

**Performance of transcriptomic clocks
(All models, sex-combined, and sex-split)**

BayesAge 2.0

Sex-combined

Tissues	# of Genes	Pearson R	R-Squared	MAE (days)
Bone	25	0.803	0.645	20.4
Brain	35	0.873	0.763	13.7
Fat	25	0.795	0.633	18.8
Gut	10	0.929	0.863	10.9
Heart	10	0.88	0.774	14.2
Kidney	20	0.776	0.603	19.4
Liver	25	0.735	0.54	21.9
Muscle	10	0.855	0.732	15.5
Ovary	50	0.716	0.513	19.1
Retina	20	0.749	0.562	18.4
Skin	20	0.852	0.726	15.9
Spinal Cord	45	0.87	0.757	14.1
Spleen	50	0.768	0.591	18.9
Testis	15	0.925	0.856	10.7

BayesAge 2.0

Female

Tissues	# of Genes	Pearson R	R-Squared	MAE (days)
Bone	10	0.814	0.663	20.762
Brain	50	0.911	0.829	12.7
Fat	10	0.847	0.718	15.174
Gut	35	0.851	0.725	13.2
Heart	10	0.705	0.497	19.8
Kidney	45	0.683	0.467	24
Liver	10	0.849	0.721	15.217
Muscle	15	0.902	0.813	12.6
Ovary	50	0.716	0.513	19.1
Retina	30	0.829	0.686	10.857
Skin	10	0.918	0.843	11.6
Spinal Cord	10	0.941	0.885	9.870
Spleen	20	0.885	0.784	12.348

BayesAge 2.0

Male

Tissues	# of Genes	Pearson R	R-Squared	MAE (days)
Bone	30	0.739	0.546	21.533
Brain	35	0.811	0.658	16.2
Fat	10	0.658	0.434	24.300
Gut	20	0.897	0.804	13.2
Heart	15	0.935	0.873	9.969
Kidney	50	0.821	0.674	19.2
Liver	15	0.857	0.735	16.419
Muscle	40	0.902	0.814	12.688
Retina	20	0.799	0.638	20.000
Skin	45	0.855	0.73	16.4
Spinal Cord	20	0.861	0.741	16.387
Spleen	35	0.789	0.622	17.125
Testis	15	0.925	0.856	10.7

Elastic Net Regression

- Random seeding = 42 for reproducibility for all the tissues.
- First pass max iteration = 10,000 and second pass max iteration = 100,000 for all the tissues.
- LOOCV

Sex-combined

Tissues	Pearson R	R-Squared	MAE (days)
Bone	0.803	0.644	20.156
Brain	0.857	0.731	16.502
Fat	0.851	0.716	18.365
Gut	0.930	0.854	12.386
Heart	0.888	0.788	14.447
Kidney	0.912	0.825	12.564
Liver	0.951	0.899	8.882
Muscle	0.893	0.796	14.688
Ovary	0.706	0.486	20.697
Retina	0.825	0.666	16.917
Skin	0.907	0.819	14.126
Spinal Cord	0.917	0.828	13.326
Spleen	0.866	0.750	15.450
Testis	0.983	0.949	7.938

Hyperparameter Tuning

Tissue	Alpha	L1 Ratio	MAE
Bone	0.1	0.8	20.156
Brain	0.01	0.1	16.502
Fat	0.001	0.1	18.365

Gut	0.1	0.8	12.386
Heart	0.01	1.0	14.447
Kidney	0.01	0.9	12.564
Liver	0.1	1.0	8.882
Muscle	0.01	0.9	14.688
Ovary	0.01	0.1	20.697
Retina	0.01	0.3	16.917
Skin	0.1	0.5	14.126
Spinal Cord	0.01	0.6	13.326
Spleen	0.01	1.0	15.450
Testis	0.1	1.0	7.938

Elastic Net Regression

Female

Tissues	Pearson R	R-Squared	MAE (days)
Bone	0.900	0.772	13.982
Brain	0.923	0.840	13.024
Fat	0.736	0.536	21.328
Gut	0.921	0.835	11.917
Heart	0.702	0.443	21.860
Kidney	0.685	0.440	22.839
Liver	0.847	0.702	16.921
Muscle	0.755	0.570	21.304
Ovary	0.706	0.486	20.697
Retina	0.578	0.159	18.037
Skin	0.901	0.802	15.105
Spinal Cord	0.659	0.377	23.302
Spleen	0.831	0.681	17.555

Hyperparameter Tuning (Female)

Tissue	Alpha	L1 Ratio	MAE
Bone	0.01	1.0	13.982
Brain	0.001	0.9	13.024
Fat	0.01	0.0	21.328
Gut	1.0	1.0	11.917
Heart	0.0001	0.0	21.860
Kidney	0.1	0.9	22.839
Liver	0.1	1.0	16.921
Muscle	0.001	0.0	21.304

Ovary	0.01	0.1	20.697
Retina	0.0001	0.300000000 0000004	18.037
Skin	0.01	1.0	15.105
Spinal Cord	0.001	0.8	23.302
Spleen	0.01	0.9	17.555

Elastic Net Regression

Male

Heart: First pass max iteration 30,000, second iteration 100,000

Bone: No matter the number of iterations in the first pass, it did not improve the results.

Tissues	Pearson R	R-Squared	MAE (days)
Bone	0.323	-100.087	103.854
Brain	0.852	0.709	17.394
Fat	0.805	0.646	21.284
Gut	0.916	0.839	13.666
Heart	0.895	0.792	14.660
Kidney	0.907	0.807	14.304
Liver	0.859	0.737	17.235
Muscle	0.952	0.900	9.554
Testis	0.983	0.949	7.938
Retina	0.856	0.717	16.350
Skin	0.952	0.904	9.996
Spinal Cord	0.849	0.716	17.174
Spleen	0.866	0.745	14.893

Hyperparameter Tuning (Male)

Tissue	Alpha	L1 Ratio	MAE
Bone	1.0	1.0	103.854
Brain	0.1	0.9	17.394
Fat	0.001	0.0	21.284
Gut	0.01	1.0	13.666
Heart	0.001	0.8	14.660
Kidney	0.001	0.6	14.304

Liver	1.0	1.0	17.235
Muscle	0.1	1.0	9.554
Retina	1.0	1.0	16.350
Skin	0.1	1.0	9.996
Spinal Cord	0.01	1.0	17.174
Spleen	1.0	1.0	14.893
Testis	0.1	1.0	7.938

Principal Component Regression

- Seeding number = 1
- PC Tested:
 - 1 to 20 and report on the best performing one

Sex-combined

Tissues	PC #	Pearson R	R-Squared	MAE (days)	Variance Explained
Bone	12	0.63	0.26	27.96	0.6578
Brain	11	0.87	0.75	15.30	0.5702
Fat	18	0.80	0.58	19.04	0.7296
Gut	17	0.85	0.71	17.06	0.6040
Heart	14	0.92	0.85	12.89	0.6033
Kidney	17	0.87	0.74	16.51	0.6821
Liver	11	0.82	0.64	20.17	0.5489
Muscle	15	0.91	0.83	13.61	0.5968
Retina	9	0.72	0.46	19.97	0.6479
Skin	9	0.88	0.77	16.58	0.5765
Spinal Cord	16	0.84	0.67	16.96	0.6749
Spleen	9	0.79	0.62	20.26	0.5856

Principal Component Regression

Female

Tissues	PC #	Pearson R	R-Squared	MAE (days)	Variance Explained
Bone	7	0.57	0.05	26.37	0.6348
Brain	17	0.91	0.78	13.60	0.8859
Fat	3	0.79	0.61	19.37	0.4626
Gut	10	0.71	0.35	22.76	0.6424
Heart	14	0.88	0.69	16.24	0.8176
Kidney	7	0.67	0.25	21.97	0.5977
Liver	5	0.68	0.44	23.48	0.4606
Muscle	4	0.77	0.59	19.67	0.4097
Ovary	14	0.71	0.50	20.17	1.000
Retina	13	0.76	0.57	14.76	1.0
Skin	7	0.82	0.60	20.43	0.6494
Spinal Cord	3	0.81	0.64	19.19	0.4813
Spleen	9	0.73	0.46	22.55	0.7070

Principal Component Regression

Male

Tissues	PC #	Pearson R	R-Squared	MAE (days)	Variance Explained
Bone	12	0.67	0.18	29.80	0.7641
Brain	10	0.83	0.67	19.57	0.6432
Fat	6	0.78	0.57	23.03	0.5799
Gut	10	0.86	0.73	17.89	0.5972
Heart	15	0.95	0.89	11.40	0.7431
Kidney	11	0.87	0.74	16.48	0.6836
Liver	16	0.81	0.55	20.88	0.7588
Muscle	8	0.89	0.78	15.36	0.5771
Retina	6	0.55	-0.35	30.06	0.5772
Skin	5	0.87	0.75	16.71	0.4902
Spinal Cord	16	0.86	0.65	17.86	0.7873
Spleen	7	0.69	0.38	23.32	0.6063
Testis	8	0.85	0.62	16.09	0.5193