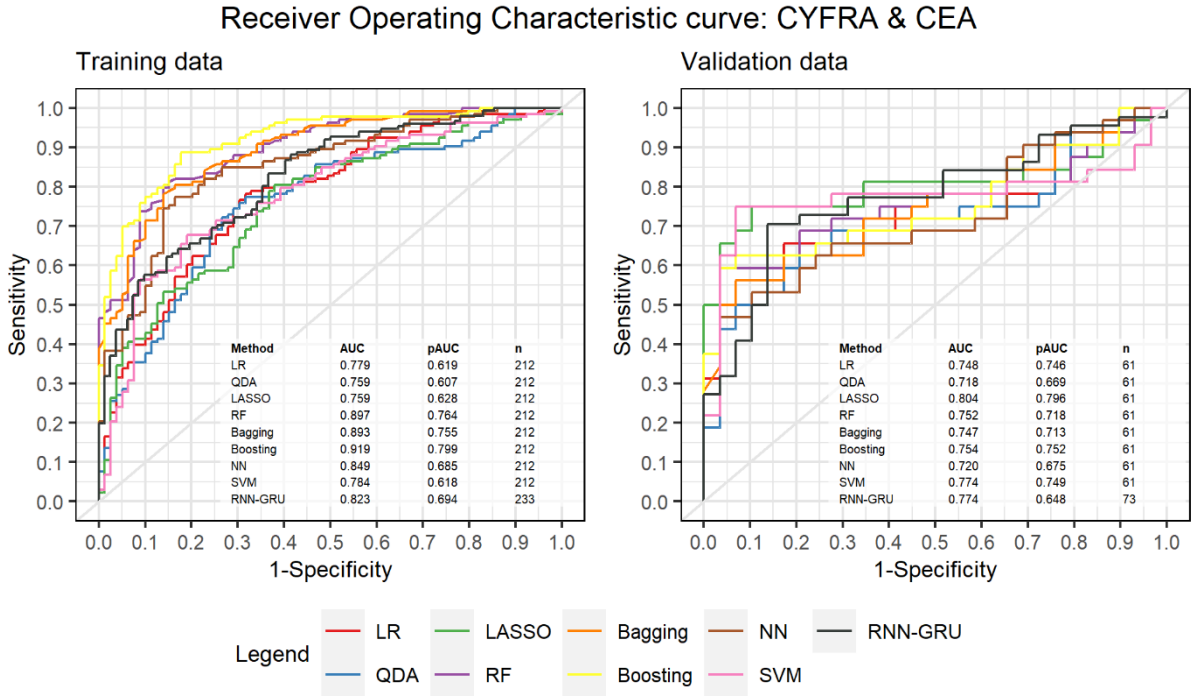
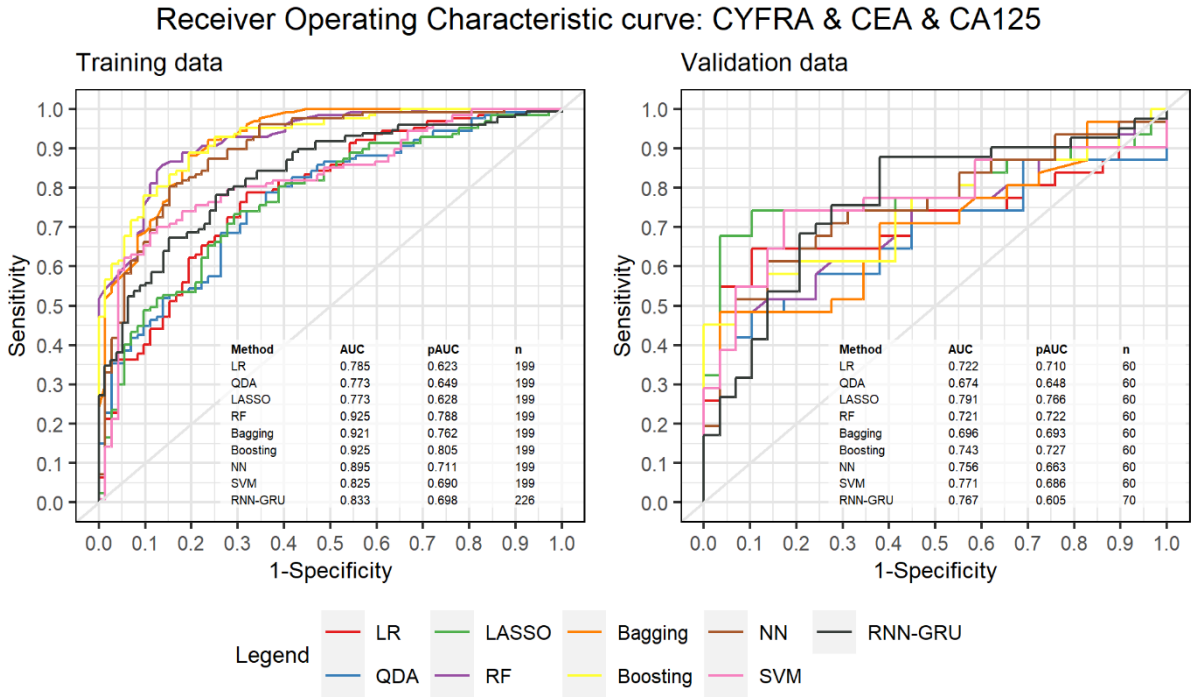
Supplementary materials

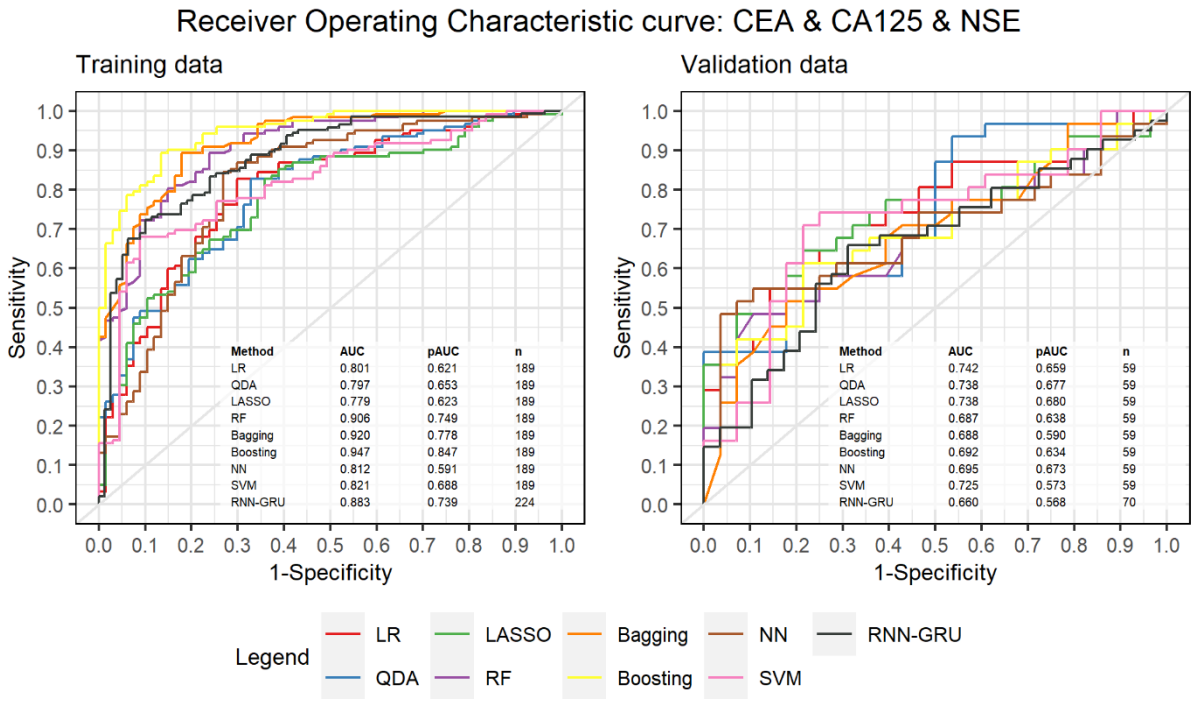
S1: Receiver operating characteristic curve for the training and validation data based on CYFRA and CEA. The partial area under curve is calculated for the specificity range 0.9 to 1.



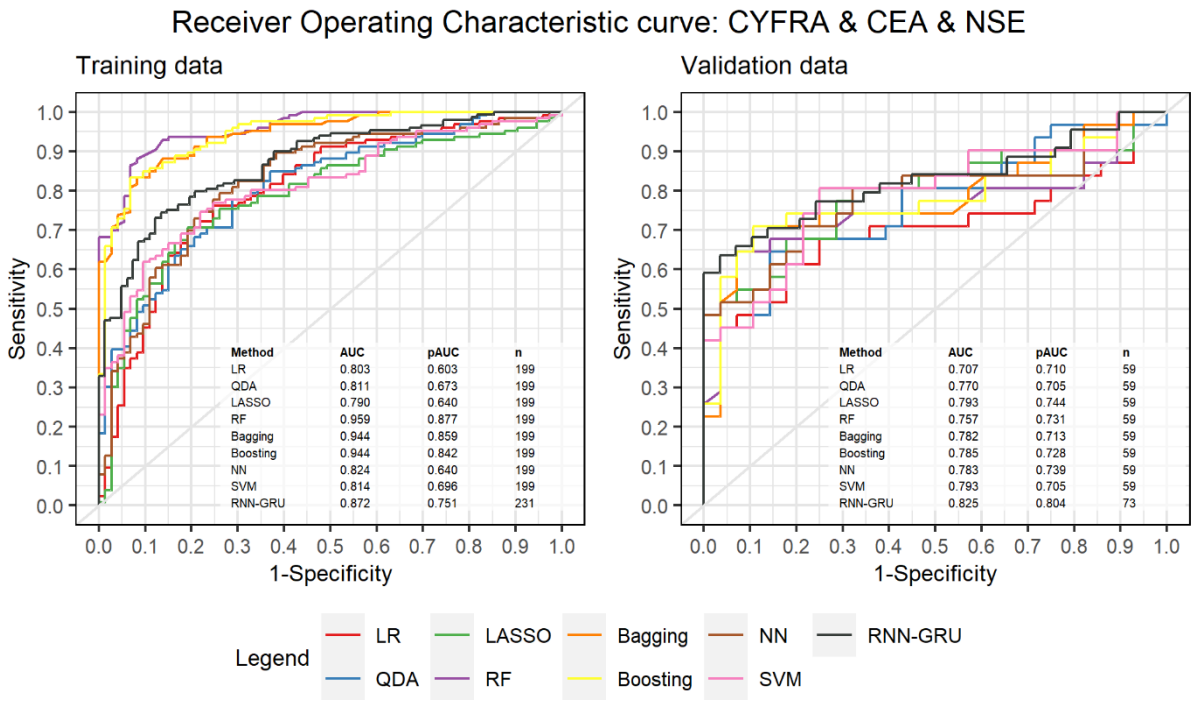
S2: Receiver operating characteristic curve for the training and validation data based on CYFRA, CEA, and CA125. The partial area under curve is calculated for the specificity range 0.9 to 1.



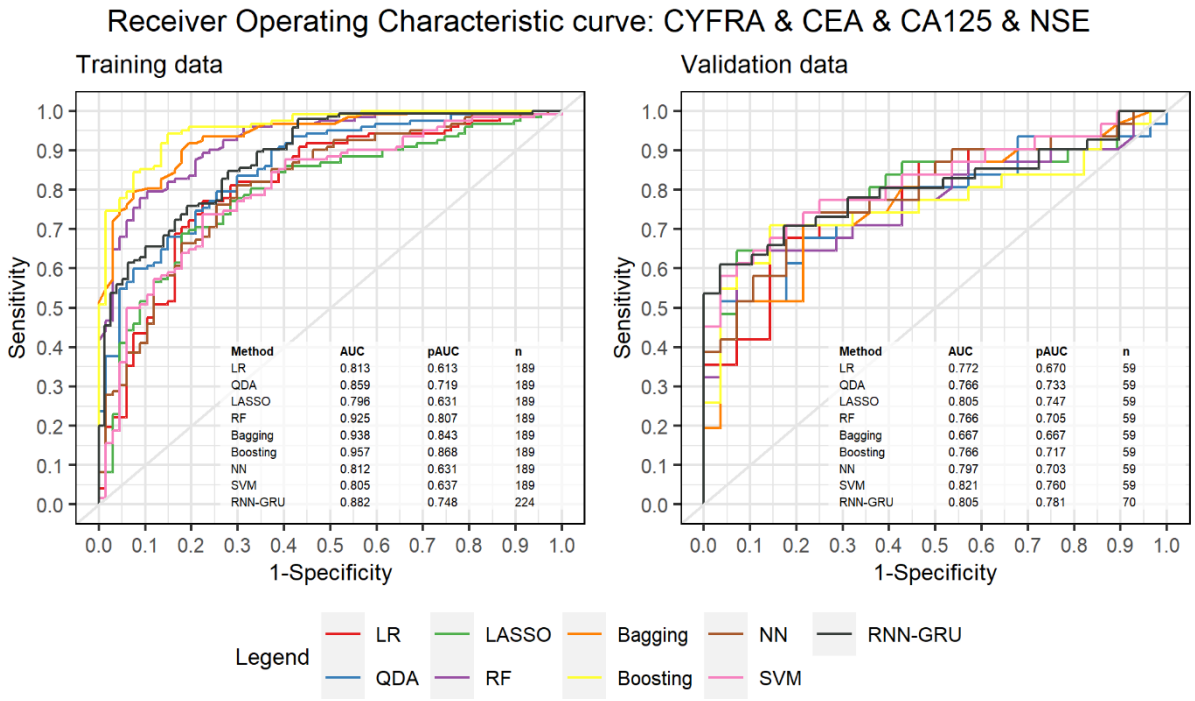
S3: Receiver operating characteristic curve for the training and validation data based on CEA, CA125, and NSE. The partial area under curve is calculated for the specificity range 0.9 to 1.



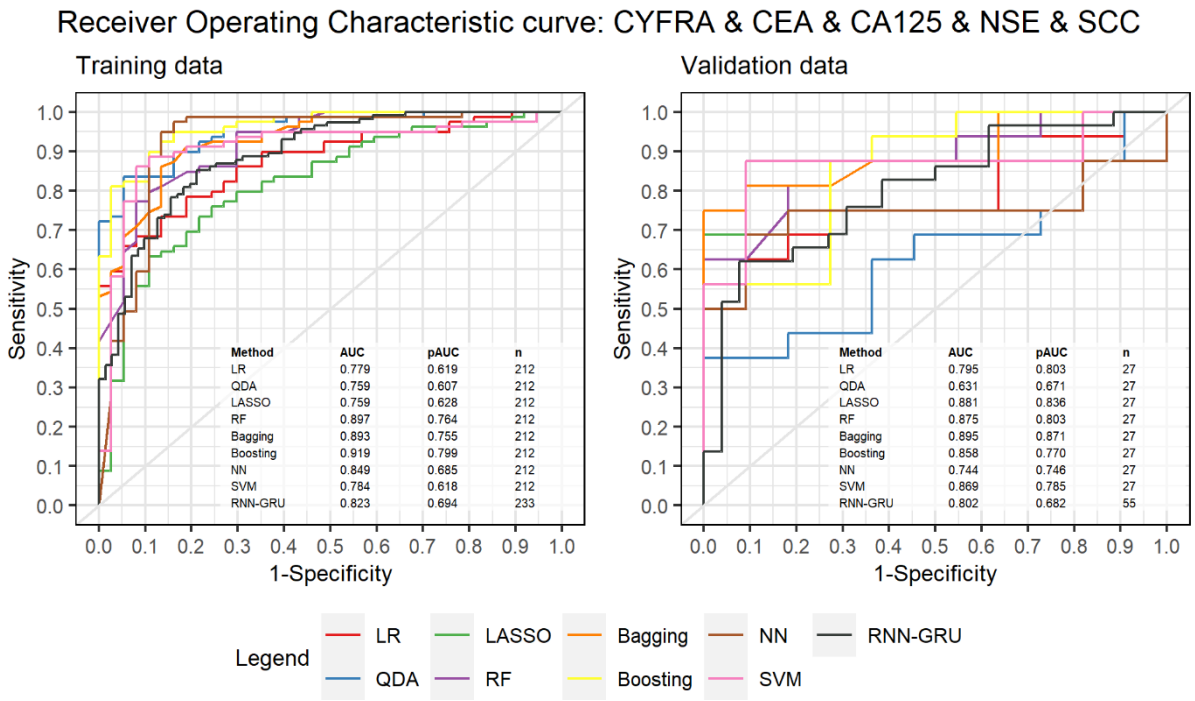
S4: Receiver operating characteristic curve for the training and validation data based on CYFRA, CEA, and NSE. The partial area under curve is calculated for the specificity range 0.9 to 1.



S5: Receiver operating characteristic curve for the training and validation data based on CYFRA, CEA, CA125, and NSE. The partial area under curve is calculated for the specificity range 0.9 to 1.



S6: Receiver operating characteristic curve for the training and validation data based on CYFRA, CEA, CA125, NSE, SCC. The partial area under curve is calculated for the specificity range 0.9 to 1.



S7: Average sensitivity and specificity found in the bootstrap analysis per method and serum tumor marker combination. The yellow fields indicate the sensitivity >20% and <30%, the green fields indicate that the sensitivity >30%. The thick black boarder indicates the method achieving the highest average sensitivity for that specific serum tumor marker combination.

	CYFRA / CEA	CYFRA / CEA / CA125	CYFRA / CEA / NSE	CEA / CA125 / NSE	CYFRA / CEA / CA125 / NSE	CYFRA / CEA / CA125 / NSE / SCC
Method	**Specificity (Bootstrap average (95%CI))**					
LR	0,963 (0,962-0,964)	0,951 (0,949-0,952)	0,960 (0,959-0,962)	0,969 (0,968-0,970)	0,968 (0,967-0,969)	0,958 (0,956-0,960)
QDA	0,953 (0,952-0,955)	0,950 (0,949-0,952)	0,961 (0,959-0,962)	0,968 (0,967-0,969)	0,958 (0,957-0,959)	0,832 (0,829-0,835)
LASSO	0,963 (0,962-0,964)	0,961 (0,959-0,962)	0,960 (0,959-0,962)	0,990 (0,989-0,990)	0,968 (0,967-0,969)	0,936 (0,934-0,939)
Random Forest	0,953 (0,952-0,954)	0,941 (0,939-0,942)	0,940 (0,938-0,941)	0,947 (0,946-0,948)	0,936 (0,935-0,938)	0,958 (0,956-0,960)
Bagging	0,953 (0,952-0,954)	0,980 (0,979-0,981)	0,950 (0,948-0,951)	0,936 (0,935-0,938)	0,946 (0,945-0,948)	0,958 (0,956-0,960)
Boosting	0,953 (0,952-0,955)	0,920 (0,919-0,922)	0,940 (0,938-0,941)	0,905 (0,904-0,907)	0,947 (0,946-0,948)	0,895 (0,892-0,898)
NN	0,954 (0,953-0,955)	0,950 (0,949-0,952)	0,960 (0,959-0,961)	0,969 (0,968-0,970)	0,969 (0,968-0,970)	0,958 (0,956-0,960)
SVM	0,954 (0,952-0,955)	0,950 (0,948-0,951)	0,960 (0,959-0,961)	0,926 (0,925-0,928)	0,968 (0,967-0,969)	0,958 (0,956-0,960)
RNN GRU	0,936 (0,935-0,938)	0,944 (0,943-0,945)	0,964 (0,963-0,965)	0,907 (0,905-0,908)	0,963 (0,962-0,964)	0,959 (0,958-0,960)
	CYFRA / CEA	CYFRA / CEA / CA125	CYFRA / CEA / NSE	CEA / CA125 / NSE	CYFRA / CEA / CA125 / NSE	CYFRA / CEA / CA125 / NSE / SCC
Method	**Sensitivity (Bootstrap average (95%CI))**					
LR	0,292 (0,290-0,294)	0,355 (0,353-0,357)	0,243 (0,240-0,245)	0,276 (0,274-0,278)	0,203 (0,202-0,205)	0,581 (0,578-0,584)
QDA	0,255 (0,253-0,257)	0,336 (0,334-0,338)	0,395 (0,392-0,397)	0,314 (0,312-0,316)	0,530 (0,527-0,532)	0,727 (0,724-0,729)
LASSO	0,364 (0,362-0,366)	0,304 (0,302-0,306)	0,358 (0,356-0,360)	0,150 (0,148-0,152)	0,381 (0,378-0,383)	0,538 (0,535-0,541)
Random Forest	0,508 (0,506-0,511)	0,576 (0,574-0,579)	0,701 (0,696-0,703)	0,465 (0,462-0,467)	0,641 (0,639-0,643)	0,508 (0,504-0,511)
Bagging	0,491 (0,489-0,493)	0,367 (0,365-0,369)	0,701 (0,699-0,703)	0,524 (0,522-0,526)	0,700 (0,697-0,702)	0,590 (0,587-0,593)
Boosting	0,619 (0,617-0,621)	0,602 (0,599-0,604)	0,708 (0,706-0,710)	0,693 (0,691-0,695)	0,745 (0,743-0,747)	0,812 (0,809-0,814)
NN	0,370 (0,368-0,373)	0,450 (0,447-0,452)	0,358 (0,356-0,360)	0,209 (0,207-0,211)	0,296 (0,294-0,298)	0,399 (0,396-0,402)
SVM	0,255 (0,253-0,257)	0,538 (0,536-0,541)	0,377 (0,375-0,379)	0,484 (0,482-0,487)	0,367 (0,365-0,370)	0,527 (0,524-0,530)
RNN GRU	0,447 (0,445-0,449)	0,356 (0,354-0,358)	0,561 (0,559-0,564)	0,539 (0,537-0,541)	0,550 (0,548-0,552)	0,480 (0,478-0,483)

Logistic regression: LR, Quadratic discriminant analysis: QDA, Least absolute shrinkage and selection operator: LASSO, Random forest: RF, Neural network: NN, Support vector machine: SVM, Recurrent neural network: RNN, Gated recurrent unit: GRU.

S8: The correlation between the sensitivity and specificity found in the bootstrap analysis.

Correlation sensitivity-specificity for bootstrap results									
Serum tumor marker combination	Method								
	LR	QDA	LASSO	RF	Bagging	Boosting	NN	SVM	RNN_GRU
CYFRA & CEA	0,0241714	-0,032613	-0,052319	-0,016256	-0,01442	-0,029817	-0,029342	0,0317052	-0,003449
CYFRA & CEA & CA125	-0,024056	-0,007073	-0,050428	-0,003875	0,0152001	-0,015714	-0,019376	-0,017946	-0,001009
CYFRA & CEA & NSE	-0,006558	-0,013615	-0,03962	-0,011845	-0,006721	0,0298479	0,0088913	-0,040521	0,02132
CEA & CA125 & NSE	-0,019242	0,0736918	0,0507428	0,1057917	0,0762252	0,0586062	0,0269763	-0,003965	0,0251674
CYFRA & CEA & CA125 & NSE	0,0656086	-0,011035	-0,040144	-0,023073	-0,0323	0,0166766	0,0314058	-0,045716	-0,015945
CYFRA & CEA & CA125 & NSE & SCC	0,035549	-0,018862	0,0307158	0,0210609	0,0128864	0,0258275	0,0143783	0,0051225	-0,013322

S9: The covariance between the sensitivity and specificity found in the bootstrap analysis.

Covariance sensitivity-specificity for bootstrap results									
Serum tumor marker combination	Method								
	LR	QDA	LASSO	RF	Bagging	Boosting	NN	SVM	RNN_GRU
CYFRA & CEA	1,43E-05	-2,01E-05	-3,31E-05	-1,23E-05	-1,08E-05	-2,03E-05	-1,97E-05	1,98E-05	-2,41E-06
CYFRA & CEA & CA125	-1,71E-05	-5,34E-06	-3,13E-05	-3,35E-06	7,27E-06	-1,51E-05	-1,47E-05	-1,46E-05	-6,95E-07
CYFRA & CEA & NSE	-3,86E-06	-9,33E-06	-2,69E-05	-9,73E-06	-5,08E-06	2,31E-05	5,93E-06	-2,92E-05	1,25E-05
CEA & CA125 & NSE	-1,15E-05	4,33E-05	1,42E-05	8,70E-05	6,74E-05	6,19E-05	1,43E-05	-3,96E-06	2,33E-05
CYFRA & CEA & CA125 & NSE	3,42E-05	-8,07E-06	-2,62E-05	-2,11E-05	-2,52E-05	1,22E-05	1,87E-05	-2,97E-05	-9,57E-06
CYFRA & CEA & CA125 & NSE & SCC	4,85E-05	-4,27E-05	5,37E-05	3,10E-05	1,83E-05	4,35E-05	1,87E-05	7,29E-06	-1,04E-05