Results

- The table below (**Table**) shows the estimate, standard error, test statistic, and p-values associated with the fixed-effect slope parameter as estimated by each modeling method for the $MALAT1 \sim CD19$ variable pairing.

Model Designation	Model Description	Estimate	Std. Error	Test Statistic	p-value
LM	Linear Model	4.918e-2	1.455e-2	3.381*	7.47e-4
LM-FE	Linear Model with Fixed-Effect Intercept	4.833e-2	1.381e-2	3.500*	4.84e-4
LMM-RI	Linear Mixed Model with Random Intercept	4.920e-2	1.374e-2	3.579*	3.6e-4
LMM-RS	Linear Mixed Model with Random Slope	5.938e-2	3.538e-2	1.678*	1.19e-1
GEE	Generalized Estimating Equations	4.918e-2	1.455e-2	3.381**	7.47e-4

Table : Summary table for each model method, $MALAT1 \sim CD19$ variable pairing. ** Approximate Wald-Z distribution

- The table below (**Table**) shows the estimate, standard error, test statistic, and p-values associated with the fixed-effect slope parameter as estimated by each modeling method for the $FBLN1 \sim CD34$ variable pairing.

Model Designation	Model Description	Estimate	Std. Error	Test Statistic	p-value
LM	Linear Model	7.884e-1	4.92e-2	4.002*	<2e-16
LM-FE	Linear Model with Fixed-Effect Intercept	1.31e-1	3.42e-2	3.818*	1.42e-4
LMM-RI	Linear Mixed Model with Random Intercept	1.35e-1	3.42e-2	3.95*	8.4e-5
LMM-RS	Linear Mixed Model with Random Slope	1.705e-1	7.29e-2	2.34*	6.7e-2
GEE	Generalized Estimating Equations	7.884e-1	4.92e-2	4.002**	< 2e-16

Table : Summary table for each model method, $FBLN1 \sim CD34$ variable pairing. ** Approximate Wald-Z distribution

- The fixed effect slope parameter is being considered for comparison because we are interested in quantifying correlation between single-cell values at the subject level.

- Displayed in **table** , **table** , and **table** below are percent change in: parameter estimate, standard error, and test statistic (respectively) for the $MALAT1 \sim CD19$variable pairing as defined by:

$$\text{Percent Change } [A]_{ij} = \left(\frac{A_j - A_i}{A_i}\right) * 100$$

Parameter Estimate Percent Change

Model	LM	LM-FE	LMM-RI	LMM-RS	GEE
LM	0	-1.7283	0.0407	20.7401	0.0000
LM-FE	1.7587	0	1.8001	22.8636	1.7587
LMM-RI	-0.0407	-1.7683	0	20.6911	-0.0407
LMM-RS	-17.1775	-18.6090	-17.1438	0	-17.1775
GEE	0.0000	-1.7283	0.0407	20.7401	0

Table : Main effect slope percent change matrix, $MALAT1 \sim CD19$ variable pairing

Standard Error Percent Change

Model	LM	LM-FE	LMM-RI	LMM-RS	GEE
LM	0	-5.0859	-5.5670	143.1615	0.0000
LM-FE	5.3584	0	-0.5069	156.1912	5.3584
LMM-RI	5.8952	0.5095	0	157.4964	5.8952
LMM-RS	-58.8751	-60.9666	-61.1645	0	-58.8751
GEE	0.0000	-5.0859	-5.5670	143.1615	0

Table : Main effect slope standard error percent change matrix, $MALAT1 \sim CD19$ variable pairing

Test Statistic Percent Change

Model	LM	LM-FE	LMM-RI	LMM-RS	GEE
LM	0	3.5197	5.8563	-50.3697	0.0000
LM-FE	-3.4000	0	2.2571	-52.0571	-3.4000
LMM-RI	-5.5323	-2.2073	0	-53.1154	-5.5323
LM-RS	101.4899	108.5816	113.2896	0	101.4899
GEE	0.0000	3.5197	5.8563	-50.3697	0

Table : Main effect slope test statistic percent change matrix, $MALAT1 \sim CD19$ variable pairing

- Displayed in **table** , **table** , and **table** below are percent change in: parameter estimate, standard error, and test statistic (respectively) for the $FBLN1 \sim CD34$ variable pairing as defined by:

$$\text{Percent Change } [A]_{ij} = \left(\frac{A_j - A_i}{A_i}\right) * 100$$

Parameter Estimate Percent Change

Model	LM	LM-FE	LMM-RI	LMM-RS	GEE
LM	0	-83.3841	-82.8767	-78.3739	0.0000
LM-FE	501.8321	0	3.0534	30.1527	501.8321
LM-RI	484.0000	-2.9630	0	26.2963	484.0000
LM-RS	362.4047	-23.1672	-20.8211	0	362.4047
GEE	0.0000	-83.3841	-82.8767	-78.3739	0

Table : Main effect slope percent change matrix, $FBLN1 \sim CD34$ variable pairing

Standard Error Percent Change

Model	LM	LM-FE	LMM-RI	LMM-RS	GEE
LM	0	-30.4878	-30.4878	48.1707	0.0000
LM-FE	43.8596	0	0.0000	113.1579	43.8596
LM-RI	43.8596	0.0000	0	113.1579	43.8596
LM-RS	-32.5103	-53.0864	-53.0864	0	-32.5103
GEE	0.0000	-30.4878	-30.4878	48.1707	0

Table : Main effect slope standard error percent change matrix, $FBLN1 \sim CD34$ variable pairing

Test Statistic Percent Change

Model	LM	LM-FE	LMM-RI	LMM-RS	GEE
LM	0	-4.5977	-1.2994	-41.5292	0.0000
LM-FE	4.8193	0	3.4573	-38.7114	4.8193
LM-RI	1.3165	-3.3418	0	-40.7595	1.3165
LM-RS	71.0256	63.1624	68.8034	0	71.0256
GEE	0.0000	-4.5977	-1.2994	-41.5292	0

Table : Main effect slope test statistic percent change matrix, $FBLN1 \sim CD34$ variable pairing

Parameter Estimates

- Models LM and GEE have similar estimates
- Models LM-FE, LM-RI, and LM-RS are also all similar
- Estimates are less similar when comparing between the two clusters of similarity mentionioned
- Accounting for subject-specific outcomes results in a different estimate than when modeling population-averages, i.e. there is an effect from subject-level correlation
- The effect is more pronounced in the FBLN1~CD34 pairing than the MALAT1~CD19 pairing

Standard Error Estimates

- The standard error of the fixed effect slope parameter estimate is highest for the random slope model
- The SE is lowest for the random intercept model
- The fixed-effect subject-specific intercept had a lower SE than either of the population-average parameter interpretaion models LM and GEE.

Test Statistics

- Changes in test statistics for the fixed-effect main-effect slope were smaller between LM and GEE, as well as between LM-FE, LMM-RI, and LMM-RS with few exceptions.
- There were very small differences between LM and GEE
- Changes to the LMM-RS resulted in calculated p-value increases with two and three orders of magnitude.

Nested Model Comparisons

Test for FE Subject Specific Intercept

Variable Pair	Model	Resid DF	RSS	DF	Sum of Squares	F-stat	P(>F)
MALAT1-CD19	LM	1108	1167.76				
	LM-FE	1094	935.89	14	231.87	19.36	< 2.2e-16
FBLN1-CD34	LM	1108	650.51				
	LM-FE	1094	214.92	14	435.59	158.38	< 2.2e-16

Table : ANOVA nested model comparison table for testing the inclusion of the subject-specific fixed-effect intercept

Table above is a nested model comparison, the result of which is an F-test statistic telling us that there is very strong evidence to support the inclusion of the subject-specific fixed-effect intercept into the LM model.

Test for RE Subject Specific Intercept

Variable Pair	Model	df	AIC	logLik	L.Ratio	p-value
MALAT1-CD19	LM	3	3224.097	-1609.048		
	LMM-RI	4	3032.024	-1512.012	194.0722	<1e-4
FBLN1-CD34	LM	3	2572.807	-1283.403		
	LMM-RI	4	1438.086	-715.043	1136.72	<1e-4

Table : ANOVA nested model comparison table for testing the inclusion of the subject-specific random effect intercept

Table above is a nested model comparison, the result of which is a likelihood ratio statistic telling us that there is very strong evidence to support the inclusion of the subject-specific random effect intercept into the LM model.

Test for RE Subject Specific Slope

Variable Pair	Model	df	AIC	logLik	L.Ratio	p-value
MALAT1-CD19	LMM-RI	4	3032.024	-1512.012		
	LMM-RS	6	2993.820	-1490.910	42.20503	<1e-4
FBLN1-CD34	LMM-RI	4	1438.086	-715.043		
	LMM-RS	6	1438.068	-713.034	4.018095	0.1341

Table : ANOVA nested model comparison table for testing the inclusion of the subject-specific random effect slope

Table above is a nested model comparison, the result of which is a likelihood ratio statistic telling us that there is very strong evidence to support the inclusion of the subject-specific random effect slope into the LMM-RI model for the MALAT1~CD19 variable pairing. However, there is insufficient evidence to support the inclusion of the subject-specific random effect slope into the LMM-RI model for the FBLN~CD34 variable pairing.

References

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