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Performance and Prediction Algorithmic Methodology Applied to Assisted Procreation Technology

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Abstract

In the field of assisted reproduction, several studies suggest that the genes involved in the crosstalk of the oocyte-cumulus cell could represent candidate gene biomarkers to select embryos competent in terms of implantation.

To achieve this objective and before any processing of the acquired transcriptomic data from RT-qPCR (Real-Time Quantitative Chain Polymerase) physical system, it is necessary to ensure the reliability of the acquired data. Indeed, these acquired data are generally provided with noise from various sources, such as experimental, technical noise, etc.

The transcriptomic data correspond to the expression of 21 biomarker genes of 102 cumulus cell samples from patients undergoing in vitro fertilization. So, our goal is to test whether this genomic signature could be used as a biomarker for pregnancy prediction. If so, we can state that this transcriptome is predictive and could generate a reliable mathematical model. In this paper, we provide a typical algorithm whose task is to verify the validity of the RT-qPCR transcriptomic data.

The originality of this paper is to combine the performance, namely Binary and Multiple Logistic Regression (BMLR), and the Likelihood criterions. This is in order to maximize the probability that the test will correctly predict the event of interest (pregnancy). In this framework, the Odds-Ratio (OR) will be also analyzed to assess the robustness of the test.

Keywords: Binary and Multiple Logistic Regression; Likelihood; Noise; Odds-Ratio; Pregnancy; Reproduction; RT-qPCR.

Introduction

Multiple Logistic Regression is one of the most commonly used multivariate analysis models for prediction. It allows measuring the association between the occurrence of an event (explanatory and qualitative variable X) and the factors that may influence this occurrence.

The combination of Binary and Multiple Logistic Regression (BMLR) and the Likelihood Criterion [1-5] is very well suited for the analysis of transcriptomic data [6,7]. The variable to be explained Y which takes only two modalities: positive or negative pregnancy is random binary categorical and dependent process that follows a binomial probability distribution with the parameters (N, p). This random variable is formulated as follows:

$$Y = [y_1, y_2, \dots, \dots, y_N] \quad (1)$$

Y is the vector to be predicted at best by maximizing the Likelihood Criterion [8-12] that will be discussed later.

The knowledge of the probability P (Y = 1 | X = x) implies that P (Y = 0 | X = x). It is therefore sufficient to model the probability by: p (x) = P (Y = 1 | X = x).

The explanatory variable X represents the gene expression data. In our case, it is expressed in matrix form as follows:

$$X = \begin{bmatrix} 1\, x_{11} & \dots . & x_{1P} \\ \dots & \dots & \dots \\ \dots & \dots & \dots \\ 1\, x_{N1} & \dots . & x_{NP} \end{bmatrix} \quad (2)$$

The lines of X represent the expression data of individual cumulus samples from individual patients (N lines). The columns correspond to the expression of the 21 genes that are potential biomarkers of pregnancy outcome (P columns).

To model the dependence of Y as a function of the descriptive matrix X, according to the following matrix equation:

$$Y = X * \beta^T + \mathcal{E} \quad (3)$$

is equivalent to estimate the pregnancy optimum vector $\hat{Y}$ then generate an optimum predictor vector $\hat{\beta}$. This by maximizing the Log of Likelihood $L_N(\beta)$.

-X is the descriptive matrix ϵ $R^N.R^{P+1}$

-β is the predictor vector ϵ R^N.

-Ɛ is the residual error following a normal distribution defined on the space Ω (0, σ^2) of zero mean and of variance = σ^2.

The likelihood is defined as follow:

$$L_N(\beta) = \prod_{k=1}^{N} P_\beta(\{(Y_i = y_i | X_i = x_i\}) \quad (4)$$

$p_\beta(x) = P_\beta(\{(Y = 1|X = x\})$ With $x = (x_1, x_2, \ldots, x_N)$ a statistical realization-sample of the transcriptomic matrix $X = (X_1, X_2, \ldots, X_N)$; the logistic model proposes a modelling of the law of Y | X = x by a Bernoulli distribution with parameter:

That represents the probability of observing the pregnancy event Y=1.

The Log of $L_N(\beta)$ has to be maximized in order to compute the optimal predictor vector $\hat{\beta}$ and then $\hat{Y}$.

In addition, we focus on measuring the ROC performance, with the aim to see if the results go in the same sense as the Likelihood optimization.

At the end of this manuscript, we conclude on the validity and therefore the exploitation of these transcriptomic data for pregnancy prediction.

Likelihood Study

Our objective is to find the optimum predictor $\hat{\beta}$ by maximizing the following residuals criteria:

$$\|Y - X * \beta^T\|^2 + \mathcal{E} \quad (5)$$

As the Likelihood process is not linear, the Logit transformation (Link function) will be used. It is given by the following formula:

$$\text{Logit}(p_\beta(x)) = \text{Log}\left[\frac{p_\beta(x)}{1 - p_\beta(x)^*}\right] = \beta_0 + \sum_{j=1}^{P=21} \beta_j x_j \quad (6)$$

This transformation makes the matrix system of optimization a linear system, thus making it possible to obtain the estimated pregnancy vector Y.

This function (Logit) is bijective and differentiable, thus transforming the binary space [0,1] of Y to a real space]- ∞,+∞[.

The predicted probability is thus written as follows:

$$p_{\hat{\beta}}(x) = E[Y = 1|X = x] = \frac{\exp\left(\hat{\beta_0} + \sum_{j=1}^{p} \hat{\beta_j} x_{ij}\right)}{1 + \exp\left(\hat{\beta_0} + \sum_{j=1}^{p} \hat{\beta_j} x_{ij}\right)} \quad (7)$$

To obtain the Maximum of Likelihood, the $\text{Log}(L_N(\beta))$ is derived in order to obtain the optimal predictor vector $\hat{\beta}$, and consequently the vector Odd-Ratio OR is such that:

$$OR = \exp(\hat{\beta}^T X) \quad (8)$$

The interpretation of the coefficients β is generally done using Odds-Ratio (OR) [3][9] [10] [12].

ODDS-RATIO (OR)

The general idea is to reason in terms of probability, using the ratings (Cote = Chance). The Odd-Ratio measures the relationship between the score of an event occurring in a group of individuals A and the rating of the same event occurring in group of individuals B [1,2] [9] [11].

OR depends on the β predictor vector and it is formulated as follows:

$$OR = \frac{p_\beta(x)}{1 - p_\beta(x)} \Big/ \frac{p_\beta(\bar{x})}{1 - p_\beta(\bar{x})} \quad (9)$$

The OR parameter is optimum when the predictor β reaches its optimum $\hat{\beta}$.

ALGORITHMS

••• Initialization:

- DATA_1 (Learn Table = 2/3 of the raw data).
- DATA_2 (Test Table = 1/3 of the raw data).
- Extraction of binary vectors Y (Pr) and construction of Explicative Matrix X.

••• Predictor Processing (under R)

- β_0 initialization.

- k ← 1

- Repeat

$\beta^{k+1} \leftarrow \beta^k + A^k \nabla L_N(\beta^k)$ where $\nabla L_N(\beta^k)$ is the gradient at the point β^k with A^k is such that $A^k = (\nabla^2 L_N(\beta^k))^{-1}$ (called step matrix of the algorithm).

$k \leftarrow k + 1$

Until Kmax

••• Predicted Probability Computation.

••• Calculation of the $OR = \exp(\hat{\beta}^T X)$

Results and Discussion

Performance Results

The ROC curve has emerged as a mathematical tool for quantifying the performance and therefore the quality of a Predictive Model. It often appears as a function of the Rate of Positive True fraction actually detected as a function of the Rate of Positive False (fraction incorrectly detected). Graphically, the ROC curve is presented as Sensitivity in function of Anti-Specificity.

The AUC of the Full Model (Red Curve) is about 0.788148. For Learning Model (Blue Curve) and Test Tables Model (Green curve), the AUCs are respectively 0.70977 and 0.933333. The perfect AUC is equal to 1.(Figure 1)

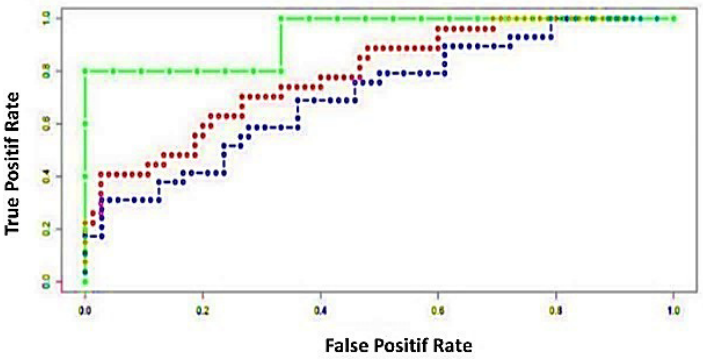

Figure 1: ROC curve in green for test data, in blue for learning data, and in red for the complete model.

The residual difference AUC between this model and the perfect model is about 20%. Therefore, this model is doubtful in terms of discrimination.

Likelihood Results: Predicted Probabilities

There is a big difference between the observed and the predicted probabilities as indicated in (Figure 2) This reinforces the doubt about the model validity.

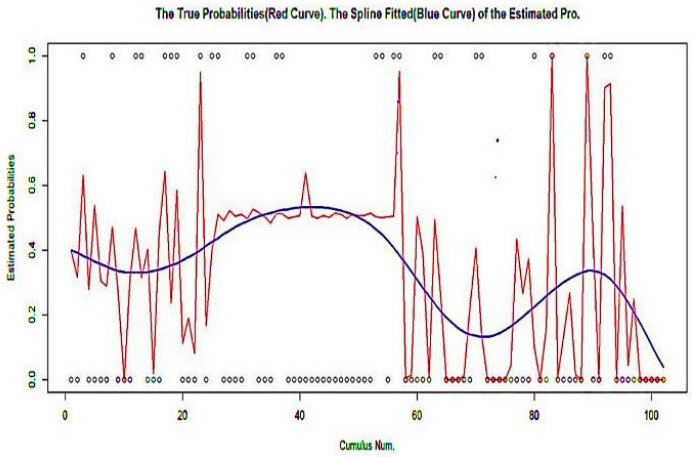

Figure 2: The observed pregnancy curve (Y) is represented as a black round- dots. The Estimated probabilies vector $\hat{Y}$ (red curve) and finally the Spline- Cubic Interpolator of Y (blue curve) are also given.

Odd-Ratio: Results

The OR parameter (black curve) and its Confidence Interval (CI) are as follow:

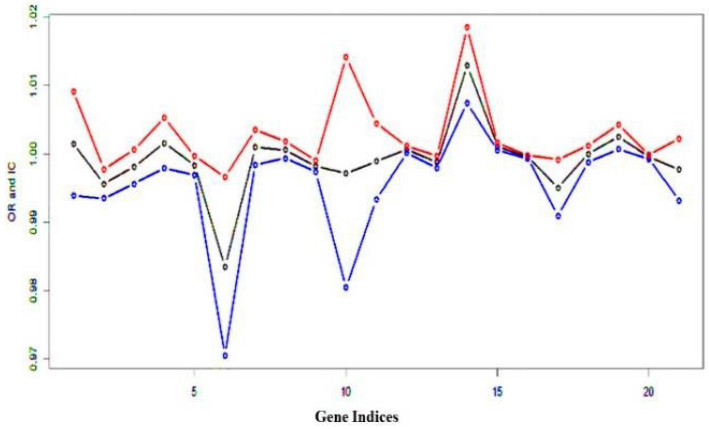

Figure 3: X axis = gene indices. Y-axis = OR, black curve. The blue and the red curves correspond respectively to the lower bound and the upper bound of the OR confidence intervals.

The Used Transcriptomic Data

The transcriptomic data used are given in the table below, in line are the cumulus of the patients, while in the columns there is the list of the used genes.

GR	G1	G2	G3	G4	G5	G6	G7	G8	G9	G10
0	83.508792	682.10791	343.42617	1033.8823	75.785828	62.850669	1085.2835	416.9863	1432.0401	33.448189
0	12.940812	191.85282	275.10836	378.42306	73.713461	25.702846	191.85282	305.25184	1402.5692	24.827312
1	14.458602	111.72871	150.52467	278.94873	109.42937	15.712667	110.19051	104.97167	273.20805	33.448189
0	10.584316	59.873935	77.37825	66.434291	35.601255	13.584186	80.664176	50.697974	288.78584	11.110534
0	40.053494	30.354872	90.751916	275.10836	82.931955	11.033787	234.56699	154.7565	271.32087	15.932008
0	50,000	193.18727	104.24658	67.361679	51.405691	3.5402621	62.416527	55.864357	217.34697	41.754396
0	5.7511728	26.980706	91.383145	262.07868	82.931955	8.7777805	200	73.204285	881.52409	5.440941
1	17.924441	17.555561	64.617642	185.31761	19.479114	7.8563336	79.004131	32.759835	156.91682	2.8359974
0	4.2985682	38.42188	67.361679	104.24658	8.0214119	1.9777447	9.4077922	17.313868	509.82425	4.2985682
0	1221.0074	1825.2219	1691.2289	1633.6194	71.20251	54.336743	350.64229	419.88667	2111.2127	358.01003
0	56.252924	92.018765	267.58551	155.83292	23.488069	10.438599	84.089642	75.785828	101.39595	14.458602
1	36.602142	114.07637	88.884268	116.47336	20.447551	3.4674046	61.985385	80.106988	123.97077	35.355339
1	8.3042863	159.1073	89.502507	115.66882	38.689125	11.502346	117.28349	38.15648	327.16082	8.5377516
0	12.074204	50	36.09823	87.660572	17.800627	5.440941	52.123288	22.531262	97.265495	17.555561
0	475.68285	204.20243	241.16157	208.49315	231.33764	53.588673	169.34906	938.26796	57.434918	6.1639544
0	8.3042863	67.361679	37.892914	212.87404	2.5737219	28.717459	122.26403	134.72336	1.884E-05	5.5552668
1	82.931955	397.237	1155.1434	1422.1483	298.96985	71.697762	1392.8809	456.30549	3550.6223	28.126462
1	19.344562	226.57678	229.73967	561.77795	34.868592	17.434296	431.69129	736.15012	475.68285	41.754396
1	100.69556	82.931955	145.39725	265.73716	72.698626	50.697974	61.132014	440.76205	305.25184	0.0214015
0	28.917205	109.42937	57.038186	288.78584	21.464136	29.524817	193.18727	102.81138	756.84612	2.9157281
0	19.751033	186.6066	303.14331	391.76812	81.22524	17.313868	546.4161	783.53624	881.52409	14.259546
0	86.453723	61.557221	195.88406	363.00766	83.508792	32.533546	554.04379	278.94873	1085.2835	21.763764
1	320.42795	900.04679	645.31341	1432.0401	1012.6053	228.15274	2617.2866	3289.9642	2581.2536	239.49574
0	2.1196943	9.944206	619.026	32.533546	2.9769937	3.3725882	20.30631	30.566007	43.527528	1.9370433
1	1.067219	1.6980232	1.8581361	5.5552668	0.2212664	0.0458751	20.447551	6.0790934	3.1906629	1.0896435
1	2.3683071	0.6215129	3.794359	4.7038961	0.0010137	0.0719858	14.358729	15.072598	0.8789519	1.6401823
0	0.7238969	1.8971795	6.515411	18.946457	5.5168937	0.2541683	12.327909	8.9622203	16.266773	0.9355302
0	1.6980232	0.9888723	9.5391201	52.123288	4.6070913	0.3353771	46.009383	21.763764	40.895103	3.4434535
0	0.3001709	1.4377932	3.901033	16.266773	2.6096497	0.0560888	21.02241	13.678671	33.680839	2.2250784
0	0.1343303	1.7579039	3.2128557	7.5362989	1.3139006	0.0560888	9.2141826	7.7481731	7.6946526	0.5448217
1	0.4742949	2.5382887	9.8073012	6.886907	3.4674046	0.6615198	19.888412	8.3620472	1.0380358	2.5737219
1	0.4710187	4.5752678	7.8020659	7.2293011	3.0395467	0.1899717	145.39725	9.6054699	0.4613253	2.9977004
0	0.2743056	1.2259127	11.343989	10.013373	2.9564301	0.2472181	3.1686234	4.6070913	0.2743056	0.2800694
0	0.1939634	1.2691444	12.940812	9.2782723	3.4674046	0.3424241	3.7162722	3.1467361	0.0109256	0.3129179
0	0.2980975	3.103414	5.440941	10.657936	1.991501	0.0631032	7.1793647	2.4688791	2.1050525	0.1797242
1	0.5336095	2.7016788	6.9830446	17.075503	1.8198962	0.0681027	21.763764	6.6985841	3.6906021	0.4334256
1	0.8200912	4.4501569	6.3372467	17.075503	2.8557233	0.0601145	24.316374	10.657936	4.2985682	0.5758864
0	0.3262062	2.351948	2.5033434	6.6063628	1.2174447	0.0644291	23.004691	4.2393885	12.413656	0.3852472
0	0.364466	1.7098339	4.0949794	9.5391201	4.6070913	0.0452436	22.845786	5.9954007	8.1333866	0.666121

0	0.7921558	1.074642	3.0819772	6.2068281	3.7681495	0.0719858	4.6070913	5.7911754	2.5737219	0.6707542
0	11.662912	6.2934722	49.311635	102.10121	49.311635	0.3988329	126.57566	191.85282	8.5971364	9.1505356
0	1.3508394	5.0765775	8.3042863	56.252924	3.1467361	0.0240779	22.687979	9.0873282	3.3492921	0.7089993
0	0.4274585	3.2128557	6.1639544	37.892914	2.2718321	0.0592869	19.344562	10.584316	8.2469244	0.4518313
0	0.3353771	0.8200912	3.1686234	5.4787858	0.8088007	0.0484908	5.5168937	2.3195681	0.5562696	0.5758864
0	2.38478	9.0245575	4.6714039	21.915143	8.0214119	0.2036066	40.332088	27.932178	0.7089993	23.325825
0	0.4710187	6.25	4.5752678	62.416527	11.343989	0.319493	37.631169	26.061644	0.5640348	8.5971364
0	0.1210652	1.6288528	2.8359974	6.4704058	2.1492841	0.0798732	3.4196678	0.9551877	1.3602353	0.0862015
0	0.1011001	3.3492921	2.8755864	6.6985841	2.9157281	0.0969817	4.4811102	1.332242	1.332242	0.1279681
0	0.4809158	0.2022002	1.6980232	3.125	1.0598471	0.0053504	9.0245575	1.9777447	1.9777447	0.1076079
0	2.0333466	0.2668047	2.5207555	7.9109787	0.6569503	0.0178721	5.7114466	1.845301	1.845301	0.1480192
0	0.3239529	0.9226505	2.0333466	12.158187	0.4710187	0.0104081	7.4842419	1.175974	0.0452436	3.97E-07
0	1.9103754	1.2691444	1.674646	15.821957	0.3043612	0.0099842	16.493849	3.742121	0.0576657	8.68E-07
1	1.4884969	0.1334024	1.6515907	2.335702	1.1048543	0.0070599	0.4245058	0.9752582	0.7139308	0.6258358
1	0.2243551	0.3721242	1.4179987	2.0193013	1.0380358	0.0192881	1.175974	0.6479059	0.3825861	0.3086099
0	0.6801176	0.3400588	1.1438169	5.4787858	1.1048543	0.0357443	2.5382887	0.8431471	1.4782151	0.3496192
1	0.4186615	0.9355302	0.9036626	2.3683071	0.1410087	2.66E-08	2.38478	0.7041019	0.9226505	0.2290693
1	0.6434305	0.8431471	1.0166733	2.4688791	0.4334256	0.0140222	1.991501	0.5640348	1.3984767	0.7598867
0	0.0015797	0.7391075	3.4434535	34.627737	5971.4111	0.1169413	0.0015797	207.05298	71.697762	0.0015797
0	0.0017167	1.277972	3.1686234	11.265631	7003.4797	0.261314	0.0017167	172.90745	25.173889	0.0017167
0	0.8088007	1.8073253	5.5552668	10.083022	2.8755864	0.1153313	7.0316155	5.041511	4.9036506	1.067219
0	6.162E-05	0.0002993	1.3048249	28.126462	33.448189	1.7337023	0.0519712	6.162E-05	6.162E-05	7.2293011
0	0.0021579	9.0873282	19.344562	26.794337	14.865089	1.074642	35.111122	32.759835	45.375958	4.6391362
1	6.4704058	50.347778	49.311635	142.40502	34.627737	2.1944451	105.7018	36.09823	181.50383	3.9554894
1	15.712667	249.66611	61.132014	153.68752	43.830286	11.502346	79.004131	38.689125	288.78584	14.55917
0	97.265495	1983.5323	246.22888	370.63522	260.26837	389.06198	431.69129	585.63428	736.15012	275.10836
0	386.37453	1123.5559	535.17102	211.40361	756.84612	0.0032935	191.85282	589.70769	6355.792	182.76629
0	0.0304768	17125.473	794.474	397.237	2082.147	324.90096	857.41877	2185.6644	1077.7869	130.13419
0	0.004822	2125.8973	887.65558	711.07414	26.609255	29.11834	101.39595	1442.0007	3779.1765	102.81138
0	11.033787	221.91389	73.204285	93.303299	31.643915	7.2795849	123.11444	60.709744	102.10121	0.7651721
1	7.5362989	100.69556	28.917205	59.460356	10.153155	2.9360086	46.65165	19.614602	57.038186	3.794359
1	0.0014139	186.6066	6.2934722	2.5033434	71.697762	9.1505356	17.555561	87.055056	82.931955	13.678671
0	159.1073	944.79413	931.78687	389.06198	220.38102	100	788.98616	751.6182	3858.585	208.49315
0	446.91486	1373.7047	5728.1605	414.10597	205.62277	311.66583	2728.4317	3701.4022	15116.706	998.66444
0	649.80192	20365.734	154137.27	22597.197	6224.9917	5808.1226	18.174656	8622.2949	507784.27	1679.5467
0	405.58379	3222.2578	1633.6194	3701.4022	520.53674	121.41949	1255.3346	1155.1434	3625.2284	256.68518
0	365.53258	3405.9846	1147.1642	1326.9113	1442.0007	334.03517	516.94113	3675.8347	4884.0295	1033.8823
0	0.4677651	171.71309	246.22888	180.25009	63.728031	18.049115	226.57678	99.30925	363.00766	17.67767
0	47.302882	108.67349	121.41949	282.84271	25.525303	6.886907	65.067093	73.204285	557.89747	35.601255
0	5.1832472	153.68752	58.641747	29.936968	53.588673	9.8073012	95.2638	31.425334	121.41949	33.217145

1	37.371231	267.58551	82.359102	110.95695	31.208264	8.8388348	91.383145	103.52649	440.76205	68.777091
0	152.62592	3453.5304	2617.2866	1800.0936	1679.5467	527.80316	373.2132	8503.5892	462.67527	502.80535
0	27.739237	263.90158	208.49315	190.5276	79.004131	34.868592	74.226179	640.8559	117.28349	29.320874
1	912.61097	3027.3845	794.474	731.06516	232.94672	200	324.90096	8100.8422	1534.8226	726.01532
0	0.0002102	462.67527	139.47437	169.34906	61.985385	22.221067	68.777091	138.51095	881.52409	16.493849
0	0.0001119	602.0987	223.45743	176.5406	502.80535	0.0018527	425.74807	5649.2992	440.76205	44.751254
0	23.004691	37.892914	17.800627	70.222244	1.2259127	26.242917	51.763246	98.62327	126.57566	5.5552668
0	7.7481731	0.0020844	845.61443	187.90455	23.325825	350.64229	0.0020844	2672.2813	8271.0581	14.968484
0	389.06198	4164.2939	2985.7056	2155.5737	2067.7645	437.71748	565.68542	9435.323	711.07414	1204.1974
1	143239703	1.122E+09	104857600	4764377.1	924345007	32724236	234312096	2.183E+09	186403821	50642883
0	21.168633	22.687979	33.448189	65.067093	17.924441	4.5122787	73.204285	110.95695	228.15274	13.773814
0	2528.1322	6268.2899	1997.3289	1402.5692	20225.058	1567.0725	29611.218	49455.94	1956.2244	833.97261
1	286.79105	343.42617	303.14331	208.49315	978.11222	284.81004	881.52409	2442.0147	506.30264	33.217145
1	150.52467	938.26796	762.1104	35.111122	2391.7588	632.03305	2125.8973	8503.5892	313.83364	97.94203
0	686.85235	1212.5733	1115.7949	119.74787	2358.8307	569.62008	4986.6533	17007.178	506.30264	39.229205
0	22.221067	303.14331	70.710678	66.896378	98.62327	117.28349	381.0552	95.926412	16.042824	0.7546378
0	450.02339	499.33222	348.22023	189.21153	355.53707	127.45606	176.5406	918.95868	212.87404	33.680839
0	10.083022	22.067575	29.730178	61.985385	5.2556026	4.9377582	19.07824	48.971015	239.49574	6.9348092
0	2358.8307	1577.9723	4463.1797	11616.245	2690.8685	489.05611	5162.5073	4494.2236	18610.848	394.49308
0	772.74906	2545.7167	557.89747	1825.2219	348.22023	156.91682	1442.0007	721.00037	805.56444	8.075E-05
0	80.664176	171.71309	59.873935	56.252924	50.347778	59.460356	54.714685	345.81489	75.785828	1.1125392
0	69.737183	108.67349	88.884268	25.173889	49.654625	10.083022	19.751033	756.84612	134.72336	5.6719947
0	71.20251	8926.3595	305.25184	128.34259	113.28839	0.0218512	1983.5323	239.49574	696.44045	7.3302184

G11	G12	G13	G14	G15	G16	G17	G18	G19	G20	G21
123.11444	4.9036506	25.348987	263.90158	3994.6578	4652.7121	381.0552	40.053494	682.10791	191.85282	472.39706
4.76956	11.033787	7.2795849	195.88406	1147.1642	2375.2377	142.40502	26.061644	453.15355	15.177436	130.13419
25.173889	2.4013675	5.2192995	123.97077	711.07414	906.30711	37.113089	24.148408	153.68752	602.0987	49.311635
6.25	1.067219	0.8789519	62.416527	453.15355	944.79413	180.25009	4.3284671	102.10121	4.3888902	59.049633
26.794337	7.9660039	1.8840747	81.790206	450.02339	1679.5467	110.19051	38.958229	236.19853	290.7945	66.434291
5.2192995	33.680839	3.7162722	85.263489	262.07868	800	25.348987	42.044821	92.018765	984.91553	32.085647
9.6722812	0.4186615	2.8164077	48.971015	450.02339	1019.6485	39.229205	10.511205	151.57166	43.527528	68.777091
7.9660039	1.1517728	1.2603777	24.148408	172.90745	123.11444	77.916458	3.103414	91.383145	12.586944	57.038186
5.9128603	25.881623	1.7217267	38.958229	249.66611	839.77335	88.884268	9.4077922	129.23528	18.049115	74.742462
422.80722	97.265495	150.52467	316.01652	5270.9825	18870.646	52.123288	303.14331	478.99148	9113.9213	97.94203
1.5197734	2.1196943	3.983002	40.895103	546.4161	1383.2596	21.168633	27.739237	73.713461	971.35591	5.6719947
20.877198	2.1944451	7.4325445	69.737183	381.0552	978.11222	50.347778	21.315872	82.931955	151.57166	48.632747
8.9622203	3.0606884	2.7204705	67.361679	585.63428	1123.5559	86.453723	18.174656	123.11444	278.94873	40.61262
6.5607293	1.1841536	6.6063628	13.584186	105.7018	400	15.496346	20.589775	43.527528	152.62592	16.15441
1204.1974	10.732068	60.709744	31.864016	1204.1974	4816.7896	185.31761	20.877198	53.588673	778.12396	30.992692

6.2934722	0.0667012	34.151006	39.776824	1.3415085	1229.5001	1.884E-05	15.821957	138.51095	1.884E-05	52.850902
133.79276	12.674493	163.58041	606.28663	6355.792	10689.125	1108.0876	220.38102	2247.1118	428.70939	247.94154
10.957572	100.69556	0.0106268	4.449E-05	610.50368	2904.0613	74.226179	788.98616	597.9397	341.05396	236.19853
30.145196	0.0001358	193.18727	184.03753	828.21194	2262.7417	45.375958	32.085647	201.39111	845.61443	105.7018
10.366494	0.4944362	57.834409	23.981603	341.05396	1534.8226	102.81138	2.7969533	212.87404	146.40857	74.742462
2.1492841	2.8755864	70.710678	115.66882	696.44045	2231.5899	253.15132	29.524817	345.81489	453.15355	70.222244
87.055056	0.2438146	28.126462	95.2638	1077.7869	3429.6751	386.37453	9.944206	422.80722	107.92282	111.72871
14.458602	0.4364403	4193.2589	2155.5737	3805.4628	8271.0581	509.82425	2067.7645	1070.342	21083.93	663.45564
0.8088007	0.4072132	7.8020659	10.584316	136.60403	236.19853	1.7824433	4.5122787	30.77861	1195.8794	8.9622203
1.314E-05	0.5190179	1.314E-05	3.7162722	11.033787	20.166044	107.17735	0.283979	19.344562	0.3239529	1.4988502
1.3984767	0.0530632	1.251E-05	3.0819772	14.968484	28.126462	15.712667	0.1521806	27.357343	2.35E-06	0.7651721
0.4456108	0.1032244	0.2259157	1.9640834	9.7395572	80.664176	5.7911754	0.2008035	14.660437	0.6215129	8.6569342
0.3988329	0.0177487	0.401607	0.854917	12.158187	51.763246	4.0949794	0.1153313	50.347778	0.1439716	14.458602
0.9685216	0.0943297	0.1129578	2.9977004	10.083022	47.302882	6.3372467	0.2355093	25	0.1161335	1.7948412
0.3799433	0.0917503	0.0815516	3.5402621	11.744034	51.405691	6.0371021	0.439476	20.026747	0.6569503	1.5953314
0.1145347	0.0022496	0.0917503	1.7948412	1.8325546	23.981603	0.1809742	0.1631031	0.9099481	0.3129179	1.8073253
0.0080536	1.30E-06	0.0004862	1.2006837	0.7704943	24.485507	0.2724109	0.2137292	0.6754197	0.2724109	1.3415085
0.1994164	0.0844275	0.2506691	5.1118879	40.895103	70.710678	0.8912217	0.3284752	4.5752678	1.991501	2.4348893
0.198039	0.0061887	0.0714886	2.664484	21.915143	47.6319	0.4072132	0.5083367	3.4915223	0.7089993	3.6146506
0.4186615	0.0997082	1.1125392	3.7162722	11.422893	160.21398	9.8755164	0.579892	2.6460791	1.7098339	1.4278616
0.0534323	0.0085128	0.1137435	1.0598471	11.422893	30.566007	1.5625	0.0338161	14.762408	0.1061265	3.7681495
0.0385762	0.0214015	0.0976563	1.19239	10.957572	40.053494	2.179287	0.0729907	20.026747	0.2668047	2.8755864
0.2489376	0.1185737	0.0821188	0.8974206	8.0772052	32.085647	6.3372467	0.1011001	13.030822	0.0416326	1.0026765
0.1688549	0.0681027	0.0443125	0.6479059	7.0316155	47.963206	2.8164077	0.0086317	13.121459	0.2762136	0.8144264
0.232267	0.196671	0.0568718	1.8073253	29.11834	54.336743	4.0386026	0.0474929	10.584316	0.1352646	2.335702
0.085606	0.0019584	1.8581361	5.9128603	46.976137	127.45606	2.8955877	0.2306626	153.68752	0.8974206	10.366494
0.0809882	4.04E-06	0.1018033	1.2174447	21.613431	92.658806	12.158187	0.196671	12.413656	0.7598867	6.2068281
0.1202289	0.3217152	0.2404579	3.742121	23.81595	110.95695	17.194273	0.4487103	10.732068	0.4157696	4.5436641
0.1642376	0.0286337	0.1083564	3.742121	22.687979	87.055056	3.3725882	0.1459814	4.0386026	0.2137292	1.9640834
0.5486113	0.0997082	0.0013284	3.3960464	35.601255	81.790206	9.3428078	0.191293	22.531262	0.0338161	3.3725882
0.1748096	2.56E-06	0.3472042	0.4334256	17.67767	67.361679	1.7457612	0.1270842	8.2469244	0.1039424	5.7511728
0.4215735	0.0242454	0.1860621	2.8359974	77.916458	133.79276	1.6630784	0.4613253	1.2958118	0.2404579	2.1944451
0.2541683	0.1129578	0.5486113	1.8073253	44.751254	112.50585	1.6176014	0.2438146	1.9103754	0.227487	1.7701311
0.0280444	0.0234195	0.1153313	1.1048543	3.5402621	25.525303	0.7598867	0.0468391	16.724094	0.1784827	4.0666933
0.3330605	0.0124635	0.3107564	0.4245058	7.1793647	24.316374	0.8608634	0.0911165	10.806715	0.0127254	2.683017
0.0045936	0.1279681	0.1469968	0.3852472	4.76956	11.110534	0.1653799	0.0068668	2.8955877	0.0364953	1.4377932
0.0182477	0.2107868	0.2137292	0.6172198	6.6985841	13.397168	0.198039	0.0068668	5.9954007	0.0055776	1.2430258
0.0667012	0.0079428	0.1553782	0.3879268	11.422893	27.168372	0.0282395	0.0766195	5.6719947	0.0211069	1.4782151
0.013451	0.0294387	0.0776891	0.4581387	4.0386026	11.582351	0.1480192	0.0419221	3.3031814	0.0212537	1.0525262
0.1809742	0.0094456	0.0001445	1.1048543	10.438599	43.830286	0.9290681	0.0404941	4.1810236	0.0150286	1.3230396

0.9355302	0.0491678	0.1575472	2.8755864	33.448189	69.737183	4.6391362	0.1597465	2.4518253	0.0370048	1.0598471
386.37453	18.301071	82.931955	1556.2479	19134.07	53745.494	2635.4913	109.42937	1.6862941	79.553648	0.9420374
20.166044	2.7969533	334.03517	237.84142	24219.076	54119.324	0.0015797	5.5552668	152.62592	0.0015797	41.754396
48.632747	25.348987	209.94334	29.524817	19267.158	29406.678	0.0017167	9.8755164	37.892914	0.0017167	57.434918
0.0804288	0.6754197	0.2182201	1.5409886	15.283003	40.61262	2.1492841	0.1480192	10.294888	0.0523327	4.0386026
0.0172633	0.026902	0.9099481	14.762408	46.329403	857.41877	62.416527	2.351948	52.850902	0.5640348	26.609255
9.2141826	175.32114	309.513	6054.7689	41587.323	178288.76	9500.9509	1354.7925	53.218509	701.28458	24.316374
1.0972226	1.9236631	2.1944451	30.145196	242.83898	462.67527	14.259546	1.0380358	0.0272775	2.9360086	3.767E-05
9.2782723	9.6054699	40.053494	61.132014	434.69395	292.81714	7.1297732	47.963206	0.0639841	778.12396	6.4704058
277.02189	151.57166	546.4161	292.81714	756.84612	1983.5323	531.47433	2200.8669	711.07414	13910.206	200
155.83292	123.11444	168.17928	475.68285	3244.6703	10469.146	136.60403	756.84612	649.80192	0.0032935	0.0032935
96.593633	237.84142	2082.147	1825.2219	4193.2589	7717.1701	1100.4335	5307.6451	2375.2377	0.0304768	0.0304768
25.702846	223.45743	368.07506	711.07414	5768.003	5930.1636	174.11011	581.58901	1714.8375	7506.1437	19.614602
30.566007	3.4434535	31.643915	0.3472042	208.49315	565.68542	19.614602	13.212726	76.843759	241.16157	1.1517728
5.4787858	0.9957505	1.6401823	17.924441	118.92071	416.9863	18.685616	1.0598471	31.425334	7.0316155	3.9554894
9.4077922	3.6146506	73.204285	0.0014139	80.664176	811.16758	0.1025114	82.931955	0.3569654	520.53674	6.6985841
105.7018	37.631169	205.62277	569.62008	3267.2388	9768.0589	198.6185	459.47934	1482.5409	8157.188	391.76812
0.0017167	365.53258	355.53707	1147.1642	1956.2244	15434.34	1264.0661	1317.7456	619.026	2082.147	1837.9174
3.6651092	1691.2289	5234.5732	2067.7645	178288.76	22132.153	2425.1465	18870.646	4311.1474	0.0220032	0.0220032
465.89343	236.19853	130.13419	581.58901	7770.8473	27059.662	5728.1605	419.88667	3550.6223	100	100
205.62277	437.71748	1195.8794	2884.0015	14104.385	14301.275	478.99148	3382.4577	5889.201	51200	1863.5737
14.762408	2.4688791	37.371231	142.40502	672.71713	1567.0725	81.22524	40.61262	212.87404	557.89747	60.290391
48.632747	3.6906021	7.9109787	73.713461	569.62008	1825.2219	89.502507	25.173889	80.664176	102.81138	23.981603
5.5552668	4.6070913	8.1333866	53.588673	632.03305	1432.0401	40.332088	15.712667	126.57566	212.87404	24.827312
22.067575	14.762408	31.208264	21.763764	246.22888	668.07034	22.221067	40.895103	69.737183	520.53674	30.354872
0.6003419	456.30549	40450.115	3267.2388	1281.7118	2476.104	66.896378	1085.2835	12025.891	29611.218	875.43496
9.4077922	13.304627	1383.2596	186.6066	273.20805	2884.0015	16.493849	16.042824	531.47433	1492.8528	77.916458
172.90745	35458.802	345.81489	900.04679	2476.104	10182.867	636.42919	3289.9642	282.84271	16542.116	194.53099
26.425451	7.5362989	0.0162193	0.0002102	581.58901	1556.2479	78.45841	1.2603777	1.3139006	331.72782	39.502066
33.448189	92.658806	7.9660039	0.0001119	606.28663	1812.6142	20.877198	5307.6451	2.0193013	1255.3346	87.055056
11.662912	0.4518313	61.985385	40.332088	1.3792234	736.15012	31.425334	23.81595	40.053494	767.4113	27.739237
0.0020844	0.0020844	1085.2835	794.474	6224.9917	3453.5304	142.40502	4525.4834	1299.6038	0.0020844	0.0020844
863.38259	0.0018146	9177.3136	1929.2925	1577.9723	4311.1474	3753.0718	263.90158	4022.4428	6534.4776	414.10597
15221.851	46144.024	8.917E+09	1.43E+09	99891334	80576522	6645084.8	475165941	95160281	1.678E+09	495344224
9.944206	0.1352646	60.709744	31.864016	168.17928	389.06198	35.111122	16.379918	52.123288	38.689125	50
0.0022652	23.164702	58003.655	20507.389	1983.5323	4164.2939	360.50019	30443.702	2672.2813	374305.36	10042.676
69.737183	5.4787858	2672.2813	1108.0876	991.76616	2262.7417	74.226179	746.42639	358.01003	3779.1765	469.13398
0.7494251	19.751033	6224.9917	2563.4236	1345.4343	984.91553	127.45606	1326.9113	258.47057	14006.959	1679.5467
87.660572	3.901033	12109.538	1588.948	1513.6922	29817.18	208.49315	3967.0646	446.91486	9904.416	2528.1322
0.4677651	288.78584	156.91682	301.04935	585.63428	81.790206	253.15132	25.881623	13.869618	48.971015	3.4196678

8.478777	22.221067	313.83364	378.42306	179.00501	1679.5467	88.884268	696.44045	177.76854	5091.4335	107.92282
13.304627	3.5402621	6.9348092	14.161049	155.83292	565.68542	26.980706	4.7366143	170.52698	1863.5737	28.519093
3267.2388	103.52649	1373.7047	1763.0482	13251.391	61310.91	4685.0742	386.37453	7052.1927	131422.81	1033.8823
98.62327	25.881623	55.478474	177.76854	2747.4094	7003.4797	569.62008	336.35857	408.40485	13159.857	169.34906
0.0003298	0.0003298	214.35469	17.075503	114.07637	741.27045	0.6434305	21.464136	60.709744	36709.254	365.53258
2.7016788	1.4680043	9370.1485	172.90745	150.52467	778.12396	41.465977	126.57566	61.985385	4620.5734	39.229205
187.90455	0.4842608	152015.21	5021.3382	453.15355	1085.2835	106.43702	1402.5692	126.57566	606.28663	125.70134

Conclusion

The ROC curve indicates that the AUC is 0.788, so far from the perfectly discriminating model of about 20%. It can therefore be deduced from the obtained results that these transcriptomic data do not allow obtaining a model that discriminates in the absolute sense, despite the relatively near-acceptable performance. Therefore, these data are not exploitable.

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