Introduction of Products

Automated JCA-BM6010/C Clinical Chemistry Analyzer

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INTRODUCTION

JCA-BM6010/C (hereinafter called "BM6010/C") is an automatic clinical chemistry analyzer that follows the basic technology of the BioMajesty® Series. It has high accuracy and stability of measurement and is capable of micro-volume analysis with a minimum reaction solution volume of 80 µL and minimum sample volume of 1.0 µL. Its throughput is 800 tests/h (1200 tests/h including ISE measurements). It is the most compact analyzer in its class and allows great flexibility of installation. Since its launch in 2011, approx. 600 units have been sold in Japan, and about 300 overseas (as of March 2017). It is capable of automated onboard sample pre-treatment and measurement of HbA1c with a throughput of 400 tests/h. Characteristics of the BM6010/C and some measurement data by the analyzer are outlined in this document.

TECHNICAL SPECIFICATIONS

The major specifications of BM6010/C are shown in ***Table 1*** and ***Fig. 1***.

Date Revised: April 25, 2017

Table 1 *Technical specifications of BM6010/C*

Throughput	Maximum 1200 tests/hour (including ISE tests)
Chemistry	Maximum 800 tests/hour
ISE	Maximum 600 tests/hour
Sample throughput	Maximum 800 samples/hour
No. of registrable tests	Maximum 100 tests (103 tests including ISE tests)
Samples	Turntable system with on-board barcode reader
Sample tray	84 positions for samples, sample ID barcodes
	Refrigerated parts (dedicated diluent, calibrators, controls): 61 positions
	Point-in-space sampling for LAS
Sample volume	1 to 25 μL/test (0.1 μL/step)
Dilution function	Dilution ratio 1-301 folds in Dilution cuvettes and Reaction cuvettes
Reagents	Turntable with on-board barcode readers
Reagent containers	20 mL, 40 mL and 70 mL; all reagents refrigerated
Reagent volume per assay	5-300 μL of each reagent (0.1 μL steps)
Reaction carousel	Turntable
Reaction volume	80-430 μL
Mixing	SSR-Spin Mixer
Measurement	All reaction processes
Measurement points	Maximum 63 points (at 13.5 sec intervals in 15 minutes)
Measurement wavelengths	340-884 nm (14 wavelengths), single-wavelength or dual-wavelength options for calculation
Dimensions (mm)	Analyzer: 1220 (W) × 850 (D) × 1108 (H)
	Workstation: 500 (W) × 610 (D) × 1104 (H)
Weight	Approximately 450 kg
Power consumption	Maximum 2.6 kVA

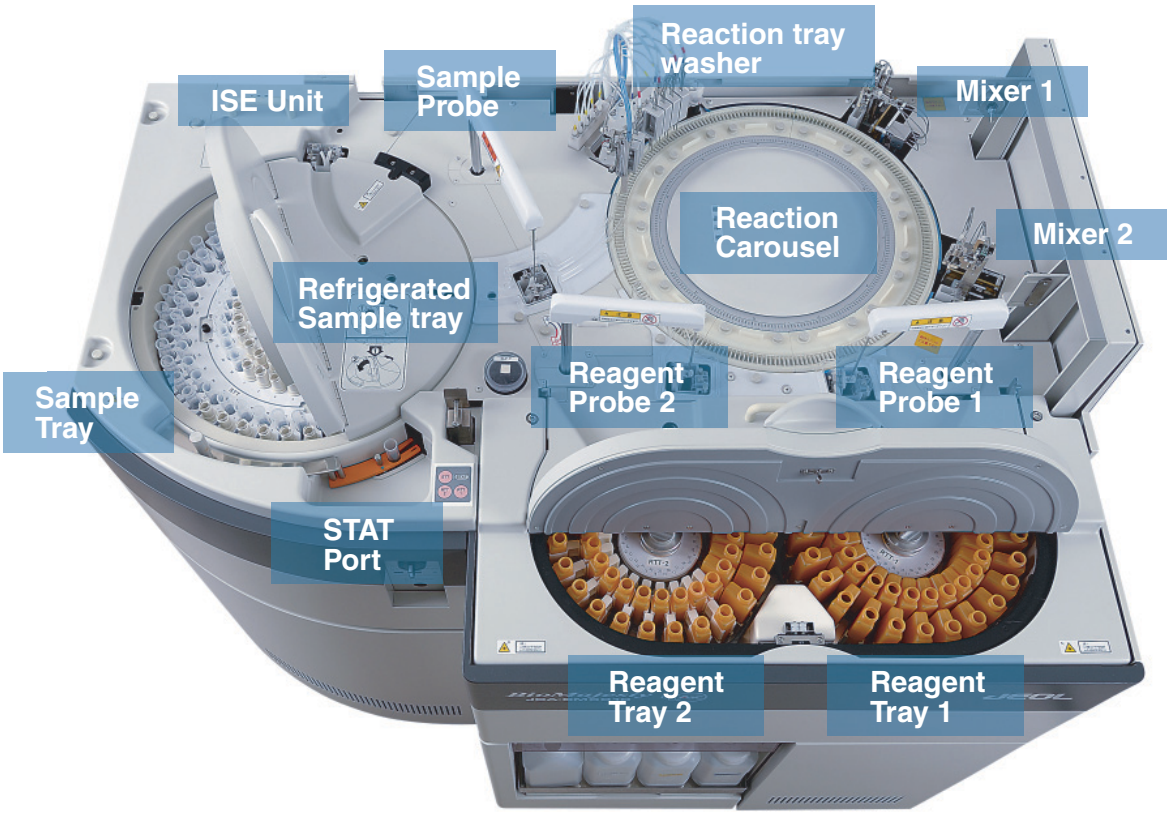

Fig. 1 *Components of JCA BM6010/C*

TECHNICAL CHARACTERISTICS

1) Sampling accuracy

Table 2 [2] shows the sampling accuracy of the BM6010/C sample probe measured by the dye dilution method, following the standard evaluation procedure used in Japan [1]. The CV was 0.06-0.16% for nominal sample volumes 1.0-25.0 µL.

2) Accuracy of reagent dispensing

Table 3 [2] shows the dispensing accuracy of the BM6010/C reagent probe measured by the gravimetric method, following the standard evaluation procedure [1] used in Japan.

The CV was 0.04-2.68% for nominal reagent volumes 5.0-300.0 µL.

Table 2 *Sampling Accuracy (N=20)*

Sample volume (µL)	MEAN(µL)	SD	CV(%)
1.0	1.07	0.00	0.16
2.0	2.10	0.00	0.13
3.0	3.10	0.00	0.15
5.0	5.22	0.01	0.13
10.0	10.45	0.01	0.13
15.0	15.48	0.01	0.07
20.0	20.43	0.03	0.16
25.0	25.36	0.02	0.06

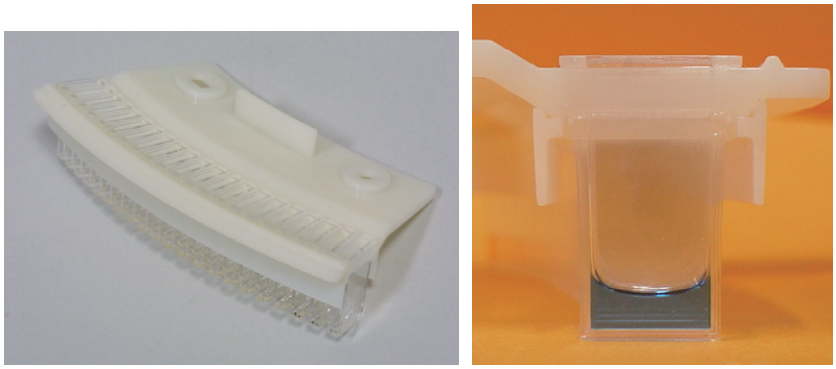

Fig. 2 *Reaction cuvettes*

Table 3 *Reagent dispensing accuracy (N=10)*

Reagent volume (µL)	MEAN(µL)	SD	CV(%)
5.0	5.66	0.15	2.68
10.0	10.24	0.21	2.03
20.0	20.36	0.30	1.50
40.0	40.30	0.12	0.30
70.0	70.16	0.05	0.06
100.0	100.02	0.16	0.16
150.0	149.92	0.16	0.12
200.0	198.72	0.75	0.38
250.0	249.44	0.27	0.11
300.0	299.98	0.13	0.04

3) Within-run reproducibility for chemistry tests

Tables 4 and ***Table 5*** show the within-run reproducibility in chemistry test measurements, sample volume and reagent volumes for each test [3)]. All the test results showed good reproducibility, including measurements with 1.0 µL sample volume.

Table 4 *Within-run reproducibility of measurements with low-level samples (N=20)*

	LDH	AST	ALT	CPK	AMY	TP	CRE	UA	GLU	Ca	IP	HDL
Unit	U/L	U/L	U/L	U/L	U/L	g/L	µmol/L	µmol/L	mmol/L	mmol/L	mmol/L	mmol/L
Sample (µL)	2.0	2.4	2.4	2.0	1.0	1.1	2.1	2.0	1.0	1.6	1.0	1.1
R-1(µL)	80.0	80.0	80.0	80.0	80.0	80.0	80.0	80.0	80.0	80.0	80.0	80.0
R-2(µL)	20.0	20.0	20.0	20.0	20.0	0.0	27.0	40.0	20.0	20.0	40.0	27.0
MEAN	113.0	33.5	32.1	173.0	126.6	49.2	111.5	260.8	4.086	2.126	1.043	1.204
MAX	114	34	33	175	128	50	117	262	4.11	2.17	1.07	1.22
MIN	111	33	31	171	125	49	108	256	4.00	2.10	1.00	1.17
RANGE	3	1	2	4	3	1	9	6	0.11	0.07	0.06	0.04
SD	0.8	0.5	0.6	1.2	0.7	0.4	2.1	2.2	0.033	0.024	0.018	0.009
CV(%)	0.70	1.52	1.82	0.70	0.54	0.83	1.87	0.84	0.81	1.12	1.77	0.74

Table 5 *Within-run reproducibility of measurements with high-level samples (N=20)*

	LDH	AST	ALT	CPK	AMY	TP	CRE	UA	GLU	Ca	IP	HDL
Unit	U/L	U/L	U/L	U/L	U/L	g/L	µmol/L	µmol/L	mmol/L	mmol/L	mmol/L	mmol/L
Sample (µL)	2.0	2.4	2.4	2.0	1.0	1.1	2.1	2.0	1.0	1.6	1.0	1.1
R-1(µL)	80.0	80.0	80.0	80.0	80.0	80.0	80.0	80.0	80.0	80.0	80.0	80.0
R-2(µL)	20.0	20.0	20.0	20.0	20.0	0.0	27.0	40.0	20.0	20.0	40.0	27.0
MEAN	453.0	184.6	88.5	462.5	463.2	64.4	395.5	471.4	14.011	3.130	2.304	2.039
MAX	458	186	89	468	469	66	407	476	14.16	3.17	2.32	2.06
MIN	449	184	88	458	458	63	390	464	13.82	3.09	2.23	2.00
RANGE	9	2	1	10	11	3	17	12	0.33	0.07	0.10	0.05
SD	2.7	0.6	0.5	2.6	2.6	0.7	3.8	3.3	0.083	0.021	0.026	0.014
CV(%)	0.61	0.31	0.57	0.57	0.56	1.04	0.96	0.69	0.59	0.66	1.14	0.69

4) Linearity of absorbance

Fig. 3 - ***Fig. 6*** show linearity of absorbance measured at 340, 410, 478 and 751 nm wavelengths with BM6010/C.

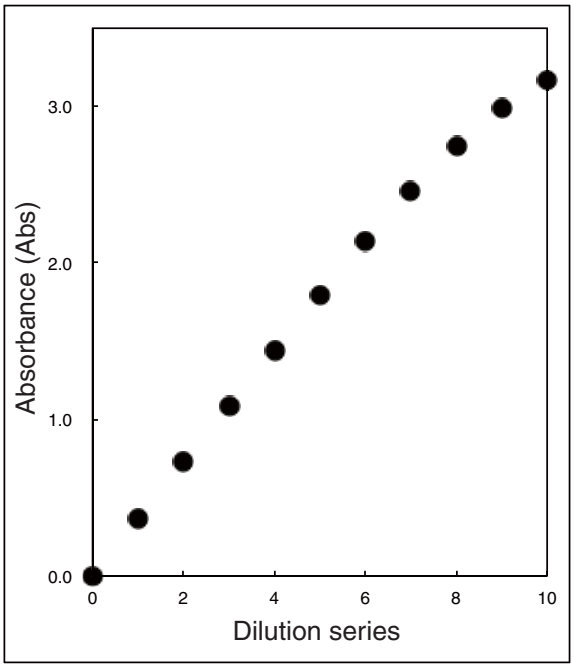

Fig. 3 *Linearity of absorbance (340 nm)*

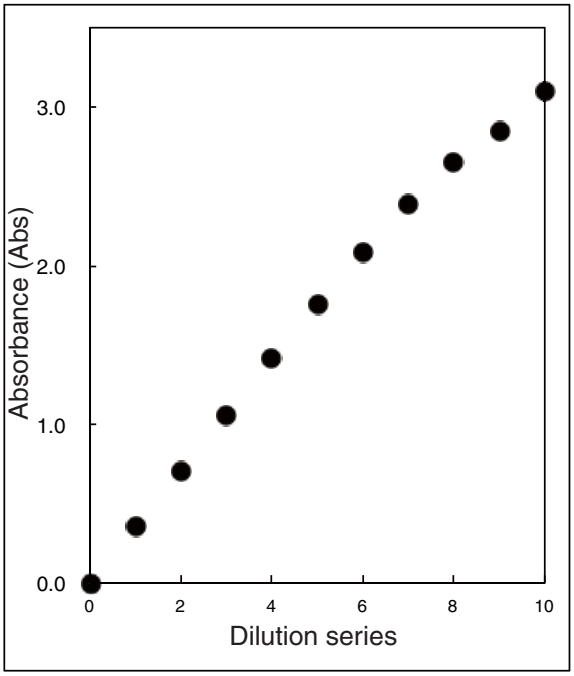

Fig. 4 *Linearity of absorbance (410 nm)*

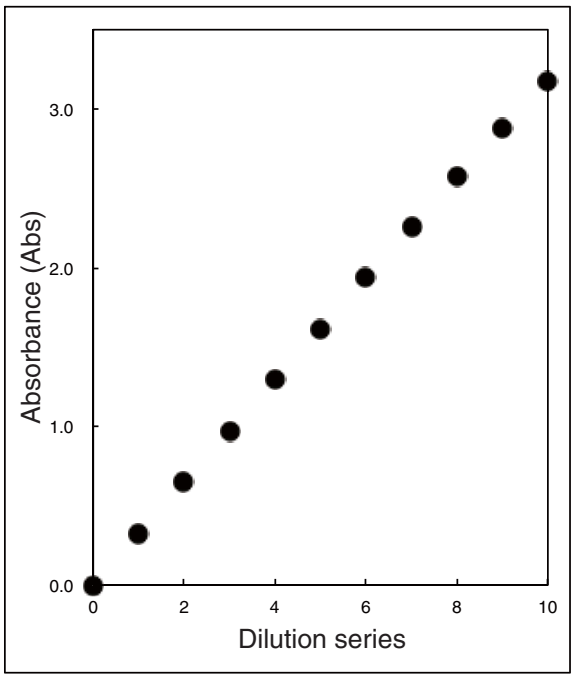

Fig. 5 *Linearity of absorbance (478 nm)*

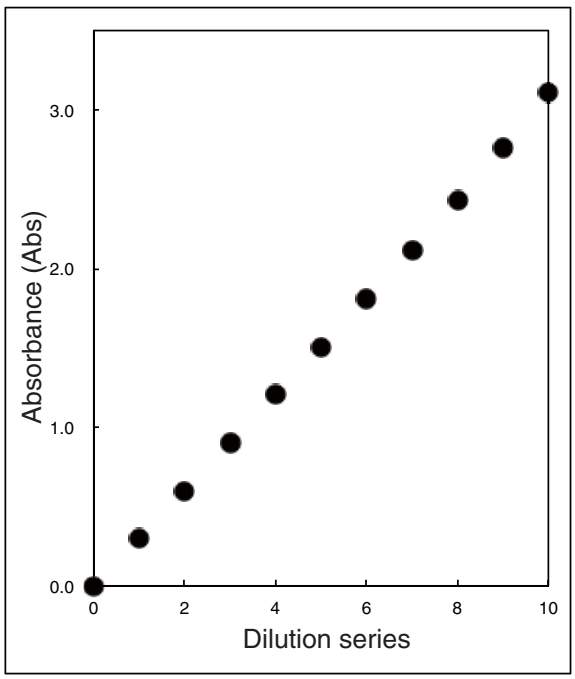

Fig. 6 *Linearity of absorbance (751 nm)*

The linearity of absorbance described here depends on the performance of the spectrophotometer. However, if any measurement result exceeds the upper limit of linearity, BM6010/C can change the range of measurement points to be used for calculation to improve the linearity, thus avoiding reruns. (***Fig. 7***)
Compared to the normal Reaction A, Reaction B requires exclusion of the absorbance values that exceed the upper limit of linearity (approx.2.8 Abs in this case) for correct calculation of measurement value. In Reaction C, the range of measurement points is expanded because too many points to be used for calculation are excluded in the original range. (***Fig. 8***)

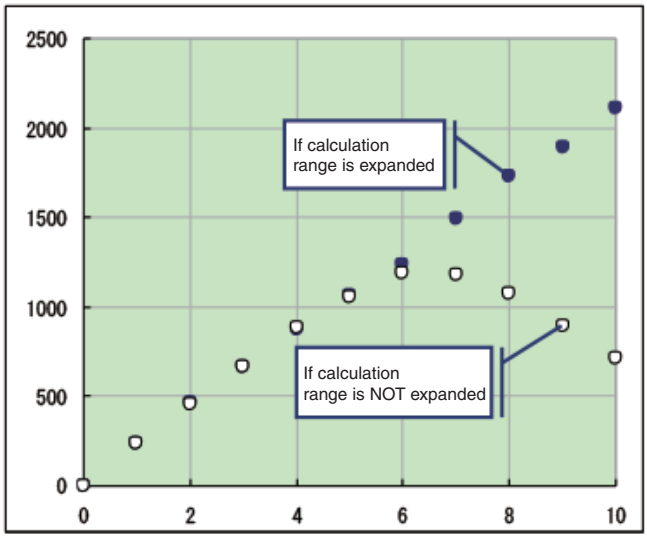

Fig. 7 *Comparison of measurement range (AMY) with or without expansion*

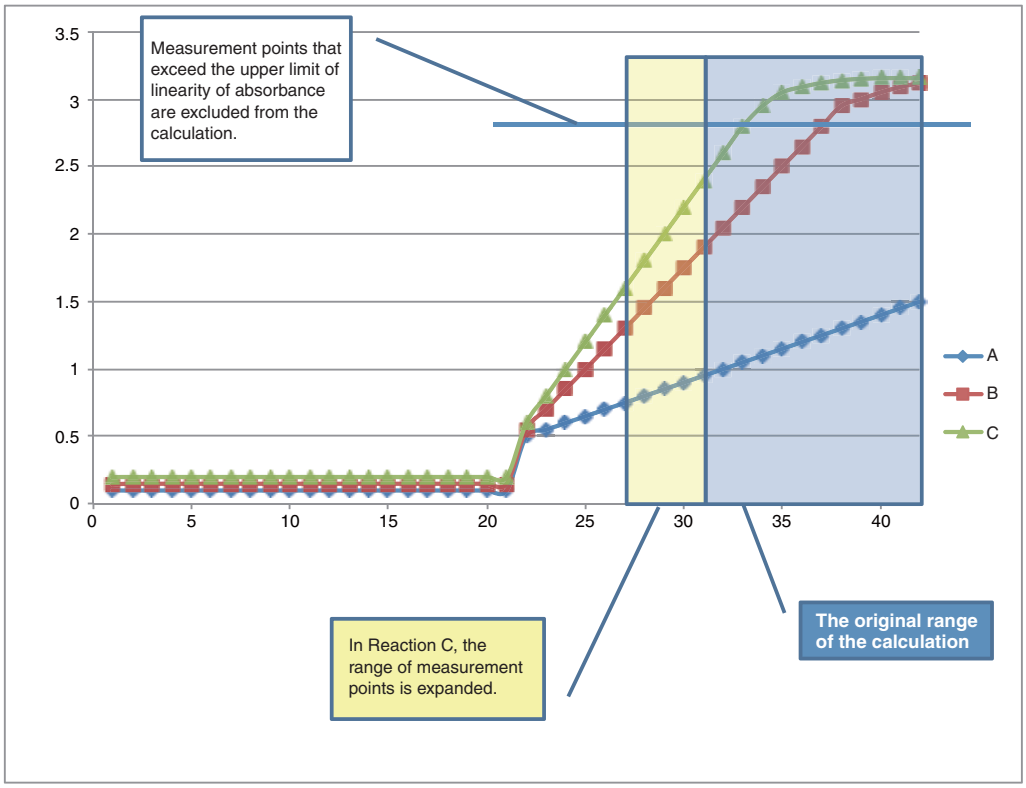

Fig. 8 *An example of expansion of the calculation range*

5) Mechanism of HbA1c measurement

1) Mechanism of HbA1c measurement

The BM6010/C has an automated onboard pre-treatment (hemolysis) mechanism for measuring HbA1c. The procedures used for measurement of chemistry tests and HbA1c are shown in ***Fig. 9***. For chemistry tests, BM6010/C first dispenses reagents, and then dispenses the sample into a reaction cuvette to measure absorbance. In this process, the sample probe detects the level of the sample using its liquid level sensor before aspirating the sample.

For HbA1c measurements on the other hand, the analyzer dispenses the pre-treatment solution, and then blood cells into a reaction cuvette ("cuvette 1") to complete the hemolysis treatment. The reagent is then dispensed into another reaction cuvette ("cuvette 2"). The hemolyzed sample is dispensed from cuvette 1 to cuvette 2 to measure the absorbance.

In this case, the sample probe descends to the blood cell layer in the sample tube to aspirate the blood cells only. The throughput of BM6010/C is 800 tests/h for chemistry tests, however, when running HbA1c only, the throughput is 400 tests/h.

BM6010/C has a sample probe that is different from those of standard clinical chemistry analyzers in its shape and also a different wash mechanism at the wash port. These differences are illustrated in ***Fig. 10***.

The sample probe of BM6010/C is narrower than those of other analyzers. This is to minimize the contamination of the probe with blood cells as the probe descends to the bottom of the sample tube for HbA1c measurements. In addition, the sample probe on BM6010/C descends in the wash port deeper to wash the whole probe while the standard analyzers wash only the tip of the probe where it contacts the samples.

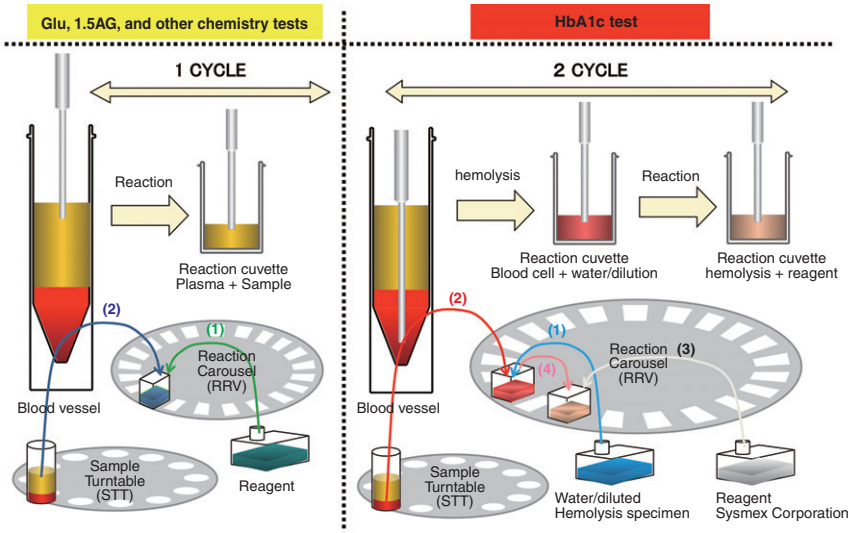

Fig. 9 *Procedures for measurement of clinical chemistry tests and HbA1c with JCA BM6010/C*

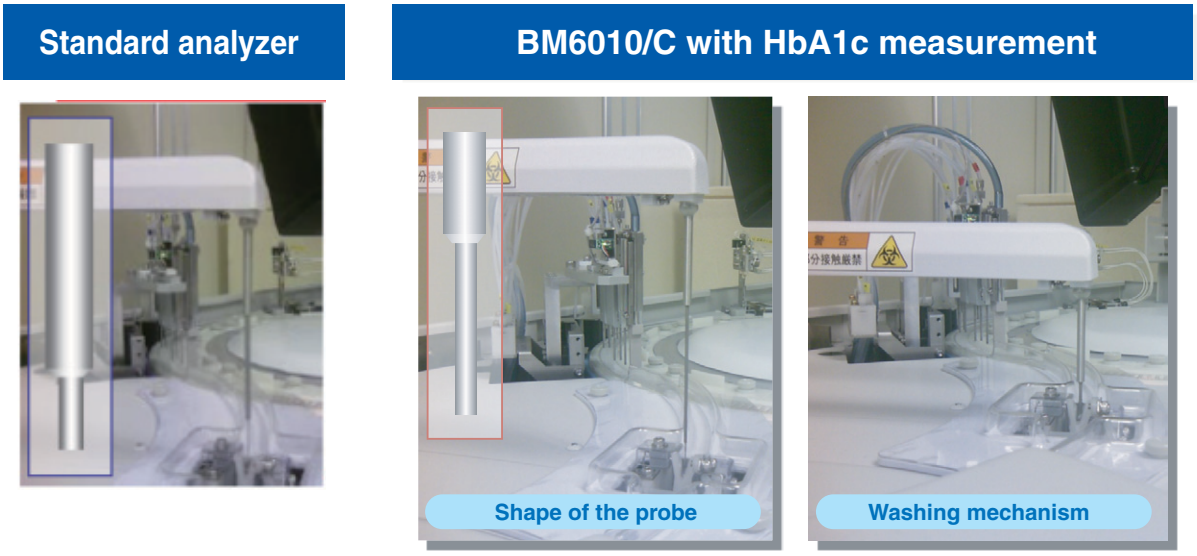

Fig. 10 *Comparison of probe shape and wash mechanism between the standard analyzer and BM6010/C with HbA1c Measurement*

2) Principle of "BM Test HbA1c" measurement

Sysmex is marketing "BM Test HbA1c" as a dedicated reagent for BM6010/C. The measurement principle with this reagent and its performance is described below.

Fig. 11 illustrates the principle of measurement with "BM Test HbA1c" and ***Fig. 12*** the standard procedure on BM6010/C. First, hemoglobin in the blood cells is oxidized to methemoglobin by the pretreatment solution. In the first reaction, glycated dideptide is generated from the N-terminus of the beta-chain of hemoglobin by the reaction with protease. Hb concentration is measured from the absorbance at 805/475 nm wavelengths at this point.

In the second reaction, glycated dipeptides reacts with fructosyl peptide oxidase (FPOX), generating hydroperoxide. The hydroperoxide allows the coloring agent to develop a color in the presence of peroxidase (POD). HbA1c concentration is calculated from the absorbance measured at 805/658 nm wavelengths.

The HbA1c% is calculated based on the Hb concentration and the HbA1c concentration obtained above.

The BM6010/C analyzer retains the absorbance measured at 14 wavelengths for all the calculation points, and up to 3 types of calculations are possible for each reaction. This feature allows BM6010/C to measure the Hb concentration and HbA1c concentration simultaneously through one reaction, using the absorbance values at different wavelengths and different calculation points with "BM Test HbA1c"

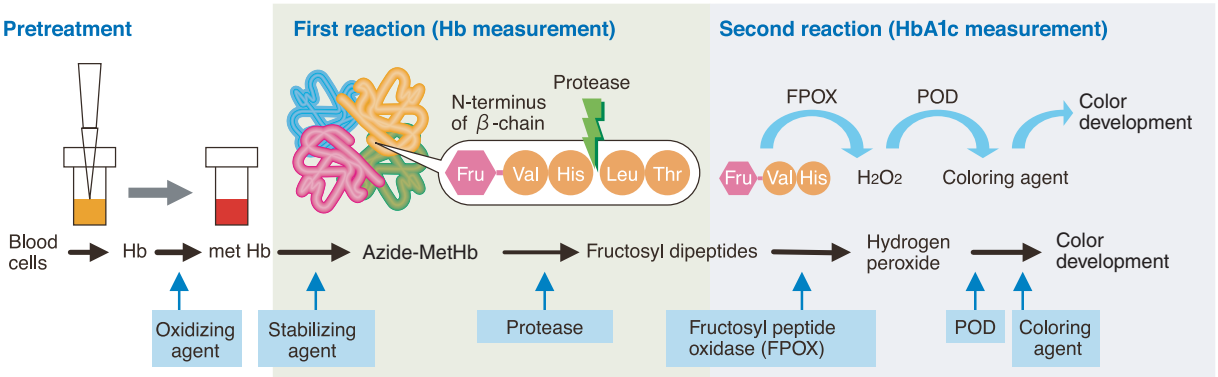

Fig. 11 *Principle of measurement with "BM Test HbA1c"*

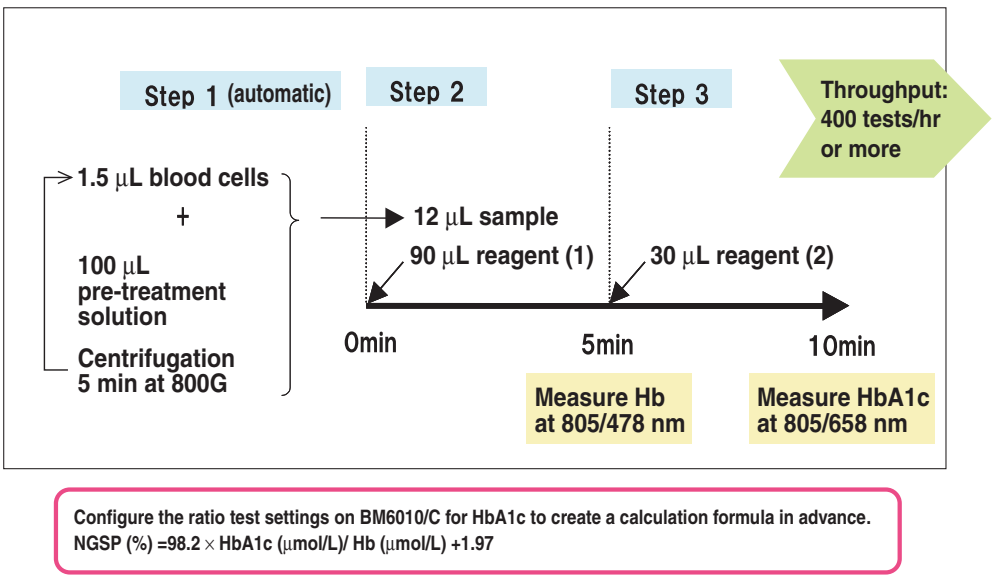

Fig. 12 *Standard procedure with "BM Test HbA1c" (JCA BM6010/C).*

3) Basic performance of "BM Test HbA1c"

Table 6 shows the within-run reproducibility of the tests with "BM Test HbA1c" and ***Fig. 13*** shows the correlation between the IFCC method results and those obtained with "BM Test HbA1c". The coefficient of variation (CV) for within-run reproducibility was not more than 0.5%. As for the correlation with the IFCC method, the correlation equation was y = 1.014x + 0.020 and the correlation coefficient was 0.998.

Table 6 *Within-run reproducibility with "BM Test HbA1c"*

	sample 1	sample 2
1	5.2	9.3
2	5.2	9.4
3	5.3	9.4
4	5.2	9.3
5	5.2	9.4
6	5.2	9.4
7	5.2	9.4
8	5.2	9.4
9	5.2	9.3
10	5.2	9.3
MEAN	5.21	9.35
S.D.	0.02	0.03
C.V.(%)	0.37	0.28
MAX	5.3	9.4
MIN	5.2	9.3
RANGE	0.1	0.1

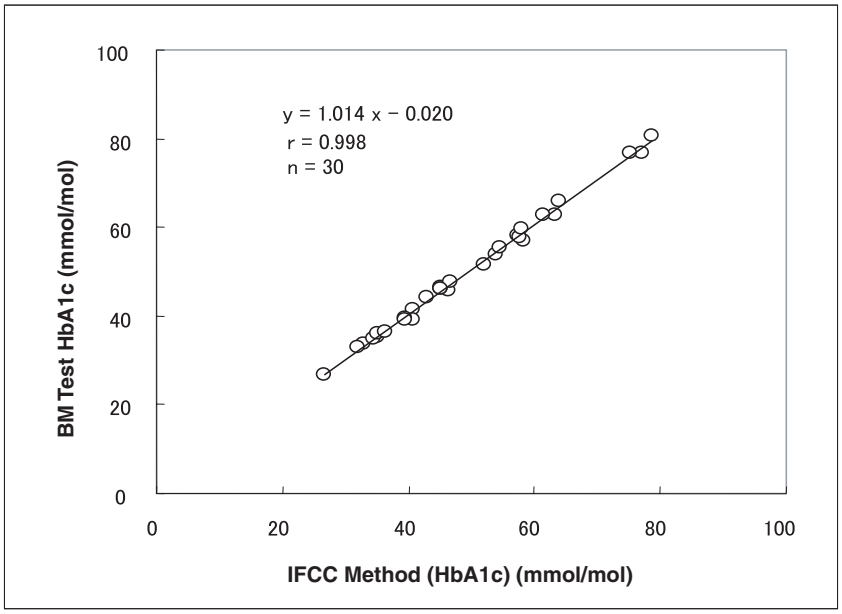

Fig. 13 *Correlation between the results with IFCC method and "BM Test HbA1c"*

6) Medium in the reaction bath

Fluorinated inert oil is used as the medium in the Reaction Bath on BM6010/C. ***Table 7*** shows the differences between the physical properties of this inert oil and water, the most typical material for the medium. The inert oil allows the Reaction Bath to be virtually maintenance-free, requiring only regular replenishment of the oil. This achieves continuous operation while maintaining a stable reaction environment.

7) Reaction cuvette washing mechanism

On BM6010/C, the reaction cuvettes are washed with water and alkaline detergent upon completion of measurement. Any remaining water in the cuvettes is vacuumed by a non-contact drain nozzle, thus making the residue in the cuvette almost zero. The rectangular nozzle is inserted into the cuvette with minimum gap between the cuvette and the nozzle. When the air is vacuumed under a non-contact condition, rapid airflow is generated in the gap between the cuvette and the nozzle, which removes the water droplets. The volume of residual water is minimized in this manner, thus achieving improved measurement accuracy. This mechanism also prevents damage to the cuvettes as the nozzle does not physically contact the cuvettes and contributes to improved cuvette life as well as reduced carryover. ***Fig. 14*** shows an enlarged view of the reaction cuvette wash mechanism and a schematic diagram of the mechanism.

Table 7 *Differences in physical properties between the inert oil and water*

Physical Property	Oil	Water	Remarks
Ingredients	Fluorine inert fluid	–	• Non-degradable, no water stains • Fully inert and does not cause corrosion to metal (reaction bath) and plastic (reaction cuvettes)
Surface tension	16 mN/m	73 mN/m	• Extremely low surface tension to prevent bubbles and dust from attaching the cuvettes • High wettability
Specific gravity	Approx. 1.9	1	• Dust and water drops stay on the surface, thus maintains clear light path
Water solubility	None	–	• Does not mix with wash water or reagents: User can easily separate and remove them should wash water or reagent be dropped in the reaction bath
Boiling point	Between 165 and 185 degrees C	100 degrees C	• Less evaporative than water

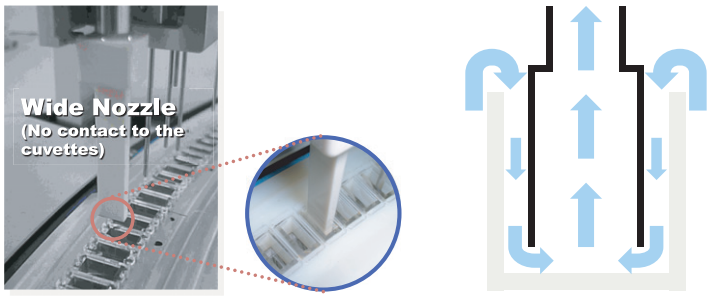

Fig. 14 *Reaction cuvette WASH mechanism*

8) Probe washing mechanism

Fig. 15 is a schematic diagram of the wash mechanism for outer wall of the probe on BM6010/C (used for both sample probe and reagent probes). The tip of the probe moves over the wash port when the probe goes to Sample Tray or Reagent Tray for sampling or when it returns to the home position after sampling. When the probe reaches the wash port, it stops and goes into the wash port whereupon the water is discharged onto the tip of the probe. The water tube has an air vent at the base, however, no water leaks from the vent during probe wash as the stream of water blocks the vent. When the water stops, the remaining water drips from the vent to be drained and the water droplets, sample and reagent on the outer wall of the probe are cleaned by the surface tension of the water.
In addition, inner wall of the probe is also washed by the stream of system water after sampling.
This wash mechanism, along with the reaction cuvette wash mechanism described in "7) Reaction cuvette washing mechanism", contributes to the accuracy of measurements on BM6010/C and reduces carryover caused by samples or reagents. ***Table 8*** shows the carryover with each unit (part) on BM6010/C [3]. This carryover data was verified with the standard procedure [1] used in Japan.

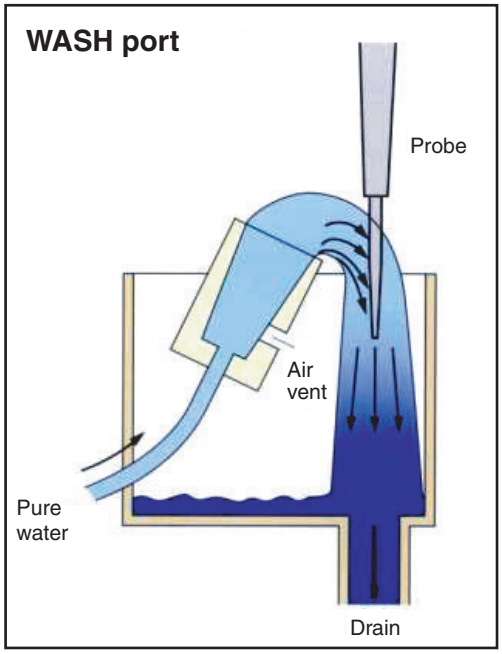

Fig. 15 *Probe outer wall WASH mechanism*

Table 8 *Carryover*

Sample probe	≤ 0.8 ppm
Reagent probe	≤ 0.1 ppm
Mixing rod	≤ 6.7 ppm
Reaction cuvette	≤ 0.01 ppm
Residual water in the cuvette	≤ 0.1 μL

9) Detection of abnormal reactions

Every assay on automatic clinical chemistry analyzer requires specific analytical conditions defined by its reagent manufacturer. These conditions include reagent volume, sample volume, measurement wavelength, assay method (end-point or reaction rate), calculation method (single-point calibration, multi-point calibration, K factor) and range for calculation.
In addition to the above analytical conditions, BM6010/C retains the absorbance for all measurement points at 14 wavelengths and is capable of generating reaction curves and quantifying noises, using the distribution and trend at each measurement point by uniquely developed calculation method. Such quantified information is output with the measurement results in real-time, which enables immediate error detection. This function prompts alarms for the errors caused by the samples, reagents or instrument and avoids erroneous reports. It is also possible to grasp a clinical diagnosis that is not made aware through the clinical examination
Fig. 16 to ***Fig. 19*** show examples of abnormal reactions that are detected by BM6010/C.

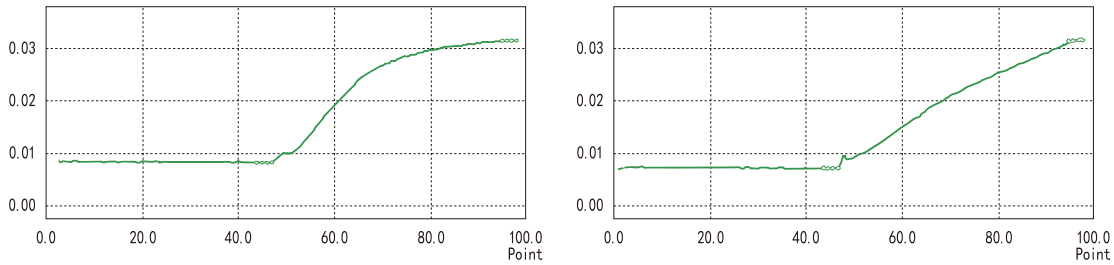

Fig. 16 *Reaction Curves with abnormal reaction speed at the end (End-point assay) (a normal curve is shown on the left).*

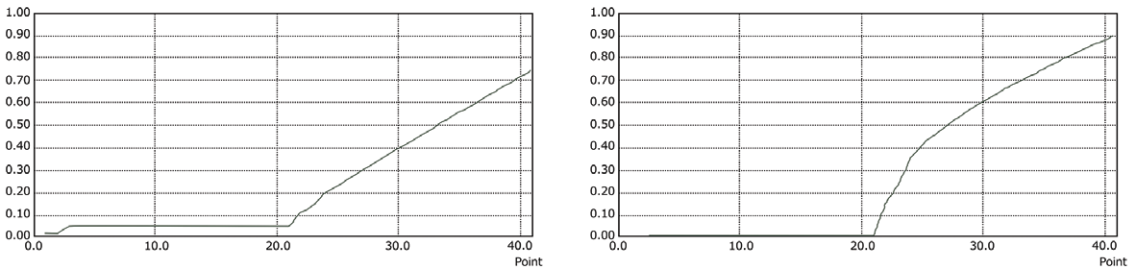

Fig. 17 *Reaction curve that has more rapid reaction only in the beginning in Reaction Rate Assay (a normal curve is shown on the left).*

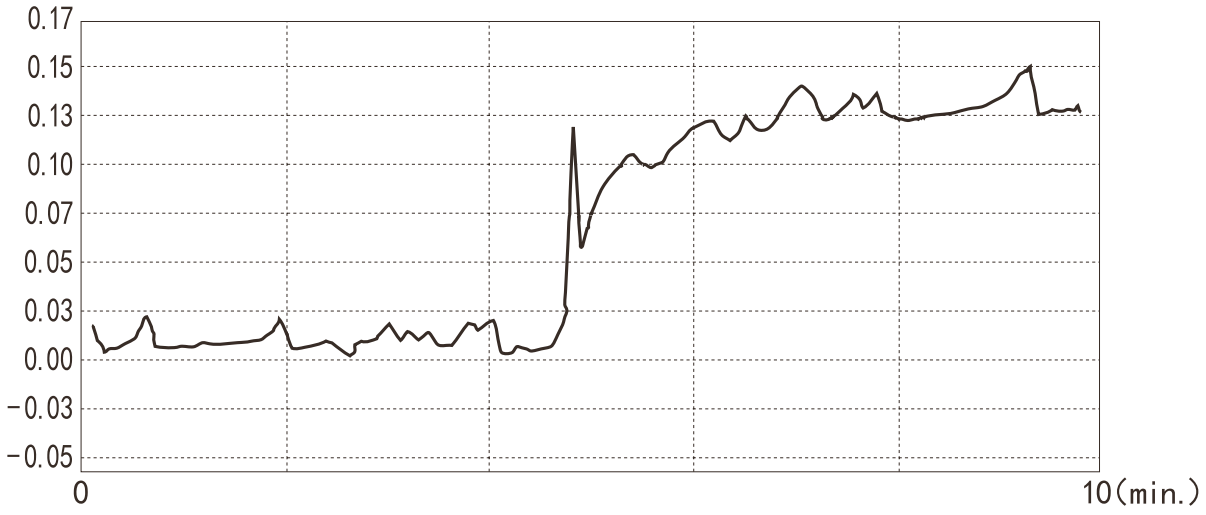

Fig. 18 *Reaction curve affected by noise throughout the reaction*

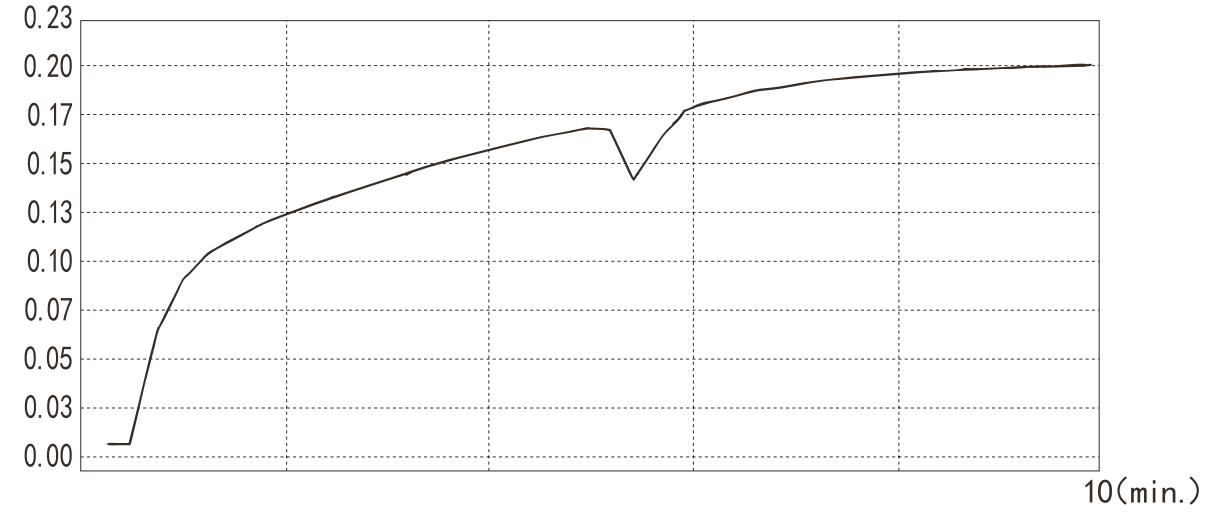

Fig. 19 *Reaction curve affected by nonspecific turbidity in the first half of the reaction*

10) ISE unit

BM6010/C runs ISE measurements using differences in the potential detected by the ion selective electrodes. In general, the potential (E) of an ion selective electrode is determined by the Nernst equation (***Fig. 20***). However, as this equation contains the temperature (T), the measurement values are sometimes affected by the ambient temperature.

ISE measurements on BM6010/C use the internal standard solution to measure the internal standard solution and the actual sample alternately and obtain the difference in the potentials between them to determine electrolyte concentration in a sample. Measurement results obtained by this measurement method with internal solution are less affected by the temperature fluctuation, therefore, it enables BM6010/C to run stable ISE measurements regardless of the ambient temperature. ***Fig. 21*** to ***Fig. 23*** illustrate the relationship between the temperature at the time of measurement and the measurement values and ***Table 9*** shows the within-run reproducibility of the ISE measurements.

In ***Fig. 21*** to ***Fig. 23***, the curves represent the temperature fluctuation and the plotted points represent electrolyte concentration. When the temperature was raised from 10°C to about 35°C and then lowered to around 10°C, the fluctuation observed with the measurement values was approx. 4 mEq/L for Na, approx. 0.3 mEq/L for K and approx. 2 mEq/L for Cl.

$$E = E_0 \pm \left(2.303 \times \frac{RT}{ZF}\right) \times Loga$$

E: Difference in potential between ion selective electrode and reference electrode (mV)

E_0: Reference potential (mV)

R: Gas constant

Z: Ion valency

F: Faraday constant

S: Ionic activity

T: Absolute temperature

Fig. 20 *The Nernst equation*

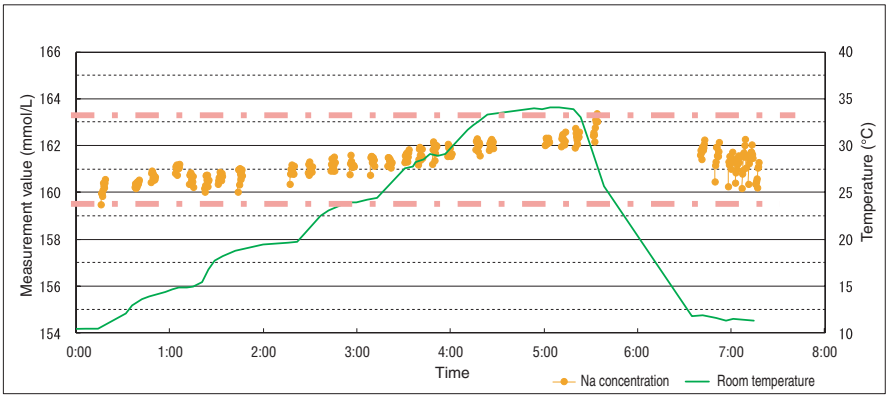

Fig. 21 *Relationship between the ambient temperature during measurement and Na concentration in measurement results*

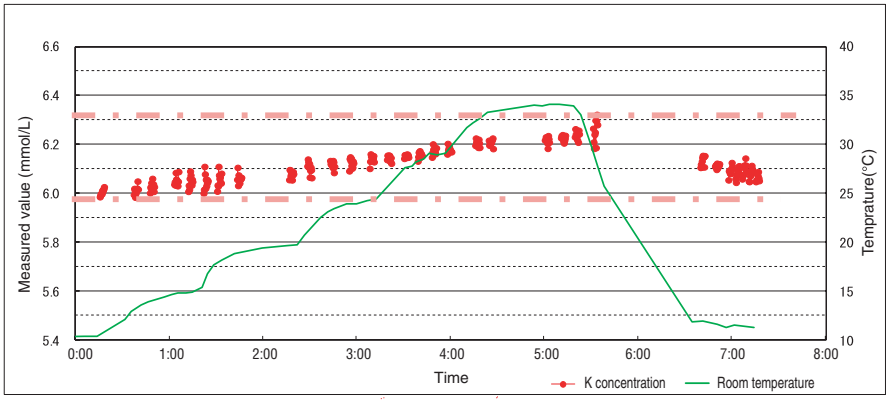

Fig. 22 *Relationship between the ambient temperature during measurement and K concentration in measurement results*

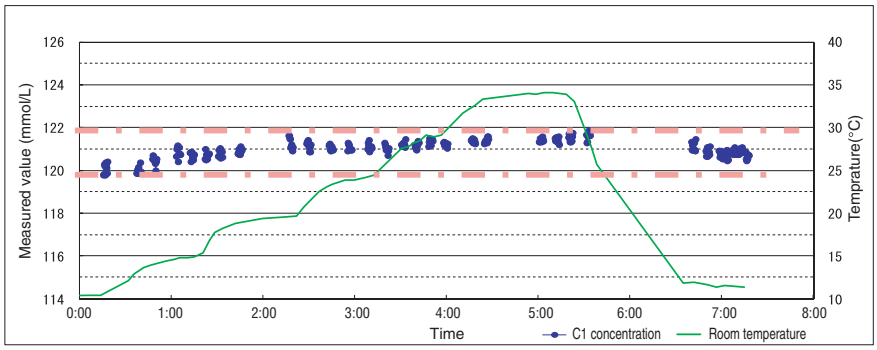

Fig. 23 *Relationship between the ambient temperature during measurement and Cl concentration in measurement results*

Table 9 *Within-run reproducibility in ISE measurements with BM6010/C (mmol/L)*

	Na		K		Cl	
	Low	High	Low	High	Low	High
1	128.8	149.5	3.89	5.82	95.5	111.2
2	129.0	150.0	3.89	5.84	95.4	111.3
3	129.2	150.1	3.90	5.84	95.4	111.0
4	129.1	150.2	3.90	5.86	95.4	111.4
5	129.0	149.9	3.90	5.82	95.4	111.2
6	129.2	149.9	3.90	5.84	95.4	111.3
7	129.1	150.1	3.89	5.85	95.5	111.2
8	129.1	149.7	3.89	5.85	95.4	111.3
9	128.9	150.1	3.89	5.84	95.4	111.2
10	129.1	150.1	3.89	5.85	95.3	111.3
11	129.3	150.2	3.91	5.85	95.5	111.4
12	129.2	149.8	3.89	5.85	95.5	111.2
13	129.1	150.4	3.90	5.84	95.4	111.4
14	129.0	150.2	3.89	5.86	95.3	111.5
15	129.1	150.2	3.89	5.84	95.3	111.3
16	129.0	150.2	3.89	5.86	95.4	111.2
17	129.0	150.2	3.89	5.82	95.5	111.2
18	128.8	150.1	3.89	5.86	95.2	111.3
19	129.2	150.1	3.90	5.86	95.5	111.3
20	128.9	150.2	3.90	5.87	95.4	111.4
MEAN	129.06	150.06	3.895	5.846	95.41	111.28
MAX	129.3	150.4	3.91	5.87	95.5	111.5
MIN	128.8	149.5	3.89	5.82	95.2	111.0
RANGE	0.5	0.9	0.02	0.05	0.3	0.5
SD	0.14	0.21	0.006	0.014	0.08	0.11
CV(%)	0.11	0.14	0.16	0.24	0.09	0.10

CONCLUSION

In this essay, we have outlined the characteristics of the automatic clinical chemistry analyzer BM6010/C. The accuracy of sampling and reagent dispensing was good and the precision is confirmed from the reproducibility of the chemistry test results. BM6010/C realizes a wider range of measurements through the unique calculation processing to raise the upper limit of the linearity in addition to the wide measurement range of the spectrophotometer.
Furthermore, the analyzer has an automatic onboard pre-treatment mechanism for HbA1c measurements and is capable of supporting a variety of tests on its own. This basic performance is further enhanced by the special wash mechanisms for reaction cuvettes and probes and a stable measurement environment is ensured by the Reaction Bath with inert oil. These advantages of BM6010/C make 24-hour operation possible for many laboratories.

BM6010/C also retains all measurement data at every measurement point with the 14 wavelengths. This feature also enables the analyzer realtime detections for measurement data as well as abnormal reactions.

Considering all the information and data presented in this essay, we conclude that BM6010/C is a highly productive and efficient analyzer for routine tests as well as STAT tests.

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