.4531 | 0.0674 |
| 44 |  |  |  | 23 | 0.6323 | 0.0527 | 0.2750 | 0.1237 | 0.4537 | 0.0672 |
| 45 |  |  | SM + SNV + WLS + MC | 3 | 0.6374 | 0.0480 | 0.1800 | 0.1076 | 0.4087 | 0.0589 |
| 46 |  |  |  | 7 | 0.6513 | 0.0579 | 0.1675 | 0.1201 | 0.4094 | 0.0667 |
| 47 |  |  |  | 11 | 0.6277 | 0.0536 | 0.1525 | 0.0955 | 0.3901 | 0.0548 |
| 48 |  |  |  | 15 | 0.6395 | 0.0549 | 0.1600 | 0.1131 | 0.3997 | 0.0628 |
| 49 |  |  |  | 19 | 0.6159 | 0.0711 | 0.1575 | 0.1179 | 0.3867 | 0.0689 |
| 50 |  |  |  | 23 | 0.6221 | 0.0595 | 0.1550 | 0.1145 | 0.3885 | 0.0645 |
| 51 |  |  | SM + SNV + N + MC | 3 | 0.6159 | 0.0493 | 0.2725 | 0.1255 | 0.4442 | 0.0674 |
| 52 |  |  |  | 7 | 0.6297 | 0.0635 | 0.2800 | 0.1373 | 0.4549 | 0.0756 |
| 53 |  |  |  | 11 | 0.6390 | 0.0677 | 0.2825 | 0.1283 | 0.4607 | 0.0725 |
| 54 |  |  |  | 15 | 0.6287 | 0.0563 | 0.2400 | 0.1402 | 0.4344 | 0.0756 |
| 55 |  |  |  | 19 | 0.6262 | 0.0595 | 0.2850 | 0.1102 | 0.4556 | 0.0626 |
| 56 |  |  |  | 23 | 0.6174 | 0.0460 | 0.2550 | 0.1359 | 0.4362 | 0.0717 |
| 57 |  |  | SM + SNV + WLS + N + MC | 3 | 0.7544 | 0.0518 | 0.1950 | 0.0805 | 0.4747 | 0.0479 |
| 58 |  |  |  | 7 | 0.7359 | 0.0516 | 0.1675 | 0.0965 | 0.4517 | 0.0547 |
| 59 |  |  |  | 11 | 0.7328 | 0.0531 | 0.1500 | 0.0875 | 0.4414 | 0.0512 |
| 60 |  |  |  | 15 | 0.7097 | 0.0476 | 0.1400 | 0.0862 | 0.4249 | 0.0492 |
| 61 |  |  |  | 19 | 0.7097 | 0.0479 | 0.1625 | 0.0986 | 0.4361 | 0.0548 |
| 62 |  |  |  | 23 | 0.7159 | 0.0480 | 0.2000 | 0.1185 | 0.4579 | 0.0639 |
| 63 |  |  | SM + WLS + MC | 3 | 0.7533 | 0.0520 | 0.1425 | 0.0911 | 0.4479 | 0.0525 |
| 64 |  |  |  | 7 | 0.7523 | 0.0413 | 0.1625 | 0.1018 | 0.4574 | 0.0549 |
| 65 |  |  |  | 11 | 0.7338 | 0.0480 | 0.1650 | 0.0854 | 0.4494 | 0.0490 |
| 66 |  |  |  | 15 | 0.7374 | 0.0590 | 0.1375 | 0.0919 | 0.4375 | 0.0546 |
| 67 |  |  |  | 19 | 0.7251 | 0.0572 | 0.1625 | 0.0809 | 0.4438 | 0.0495 |
| 68 |  |  |  | 23 | 0.7164 | 0.0612 | 0.1525 | 0.0921 | 0.4345 | 0.0553 |
| 69 |  |  | SM + WLS + N + MC | 3 | 0.7728 | 0.0536 | 0.1875 | 0.0809 | 0.4802 | 0.0485 |
| 70 |  |  |  | 7 | 0.7477 | 0.0447 | 0.1650 | 0.0854 | 0.4563 | 0.0482 |
| 71 |  |  |  | 11 | 0.7287 | 0.0568 | 0.1750 | 0.0838 | 0.4519 | 0.0506 |
| 72 |  |  |  | 15 | 0.7159 | 0.0502 | 0.1375 | 0.1049 | 0.4267 | 0.0581 |
| 73 |  |  |  | 19 | 0.7154 | 0.0392 | 0.1625 | 0.1136 | 0.4389 | 0.0601 |
| 74 |  |  |  | 23 | 0.7164 | 0.0561 | 0.1750 | 0.1071 | 0.4457 | 0.0605 |
| 75 |  |  | SM + N + MC | 3 | 0.6005 | 0.0558 | 0.3175 | 0.1293 | 0.4590 | 0.0704 |
| 76 |  |  |  | 7 | 0.6349 | 0.0631 | 0.2775 | 0.1390 | 0.4562 | 0.0763 |
| 77 |  |  |  | 11 | 0.6015 | 0.0845 | 0.3150 | 0.1389 | 0.4583 | 0.0813 |
| 78 |  |  |  | 15 | 0.5974 | 0.0692 | 0.3075 | 0.1433 | 0.4525 | 0.0796 |
| 79 |  |  |  | 19 | 0.5928 | 0.0741 | 0.3025 | 0.1496 | 0.4477 | 0.0835 |
| 80 |  |  |  | 23 | 0.5928 | 0.0629 | 0.3050 | 0.1560 | 0.4489 | 0.0841 |

*NIR: near-infrared; 2T: second trimester; R2: range 2; Sp: specificity; Se: sensitivity; NER: non-error rate; Av: average; StD: standard deviation; MC: mean centering; N: normalization; WLS: weighted least squares; SNV: standard normal variate; 1D: first derivative; 2D: second derivative; SM: smoothing.*

**Table S9.** Predictive performance of ML models using NIR spectral data from second trimester serum samples (range 3, 5100-4000 cm-1).

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Model number** | **Dataset** | **Detail** | **Pretreatment** | **Width** | **Sp (Av)** | **Sp (StD)** | **Se (Av)** | **Se (StD)** | **NER (Av)** | **NER (StD)** |
| 1 | NIR2T | R3 | MC |  | 0.7805 | 0.0421 | 0.6375 | 0.1318 | 0.7090 | 0.0692 |
| 2 |  |  | N+MC |  | 0.7626 | 0.0483 | 0.4550 | 0.0937 | 0.6088 | 0.0527 |
| 3 |  |  | WLS+MC |  | 0.8108 | 0.0401 | 0.5600 | 0.1217 | 0.6854 | 0.0641 |
| 4 |  |  | WLS+N+MC |  | 0.7497 | 0.0403 | 0.4425 | 0.1048 | 0.5961 | 0.0561 |
| 5 |  |  | SNV + MC |  | 0.8133 | 0.0411 | 0.7075 | 0.0998 | 0.7604 | 0.0540 |
| 6 |  |  | SNV + WLS + MC |  | 0.7913 | 0.0427 | 0.6125 | 0.1049 | 0.7019 | 0.0566 |
| 7 |  |  | SNV + N + MC |  | 0.7908 | 0.0467 | 0.7025 | 0.1126 | 0.7466 | 0.0610 |
| 8 |  |  | SNV + WLS + N + MC |  | 0.8426 | 0.0351 | 0.4925 | 0.1222 | 0.6675 | 0.0636 |
| 9 |  |  | 1D + MC | 3 | 0.7215 | 0.0577 | 0.1200 | 0.0944 | 0.4208 | 0.0553 |
| 10 |  |  |  | 7 | 0.7918 | 0.0465 | 0.3875 | 0.1736 | 0.5896 | 0.0899 |
| 11 |  |  |  | 11 | 0.8415 | 0.0350 | 0.5925 | 0.1179 | 0.7170 | 0.0615 |
| 12 |  |  |  | 15 | 0.8713 | 0.0361 | 0.7075 | 0.0783 | 0.7894 | 0.0431 |
| 13 |  |  |  | 19 | 0.7815 | 0.0526 | 0.5500 | 0.1383 | 0.6658 | 0.0740 |
| 14 |  |  |  | 23 | 0.7523 | 0.0490 | 0.4975 | 0.1300 | 0.6249 | 0.0695 |
| 15 |  |  | 1D + N + MC | 3 | 0.7949 | 0.0460 | 0.1600 | 0.1042 | 0.4774 | 0.0570 |
| 16 |  |  |  | 7 | 0.8082 | 0.0422 | 0.3850 | 0.1533 | 0.5966 | 0.0795 |
| 17 |  |  |  | 11 | 0.8395 | 0.0451 | 0.7200 | 0.1226 | 0.7797 | 0.0653 |
| 18 |  |  |  | 15 | 0.8415 | 0.0445 | 0.7200 | 0.1301 | 0.7808 | 0.0688 |
| 19 |  |  |  | 19 | 0.8026 | 0.0425 | 0.7100 | 0.1113 | 0.7563 | 0.0596 |
| 20 |  |  |  | 23 | 0.7723 | 0.0403 | 0.6700 | 0.1064 | 0.7212 | 0.0569 |
| 21 |  |  | 2D + MC | 3 | 0.7497 | 0.0368 | 0.0000 | 0.0000 | 0.3749 | 0.0184 |
| 22 |  |  |  | 7 | 0.8431 | 0.0416 | 0.0000 | 0.0000 | 0.4215 | 0.0208 |
| 23 |  |  |  | 11 | 0.6733 | 0.0553 | 0.0075 | 0.0300 | 0.3404 | 0.0314 |
| 24 |  |  |  | 15 | 0.7221 | 0.0428 | 0.1625 | 0.1108 | 0.4423 | 0.0594 |
| 25 |  |  |  | 19 | 0.7446 | 0.0460 | 0.1350 | 0.1067 | 0.4398 | 0.0581 |
| 26 |  |  |  | 23 | 0.7436 | 0.0455 | 0.2225 | 0.0921 | 0.4830 | 0.0513 |
| 27 |  |  | 2D + N + MC | 3 | 0.7585 | 0.0302 | 0.0000 | 0.0000 | 0.3792 | 0.0151 |
| 28 |  |  |  | 7 | 0.8441 | 0.0397 | 0.0100 | 0.0343 | 0.4271 | 0.0262 |
| 29 |  |  |  | 11 | 0.6923 | 0.0515 | 0.0100 | 0.0343 | 0.3512 | 0.0309 |
| 30 |  |  |  | 15 | 0.7528 | 0.0394 | 0.1825 | 0.1293 | 0.4677 | 0.0676 |
| 31 |  |  |  | 19 | 0.7744 | 0.0374 | 0.1350 | 0.1067 | 0.4547 | 0.0565 |
| 32 |  |  |  | 23 | 0.7641 | 0.0455 | 0.2325 | 0.1237 | 0.4983 | 0.0659 |
| 33 |  |  | SM + MC | 3 | 0.7856 | 0.0442 | 0.6200 | 0.1262 | 0.7028 | 0.0668 |
| 34 |  |  |  | 7 | 0.7708 | 0.0450 | 0.6750 | 0.1010 | 0.7229 | 0.0553 |
| 35 |  |  |  | 11 | 0.7605 | 0.0444 | 0.6500 | 0.1129 | 0.7053 | 0.0607 |
| 36 |  |  |  | 15 | 0.7682 | 0.0433 | 0.6475 | 0.0934 | 0.7079 | 0.0515 |
| 37 |  |  |  | 19 | 0.7636 | 0.0455 | 0.6400 | 0.1061 | 0.7018 | 0.0577 |
| 38 |  |  |  | 23 | 0.7759 | 0.0417 | 0.6575 | 0.1095 | 0.7167 | 0.0586 |
| 39 |  |  | SM + SNV + MC | 3 | 0.8072 | 0.0458 | 0.6925 | 0.1017 | 0.7498 | 0.0558 |
| 40 |  |  |  | 7 | 0.8015 | 0.0401 | 0.6825 | 0.0952 | 0.7420 | 0.0516 |
| 41 |  |  |  | 11 | 0.8062 | 0.0472 | 0.6800 | 0.1189 | 0.7431 | 0.0640 |
| 42 |  |  |  | 15 | 0.7964 | 0.0432 | 0.6950 | 0.1105 | 0.7457 | 0.0593 |
| 43 |  |  |  | 19 | 0.8103 | 0.0427 | 0.6875 | 0.1108 | 0.7489 | 0.0594 |
| 44 |  |  |  | 23 | 0.8041 | 0.0477 | 0.7100 | 0.1142 | 0.7571 | 0.0619 |
| 45 |  |  | SM + SNV + WLS + MC | 3 | 0.7810 | 0.0337 | 0.5950 | 0.1373 | 0.6880 | 0.0707 |
| 46 |  |  |  | 7 | 0.7938 | 0.0388 | 0.6425 | 0.1101 | 0.7182 | 0.0584 |
| 47 |  |  |  | 11 | 0.7862 | 0.0410 | 0.6250 | 0.1010 | 0.7056 | 0.0545 |
| 48 |  |  |  | 15 | 0.7846 | 0.0405 | 0.6525 | 0.1138 | 0.7186 | 0.0604 |
| 49 |  |  |  | 19 | 0.7897 | 0.0411 | 0.6475 | 0.1092 | 0.7186 | 0.0583 |
| 50 |  |  |  | 23 | 0.8010 | 0.0462 | 0.6500 | 0.1041 | 0.7255 | 0.0570 |
| 51 |  |  | SM + SNV + N + MC | 3 | 0.8026 | 0.0360 | 0.7100 | 0.0960 | 0.7563 | 0.0512 |
| 52 |  |  |  | 7 | 0.8046 | 0.0424 | 0.7075 | 0.1089 | 0.7561 | 0.0584 |
| 53 |  |  |  | 11 | 0.7954 | 0.0453 | 0.7150 | 0.1042 | 0.7552 | 0.0568 |
| 54 |  |  |  | 15 | 0.7954 | 0.0416 | 0.6650 | 0.1055 | 0.7302 | 0.0567 |
| 55 |  |  |  | 19 | 0.8092 | 0.0385 | 0.7125 | 0.1164 | 0.7609 | 0.0613 |
| 56 |  |  |  | 23 | 0.8164 | 0.0428 | 0.6825 | 0.1217 | 0.7495 | 0.0645 |
| 57 |  |  | SM + SNV + WLS + N + MC | 3 | 0.8364 | 0.0404 | 0.4975 | 0.1115 | 0.6670 | 0.0593 |
| 58 |  |  |  | 7 | 0.8436 | 0.0409 | 0.5000 | 0.1010 | 0.6718 | 0.0545 |
| 59 |  |  |  | 11 | 0.8456 | 0.0326 | 0.5300 | 0.1199 | 0.6878 | 0.0621 |
| 60 |  |  |  | 15 | 0.8374 | 0.0465 | 0.5100 | 0.1491 | 0.6737 | 0.0781 |
| 61 |  |  |  | 19 | 0.8282 | 0.0455 | 0.5225 | 0.1399 | 0.6754 | 0.0736 |
| 62 |  |  |  | 23 | 0.8431 | 0.0432 | 0.5350 | 0.1186 | 0.6890 | 0.0631 |
| 63 |  |  | SM + WLS + MC | 3 | 0.8010 | 0.0410 | 0.5850 | 0.1223 | 0.6930 | 0.0645 |
| 64 |  |  |  | 7 | 0.8159 | 0.0488 | 0.5675 | 0.1135 | 0.6917 | 0.0618 |
| 65 |  |  |  | 11 | 0.8082 | 0.0458 | 0.5650 | 0.1018 | 0.6866 | 0.0558 |
| 66 |  |  |  | 15 | 0.8159 | 0.0407 | 0.5750 | 0.0945 | 0.6954 | 0.0514 |
| 67 |  |  |  | 19 | 0.8159 | 0.0436 | 0.5725 | 0.1239 | 0.6942 | 0.0657 |
| 68 |  |  |  | 23 | 0.8056 | 0.0531 | 0.5825 | 0.1174 | 0.6941 | 0.0644 |
| 69 |  |  | SM + WLS + N + MC | 3 | 0.8328 | 0.0392 | 0.4900 | 0.1207 | 0.6614 | 0.0634 |
| 70 |  |  |  | 7 | 0.8226 | 0.0550 | 0.4975 | 0.0961 | 0.6600 | 0.0554 |
| 71 |  |  |  | 11 | 0.8328 | 0.0402 | 0.5150 | 0.1375 | 0.6739 | 0.0716 |
| 72 |  |  |  | 15 | 0.8405 | 0.0367 | 0.5175 | 0.1042 | 0.6790 | 0.0552 |
| 73 |  |  |  | 19 | 0.8369 | 0.0318 | 0.5325 | 0.1004 | 0.6847 | 0.0527 |
| 74 |  |  |  | 23 | 0.8369 | 0.0376 | 0.5300 | 0.1173 | 0.6835 | 0.0616 |
| 75 |  |  | SM + N + MC | 3 | 0.7692 | 0.0521 | 0.4475 | 0.0981 | 0.6084 | 0.0555 |
| 76 |  |  |  | 7 | 0.7692 | 0.0443 | 0.4650 | 0.1158 | 0.6171 | 0.0620 |
| 77 |  |  |  | 11 | 0.7487 | 0.0508 | 0.4775 | 0.1000 | 0.6131 | 0.0561 |
| 78 |  |  |  | 15 | 0.7426 | 0.0494 | 0.4850 | 0.1147 | 0.6138 | 0.0625 |
| 79 |  |  |  | 19 | 0.7508 | 0.0500 | 0.4750 | 0.1101 | 0.6129 | 0.0604 |
| 80 |  |  |  | 23 | 0.7549 | 0.0565 | 0.4725 | 0.1109 | 0.6137 | 0.0622 |

*NIR: near-infrared; 2T: second trimester; R3: range 3; Sp: specificity; Se: sensitivity; NER: non-error rate; Av: average; StD: standard deviation; MC: mean centering; N: normalization; WLS: weighted least squares; SNV: standard normal variate; 1D: first derivative; 2D: second derivative; SM: smoothing.*

**Table S10.** Predictive performance of ML models combining NIR spectral data of second trimester sera with medical parameters.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **NIR 2T range a** | **Plus** | **Block order b** | **Sp (Av)** | **Sp (StD)** | **Se (Av)** | **Se (StD)** | **NER (Av)** | **NER (StD)** |
| Full |  |  | 0.8133 | 0.0324 | 0.1150 | 0.0556 | 0.4642 | 0.0321 |
| Full | Medical | 1-2 | 0.8718 | 0.0398 | 0.3175 | 0.1048 | 0.5946 | 0.0560 |
| Full | Medical | 2-1 | 0.8703 | 0.0360 | 0.2950 | 0.0747 | 0.5826 | 0.0415 |
| Full simp c | Medical simp c | 1-2 | 0.6759 | 0.0915 | 0.5125 | 0.1478 | 0.5942 | 0.0869 |
| Full simp c | Medical simp c | 2-1 | 0.7600 | 0.0727 | 0.5275 | 0.1457 | 0.6438 | 0.0814 |
| R3 |  |  | 0.8713 | 0.0361 | 0.7075 | 0.0783 | 0.7894 | 0.0431 |
| R3 | Medical | 1-2 | 0.8667 | 0.0319 | 0.5750 | 0.1617 | 0.7208 d | 0.0824 d |
| R3 | Medical | 2-1 | 0.8487 | 0.0511 | 0.4875 | 0.1641 | 0.6681 | 0.0860 |
| R3 simp c | Medical simp c | 1-2 | 0.6492 | 0.0713 | 0.4625 | 0.1562 | 0.5559 | 0.0858 |
| R3 simp c | Medical simp c | 2-1 | 0.7195 | 0.0748 | 0.4750 | 0.1263 | 0.5972 | 0.0734 |

a Full: 10500-4000 cm-1; R3: 5100-4000 cm-1.

b NIR blocks were pretreated using the conditions identified as best in single-block analysis. Medical blocks were pretreated by autoscaling.

c Data obtained after variable selection, using the variable importance information from the original equivalent multi-block model.

d Best multi-block model. Its DCV-AUROC is 0.8126 ± 0.0696.

*NIR: near-infrared; 2T: second trimester; R3: range 3; Sp: specificity; Se: sensitivity; NER: non-error rate; Av: average; StD: standard deviation.*

**Table S11.** Molecular vibrations and biomolecules that have been associated with the most relevant spectral intervals of the best first trimester model.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Spectral interval** | **Tentative molecular vibration** | **Theoretical wavenumber** | **Potential biomolecule** | **Reference** |
| 10500-9828 cm-1 | Second overtone of O-H stretching | 9911, 10288-10300 cm-1 | Carbohydrates | (32,34) |
|  | Second overtone of N-H stretching | 10277-9804 cm-1 | Proteins | (32) |
| 8826-7858 cm-1 | Second overtone of C-H stretching | 8250-8696 cm-1 | Carbohydrates and lipids | (32,33) |

**Table S12.** Molecular vibrations and biomolecules that have been associated with the most relevant spectral intervals of the best second trimester model.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Spectral interval** | **Tentative molecular vibration** | **Theoretical wavenumber** | **Potential biomolecule** | **Reference** |
| 5028-4856 cm-1 | Combination of N-H stretching + C-N stretching + N-H bending | 4925, 4975, 5025 cm-1 | Proteins | (32) |
|  | Second overtone of C=O stretching | 4926 cm-1 | Proteins | (32) |
|  | Combination of N-H stretching + N-H bending | 4880-4902 cm-1 | Proteins | (32,33) |
|  | Combination of N-H bending + C-N stretching + N-H bending | 4878 cm-1 | Proteins | (32) |
|  | Combination of N-H stretching + C=O stretching | 4866 cm-1 | Proteins | (32,33) |
|  | Combination of second overtone of N-H bending + N-H stretching | 4854 cm-1 | Proteins | (32) |
|  | Combination band of N-H stretching + N-H bending | 4850 cm-1 | Proteins | (32) |
| 4764-4702 cm-1 | Third overtone of C=O-O stretching | 4762 cm-1 | Carbohydrates | (32) |
|  | Combination of O-H bending + C-O stretching | 4762 cm-1 | Carbohydrates | (32) |
| 4492-4442 cm-1 | Combination bands of C-H | 4250-4760 cm-1 | Carbohydrates | (32,34) |
| 4392-4364 cm-1 | Combination of C-H stretching + CH2 deformation | 4386 cm-1 | Carbohydrates | (32) |
| 4302-4268 cm-1 | Combination of C-H stretching + CH2 deformation | 4283, 4292 cm-1 | Carbohydrates | (32) |
| 4206-4176 cm-1 | Combination band of C-H stretching + C-H stretching | 4202 cm-1 | Lipids | (32) |
| 4096-4000 cm-1 | Combination bands of C-H | 4049 cm-1 | Lipids | (32) |
|  | First overtone of C-N-C stretching | 4049 cm-1 | Proteins | (32) |
|  | Combination of C-H stretching + C-C stretching + C-O-C stretching | 4000 cm-1 | Carbohydrates | (32) |