

iSED® ELITE: Using Rheology to Expedite ESR Testing

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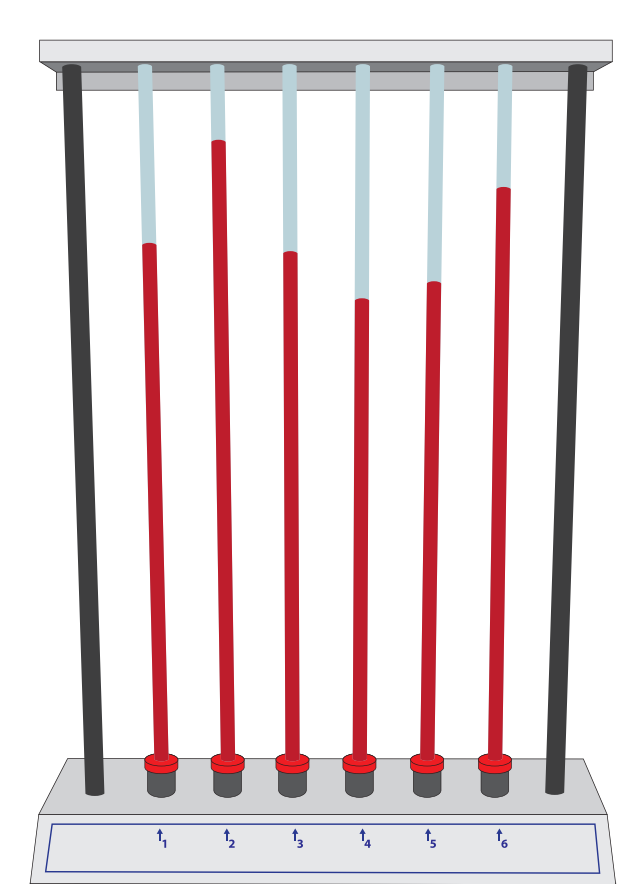


Abstract

Introduction: Erythrocyte sedimentation rate (ESR) is a common laboratory test used to help determine if a patient has an inflammatory condition or to help monitor patients with inflammatory conditions. 48 million ESR tests are performed in the US annually.¹ Traditional ESR testing is done using a manual or semi-automated version of the Westergren method. The iSED® ELITE is the latest platform in the iSED instrument family. Results are available within 20 seconds with minimal hands-on time, significantly reducing time to result and improving patient care. **Method:** The iSED technology is based on syllectometry and utilizes photometric rheology reading to quantify the rouleaux formation, which is the earliest phase of red blood cell (RBC) sedimentation. RBCs are injected into the analyzer's flow cell, and the shear stress causes them to disaggregate. Sensors capture the difference in light transmission over time as the RBCs begin to re-aggregate. The technical innovation of the iSED analyzers consists of "directly" measuring the aggregation of the RBCs, whereas traditional methods "indirectly" measure aggregation of the RBCs by recording the length at which the cells settle in a Westergren tube. The iSED ELITE technology is highly correlated to the Westergren method, but test results are available within 20 seconds without the drawbacks and inconvenience of traditional ESR testing. **Results:** Method Correlation (iSED ELITE vs Westergren) was performed according to CLSI Procedure H02-5. The method correlation (n = 200), analyzed by Passing Bablok regression, results in a regression equation of $y = 1.0 + 1.0x$, 95% CI of the slope is 0.94–1.07, 95% CI of intercept is 0.43–2.3. CuSum test is greater than 0.05, showing no deviation from linearity. Paired T-Test shows equivalence. Precision studies (40 patients X 5 replicates), across the clinical range of interest, demonstrated average precision results of 6.1% for samples less than 20 mm/hr. and 3.9%, for samples 20-60 mm/hr. Traditional ESR testing is commonly affected by environmental variables as well as variables within the sample. The iSED ELITE sample is analyzed within seconds in a closed environment, limiting potential impact of environment factors, and sampling is done by the instrument, eliminating the potential for human error and improving operator safety. **Conclusion:** The direct ESR measurement possible with the photometric determination of ESR based on syllectometry is comparable with the Westergren methodology, and results are available in seconds versus minutes to one hour, significantly improving patient care and laboratory efficiency.

Introduction

Erythrocyte sedimentation rate (ESR) is a common laboratory test used to help determine if a patient has an inflammatory condition or to help monitor patients with inflammatory conditions. 48 million ESR tests are performed in the US annually.¹ Traditional ESR testing is done using a manual or semi-automated version of the Westergren method. The iSED ELITE is the latest platform in the iSED instrument family. Results are available within 20 seconds with minimal hands-on time, significantly reducing time to result and improving patient care.



Traditional Westergren setup

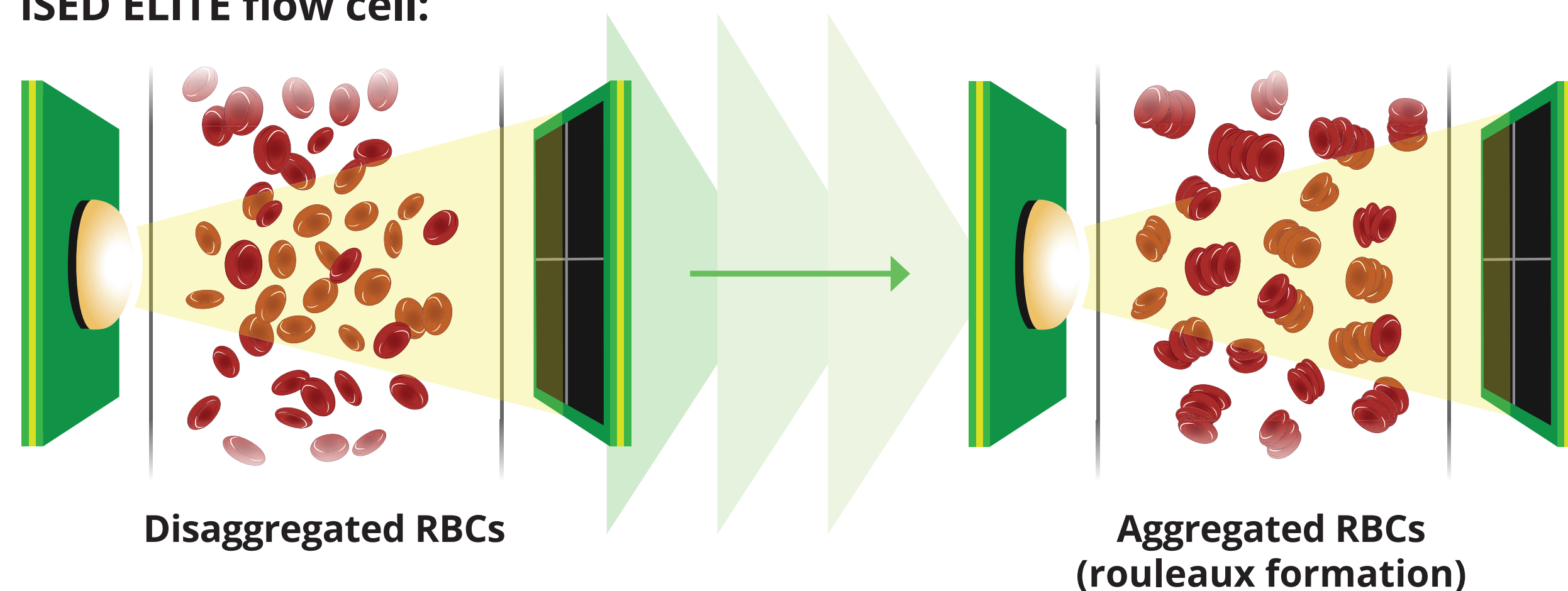


iSED ELITE

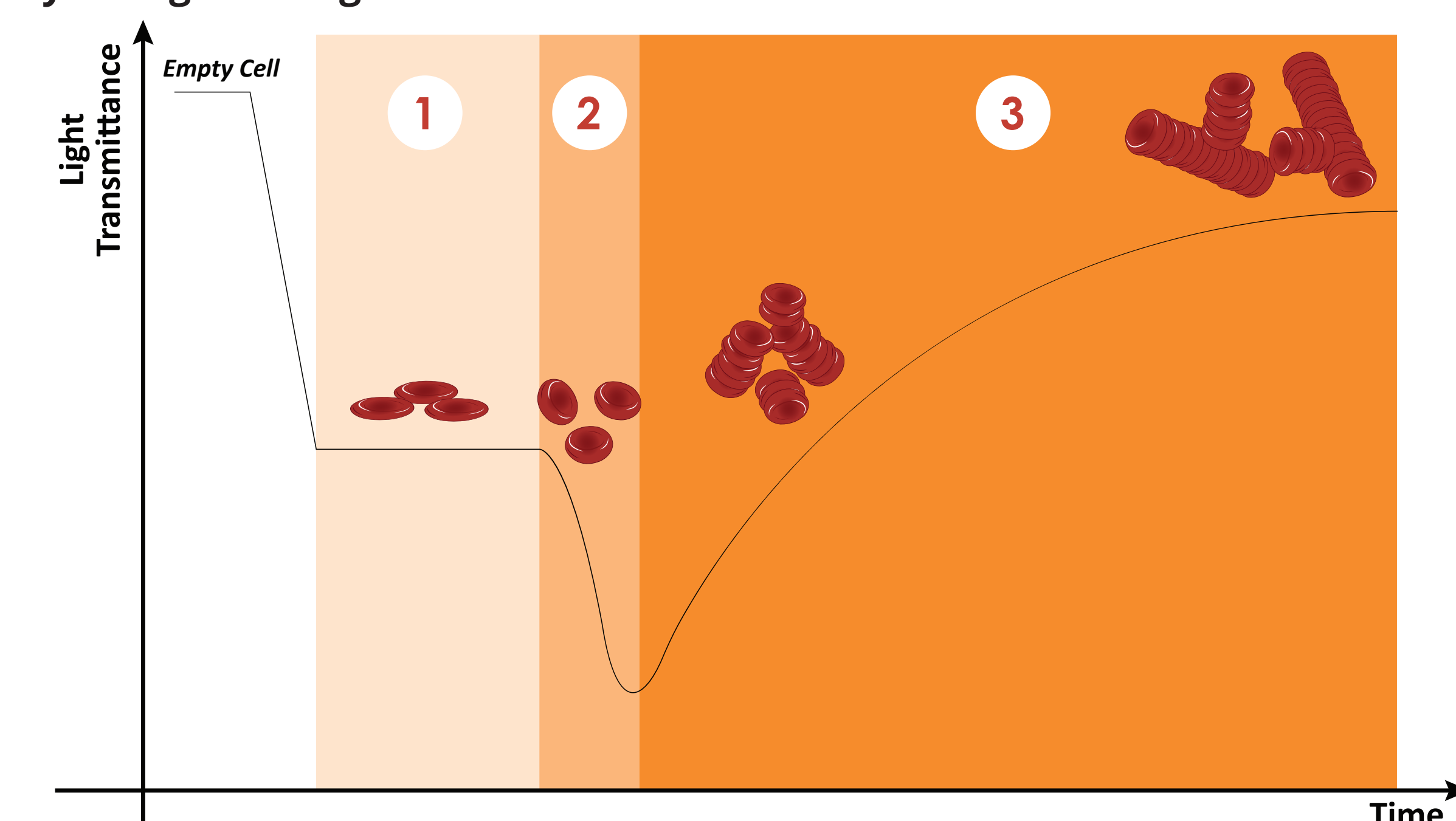
Method

The iSED technology is based on syllectometry and utilizes photometric reading to quantify the rouleaux formation, which is the earliest phase of RBC sedimentation. RBCs are injected into the analyzer's flow cell, and the shear stress causes them to disaggregate. Sensors capture the difference in light transmission over time as the RBCs begin to re-aggregate.

iSED ELITE flow cell:



Syllectogram Stages



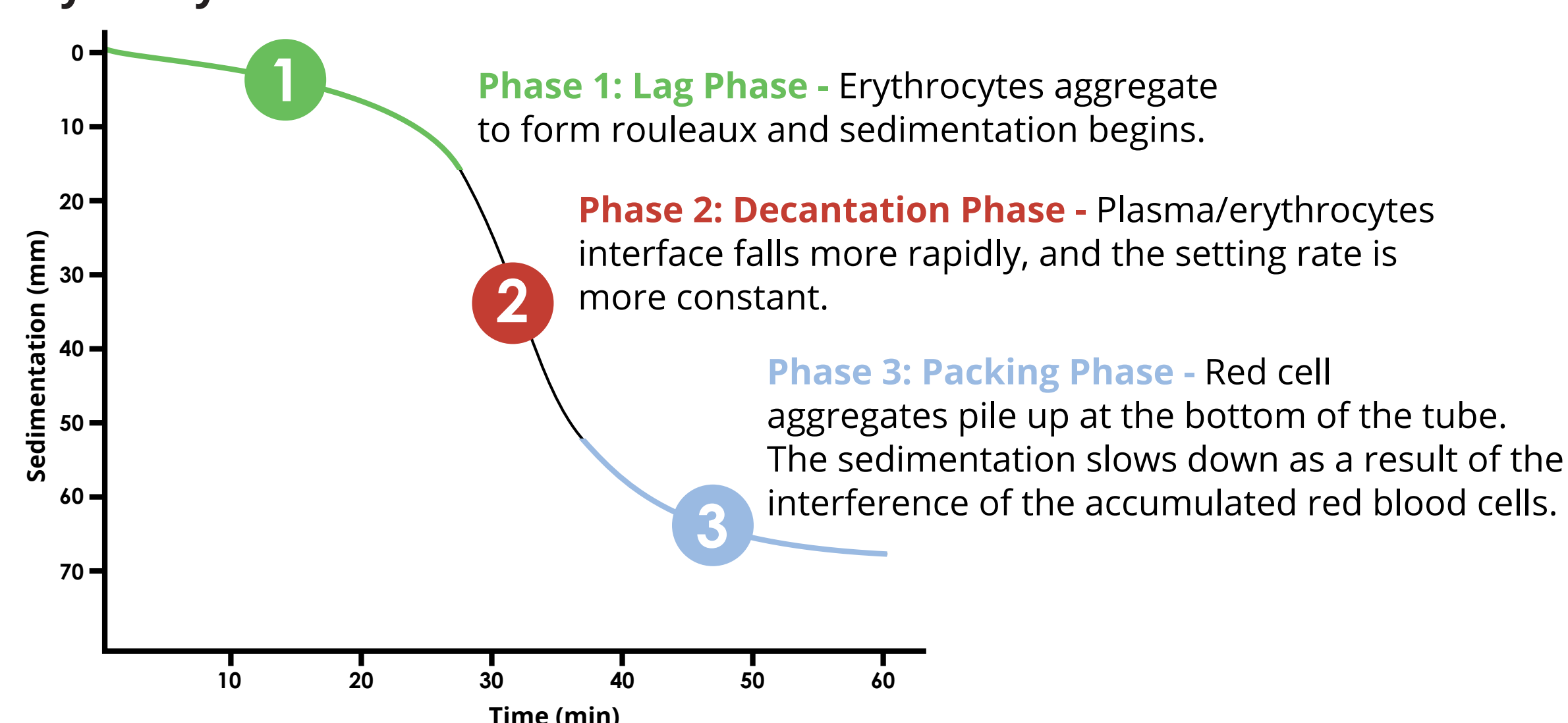
A time-dependent light intensity plot called a syllectogram is generated. In normal samples, the syllectogram has a characteristic shape and consists of 3 main stages.

Stage 1: Application of shear stress

Stage 2: RBC shape recovery and redistribution

Stage 3: RBC aggregation

Erythrocyte Sedimentation Phases



Erythrocyte sedimentation consists of 3 main phases. While traditional ESR tests measure the sedimentation after the last phase, iSED ELITE measures aggregation during the first phase. The amount of aggregation is directly correlated to the amount of sedimentation.²

The technical innovation of the iSED analyzers consists of "directly" measuring the aggregation of the RBCs, whereas traditional methods "indirectly" measure aggregation of the RBCs by recording the length at which the cells settle in a Westergren tube. The iSED ELITE technology is highly correlated to the Westergren method, but test results are available within 20 seconds and require less than 3 seconds of hands-on time per sample.

Results

Method Comparison

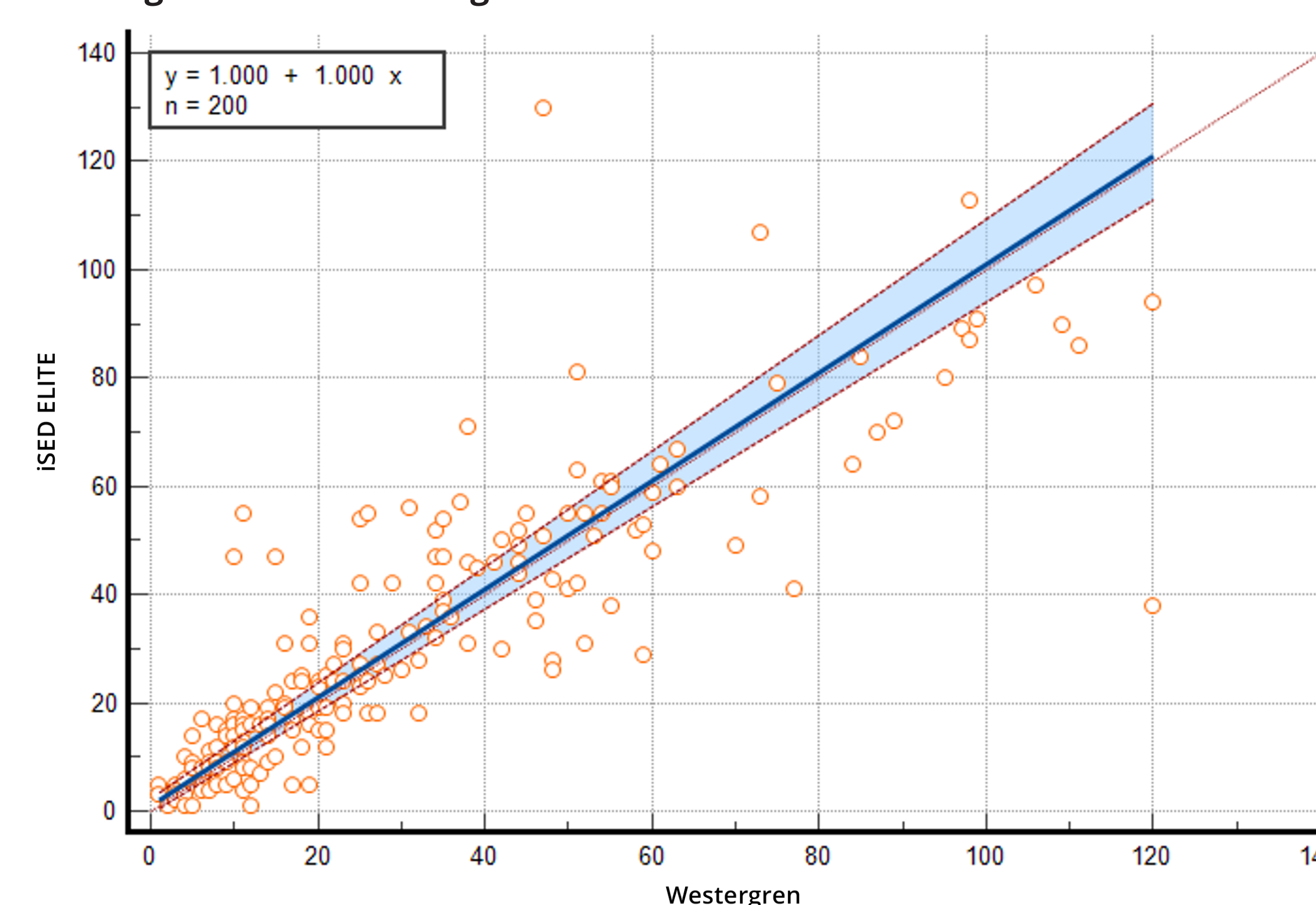
iSED ELITE ESR analyzer has been demonstrated to provide results equivalent to the CLSI approved standard methodology for ESR, the Westergren method. Since ESR is based on the physical interactions of RBCs during testing, the Westergren reference method is subject to a number of variables, including sample characteristics, testing environment, and individual operators' techniques. Therefore, Passing Bablok regression analysis is recommended for comparing two ESR methods since the reference method is known to be subject to variables.²

Results of Passing Bablok regression analysis:

Variable X	Westergren
Variable Y	iSED ELITE
Sample Size	200

$y = 1.000000 + 1.000000 x$	
Systematic Differences	
Intercept A	1.0000
95% CI	-0.4296 to 2.3056
Proportional Differences	
Slope B	1.0000
95% CI	0.9444 to 1.0704
Random Differences	
Residual Standard Deviation (RSD)	9.7999
± 1.96 RSD Interval	-19.2078 to 19.2078
Linear Model Validity	
Cusum Test for Linearity	No significant deviation from linearity (P=0.28)

Passing Bablok scatter diagram:



Precision

Samples spanning a range of ESR values (quartiles were defined as per the CLSI ESR standard) were run on the iSED ELITE analyzer a total of ten (10) times to demonstrate precision. As with other laboratory tests, higher CVs are expected when comparing lower numerical values.

Run#/Range (mm/hr)	10–20	20–40	40–60	60–105
Average	12.7	22.7	50.1	102.6
SD	0.82	1.42	2.42	4.48
% CV	6.48	6.25	4.84	4.36

Stability

Samples spanning a range of ESR values were run on the iSED ELITE analyzer at 24 hours to demonstrate stability. As with other laboratory tests, higher CVs are expected when comparing lower numerical values.

Average %CV	24 Hours Refrigerated (mm/hr)
Lower ESR Result	14.88
Medium ESR Result	6.22
High ESR Result	2.47

Carryover

Carryover testing was performed to demonstrate that the sequence of sample testing does not affect measured values (mm/hr).

Sample	Run 1	Run 2	Run 3	Run 4	Average
Sample 1a	70	68	74	67	69.8
Sample 1b	73	71	74	75	73.3
Sample 2a	7	6	7	7	6.8
Sample 2b	5	5	5	5	5.0
% Carryover	3.1	1.6	2.9	3.2	2.7

Conclusion

The direct ESR measurement possible with the photometric rheology of ESR based on syllectometry is comparable with the Westergren methodology, and results are available in seconds versus minutes to one hour, significantly improving patient care and laboratory efficiency.

References

- ALCOR Scientific Internal Data.
- CLSI. Procedures for the Erythrocyte Sedimentation Rate Test; Approved Standard—Fifth Edition. CLSI document H02-A5. Wayne, PA: Clinical and Laboratory Standards Institute; 2011.