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Electrooxidation of dissolved dsDNA backed by *in situ* UV–Vis spectroscopy

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Abstract

The electrooxidation of double-stranded DNA (dsDNA) from calf thymus was carried by using cyclic voltammetry. A glassy carbon disk-, a platinum disk-, a platinum mesh- and a carbon vapor-deposited platinum mesh electrodes were used. It is shown that the appropriate chemical and biological (steam treatment) purification of the complete cell allows, for the graphite electrode, formation of a wide anodic dsDNA signal with two visible anodic peaks. There was no necessity of preaccumulation of dsDNA on the electrode surface and of use of mediators to get well defined voltammetric signals. These peaks apparently reflect electrooxidation of the DNA's guanine and adenine. The spectrophotometric data obtained during the electrooxidation indicate that the absorbance increases with an increase in potential and electrooxidation current of dsDNA. However, the absorption band maximum either does or does not change its position depending on the mesh material. This different spectroscopic behavior may mean that the changes in the dsDNA structure upon electrooxidation are different in the case of Pt and C electrodes.

Keywords: dsDNA; Voltammetry; In-situ UV–Vis spectroelectrochemistry; Electrooxidation

1. Introduction

The electrochemistry of nucleic acid, especially DNA gets continuous attraction recently. It is well known that DNA is a polymer molecule responsible for the transfer of genetic information located in the cytosol of prokaryotic cells and in the nucleus or mitochondrium of eukaryotes [1]. It is built of heterocyclic bases (adenine, guanine, tymine and cytosine) and carbohydrate (deoxyribose) linked by the phosphate groups. Such a chain is duplicated into the form of a double helix [2].

First electrochemical investigations of DNA were done by Berg in 1957 [3]. He used cobalt ions for the detection of the proteins in RNA and DNA. A few years later Palecek and Bendich reported that only the bases from nucleic acids components undergo redox process [4–6]. Since the electroreduction of nucleic-acid bases occurs at highly negative potentials, it is attainable at mercury electrodes only [7,8]. On the other hand, the electrooxidation process of these bases takes place at potentials too positive to be studied at mercury electrodes. The voltammetric oxidation signals of nucleobases were obtained by using different solid electrodes such as gold, silver, carbon, copper and platinum. However, the voltammetric peaks were very poorly developed [9–11]. The reason for this behavior was, among others, a very high overpotential of these electrode processes and merging of the peaks with the background current. A number of papers report that to improve the visibility of the oxidation signals the differential pulse voltammetry should be employed [12–17].

It is widely accepted that guanine and adenine are the major targets in the oxidation of the DNA chain [18–20]. The analytical importance of these bases is that the determination of their individual concentrations, or of their concentration ratio, in DNA is very helpful in the measurement of the nucleic acid concentration [21]. Therefore, the work has been continued on the improvement of the voltammetric signals of DNA. Appropriate modification of the glassy carbon and gold electrode

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surfaces improved substantially the detection of DNA, its interactions with other compounds, hybridization and damage [22–30].

DNA itself can be a component of the modification layer at electrodes. The electrodes modified with DNA were used to investigate the interaction of DNA with proteins containing iron (hemoglobine and myoglobine) [31] and with other molecules in e.g. the studies on the drug action and the base-sequence recognition of DNA [32]. A useful technique reported for the modification of electrodes with DNA is adsorption of DNA on a single-crystal graphite [33–35] or on a layer of multi-wall carbon nanotubes anchored at a glassy carbon electrode [36].

The electroreduction or electrooxidation of single stranded DNA (ssDNA), with and without pre-concentration, at different types of electrodes is well known [14,37]. The detection of dissolved, not adsorbed, dsDNA in the solution was done only indirectly by watching the signal of a DNA intercalator [38]. To our best knowledge, a dsDNA direct linear-scan voltammetric signal of a good definition, in a solution, without DNA pre-concentration at the electrode surface, has not been reported yet.

In this paper, we show that the oxidation process of dsDNA can give well visible linear-scan voltammetric signals without pre-concentration or special modification of the surface of the working electrode. This, however, requires a special chemical/biological cleaning procedure. Linear-scan voltammetry might be useful for the detection of interactions of dsDNA with drugs as it provides direct currents (not its derivative) and the corresponding charges. The electrooxidation of dsDNA was also carried out with simultaneously recorded UV–Vis spectra. The electrooxidation products were stable, which was confirmed by exhaustive electrolysis of dsDNA.

2. Experimental setup

2.1. Apparatus

Electrochemical measurements were performed using an Autolab, Eco Chemie, potentiostat. In spectroelectrochemical experiments a model LAMBDA-20, UV–VIS, Perkin-Elmer spectrometer was employed. Both instruments were controlled via software. All experiments were carried out in the three-electrode system. Two platinum wires served as the counter and quasi-reference electrodes. All potentials in the paper are given vs. quasi Pt reference electrode. A regular reference electrode with a classical salt bridge was not used to prevent accumulation of DNA in the frits. A glassy-carbon disc electrode (GCDE) of 3 mm in diameter and a Pt disc electrode of 2 mm in diameter (both obtained from nLab, Poland) were applied as the working electrodes.

The home-made cell for spectroelectrochemistry was used with an optically transparent platinum electrode. The electrode was either plain platinum or carbon physically vapor deposited. Quality of the carbon coverage on Pt was inspected with SEM (Zeiss LEO 435 VP). Completeness of the coverage was also examined electrochemically by determination of hydrogen evolution over-potential in acidic media. The difference in the hydrogen evolution potential at carbon- and Pt-mesh electrodes was 0.45 V. For the vapor deposition of carbon a Polaron, model CA7625, evaporator was used. The mesh has the following parameters: the nominal aperture is 0.25 mm, the open area equals 65% of the geometric area, the wire diameter is 0.06 mm; and the no. of wires per sq. cm of the mesh is 32.3 × 32.3. The optical window is oval and of size 13 mm × 5.5 mm. During the experiments the cell was placed in a quartz cuvette (Spectrolab), see Fig. 1. The platinum counter and reference wires are appropriately smaller compared to the regular cell. The platinum mesh was supplied by Goodfellow. All electrodes were mounted in a teflon holder.

For the exhaustive electrolysis of DNA a home-made two-compartment cell was used. The counter and reference electrodes were platinum wires. The working electrodes were made from platinum and glassy carbon rods.

Each time before use, the working GCDE was polished with 0.3–0.5 μm Al_2O_3 powder on a wet pad. After each polishing, the electrode was rinsed with direct stream of ultrapure water (Milli-Q, Millipore, conductivity of ~ 0.056 mS/cm) to remove alumina completely from the electrode surface. The electrode surface was inspected optically with an Olympus, model PME 3, inverted metallurgical microscope. In all experiments, the electrochemical cell was kept in a Faraday cage to minimize the electrical noise. The potentials in figures are given *vs.* the Pt quasi-reference electrode.

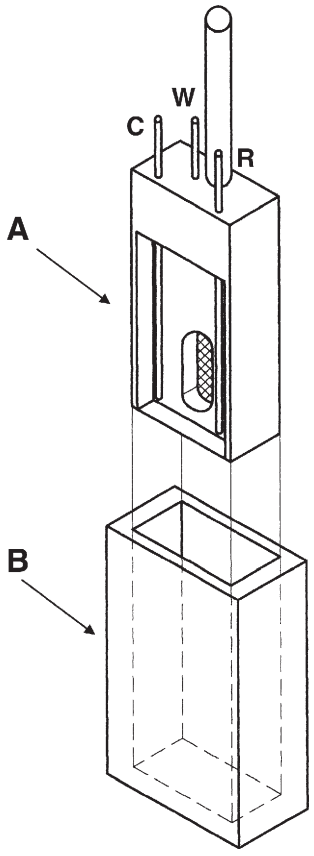

Fig. 1. Spectroelectrochemicall cell. Thickness of solution layer: 1 cm. A) Cell in a teflon holder, B) quartz cuvette.

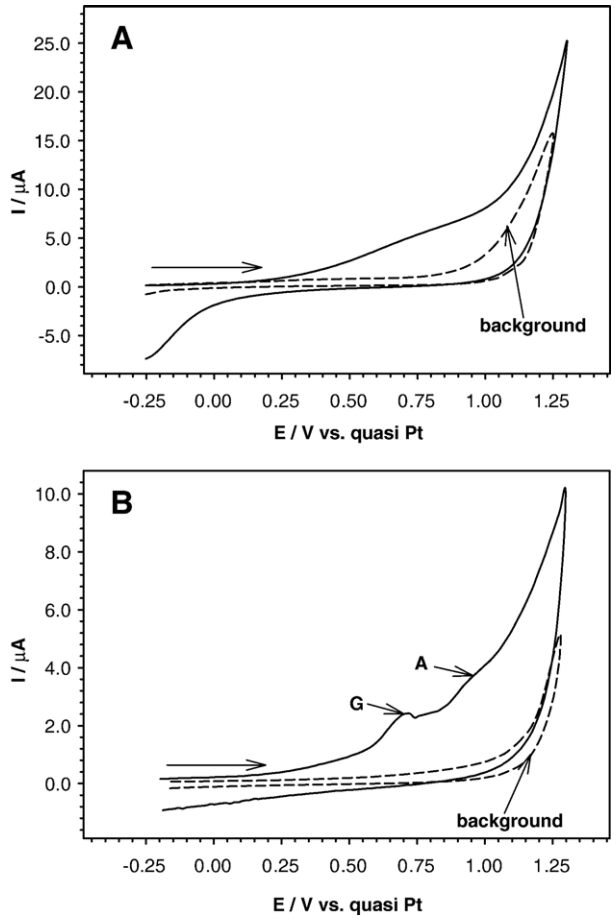

Fig. 2. Cyclic voltammograms of dsDNA at concentration of 76.4 μM base pairs in 0.05 M phosphate buffer of pH = 7.4. A) Platinum disk electrode of $\phi = 2$ mm, B) glassy carbon disk electrode of $\phi = 3$ mm. Scan rate: 100 mV s^{-1}. G stands for guanine and A stands for adenine.

2.2. Reagents

Calf thymus double stranded DNA (dsDNA) was purchased from Sigma. The dsDNA solution of 1 mg DNA/1 ml of phosphate buffer (pH ≅ 7.4) was prepared 24 (or more) h before experiments. For electrochemical and spectroelectrochemical measurements the concentration of dsDNA solution was 76.4 μM base pairs. The dsDNA concentration was determined from absorbance at $\lambda = 260$ nm using the value of $\varepsilon = 6600$ M^{-1} cm^{-1}. The phosphate buffer saline of pH = 7.4 was purchased from Sigma.

2.3. Cleaning procedure

Before each experiment the quartz cuvette, the cells and all used electrodes and accessories were cleaned according to the following procedure. First, the cell with all electrodes was immersed in ethanol to remove any adsorbed species of the oxidation products of DNA. The time of treatment was at least 30 min. Then, alcohol was replaced with ultra-pure water (Mili-Q, Millipore, conductivity of circa 0.056 μs/cm). After these two steps, the all-to-be-used accessories were exposed to hot (120 °C) water vapor. Next, the prepared cell was rinsed with a stream of phosphate buffer (pH ≅ 7.4). Finally, just before measurements, the analyzed solution was added and degassed with pure argon.

3. Results and discussion

Typical cyclic voltammograms of dsDNA at concentration 76.4 μM base pairs, obtained in pH ≅ 7.4 (0.05 M phosphate buffer) at the platinum and glassy carbon disc electrodes, are presented in Fig. 2A and B. As it was mentioned earlier, so far, no substantiated report on the electrooxidation of dsDNA in the dissolved state has been published. The only positive results that have been obtained concern the situation when dsDNA was accumulated on the electrode surface by doing appropriate polarization for 25 ÷ 40 min [33]. In our experiments we did not attempt to pre-concentrate dsDNA on the electrode surface. The dsDNA was only present in the solution. The voltammetric response obtained with the glassy carbon electrode — see Fig. 2B — exhibits two peaks at 0.72 and 1.0 V, respectively. By comparing these numbers to those corresponding to the peaks of free dissolved bases and to those of preadsorbed dsDNA, it looks as if the first peak corresponds to the oxidation of guanine (G) and the second one to adenine (A) [14,16,39]. The oxidation peaks of thymine (T) and cytozine (C) cannot be seen. It is well

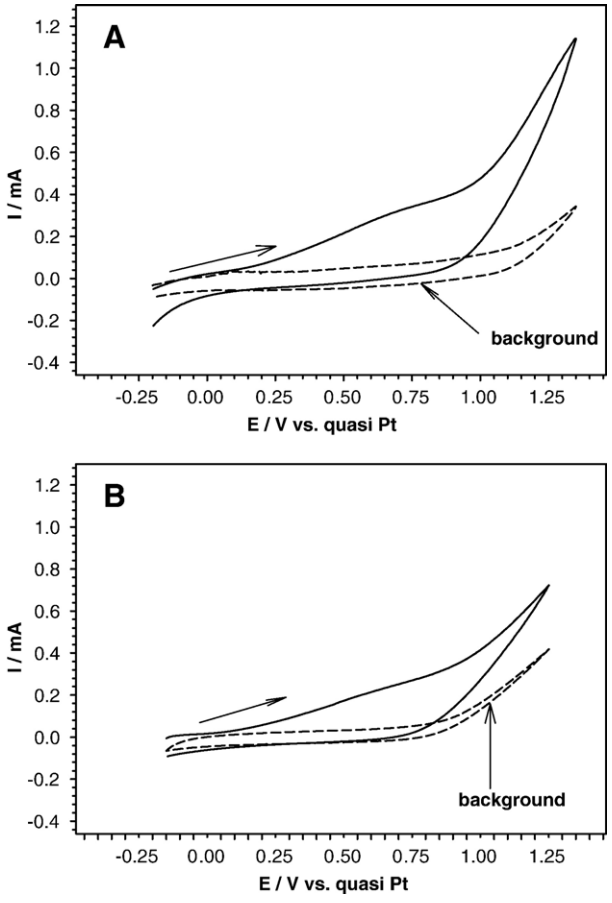

Fig. 3. Cyclic voltammograms of dsDNA at concentration of 76.4 μM base pairs in 0.05 M phosphate buffer of pH = 7.4. Platinum plain weave mesh electrodes: bare (A), carbon vapor deposited (B). Scan rate: 100 mV s^{-1}.

known, that at a potential higher than 1 V the oxidation of water starts, and the signal from cytozine and thymine is effectively covered by the water/oxygen signal. The resolution of the curves obtained with the Pt disc (Fig. 2A) has never been as good as that for the GCDE.

The voltammetric experiments with the bare-platinum transparent electrode gave also the results of poor resolution. Only one wide signal without any distinct peak was obtained in the same (compared to the disc) potential range, see Fig. 3A. Clearly, the guanine and adenine peaks could not be seen at the voltammograms. The situation was very similar at the carbon-covered mesh electrode, see Fig. 3B. There was one interesting difference between the curves obtained with Pt- and C-mesh electrodes: the "plateau" current was always higher by circa 30% in the case of Pt. Since Pt and C mesh electrodes are of the same area, this simply means that the efficiency of the oxidation process (or the percentage of the oxidized bases) is higher in the case of Pt.

The oxidation process at the transparent electrodes was accompanied by *in situ* spectroscopy (UV–Vis). The double potential sequence applied to the working electrode in spectroelectrochemical experiments was the following: for 3 s the electrode was kept at 0 V, where no Faradic current could flow, then, for 10 min, the electrode was held at increasingly positive potentials: 0.1, 0.5, 0.9 and 1.1 V. The values 0.5 and 0.9 V sit well on the DNA voltammetric signal. Several spectra were collected during the imposition of the second pulse. Fig. 4A (platinum mesh) and 4B (physically deposited carbon) present each first spectrum obtained at the second pulse potential. The collected successive spectra for each chronoammperogram were similar to the first one. After each double-potential-step measurement the cell and the electrodes were appropriately cleaned.

The spectroelectrochemical experiments revealed that the 260 nm absorption peak of dsDNA increases as dsDNA is electrooxidized. The height of the peak increases for both mesh electrodes. For the platinum mesh the increase in absorbance amounts to circa 32%, and for the carbon mesh to 11%. Also, the results obtained with Pt electrode vary much from the carbon data regarding the position of the absorbance peak of the electrooxidized species. This is illustrated in Fig. 4A and B. In the case of platinum electrode, there was no change in the absorbance peak position. The lack of changes in the position of the absorbance maximum in the dsDNA spectra obtained with the Pt electrode indicates that the electrochemical anodic process of dsDNA may not trigger the transformation of the double helix. On the other hand, there is a substantial increase in the absorbance peak. This could be interpreted in terms of the anchoring of the long dsDNA chains at the surface of the Pt mesh, however, after exhaustive electrolysis with Pt rod and removal of the working mesh electrode the absorbance was still much higher. The latter fact means that the absorption (and therefore accumulation) is not the major factor in the absorbance increase. Certainly, we have made sure that the absorbance changes shown in Fig. 4A (and in Fig. 4B) have not been caused by possible instability of the dsDNA solution.

For the carbon transparent electrode the shift of the peak wavelength was hipsochromic and amounted to circa 7.5 nm, see Fig. 4B. Interestingly, an increase in the absorbance peak of dsDNA together with identical change in its position in the spectrum was reported for the electroreduction of dsDNA at glassy carbon electrodes modified with methylene green [40]. It may mean that the configuration change of DNA upon reduction and oxidation at GC electrodes is identical. Regarding the comparison of Pt and GC electrodes: apparently, the electrooxidation of dsDNA at platinum and carbon transparent electrodes leads to the products of different conformation. To make sure the electrooxidation products are stable we have made some exhaustive electrolysis experiments. There was no major difference between the absorbance plots obtained after 2 h of exhaustive electrolysis with large-area electrodes and those taken during the spectroelectrochemical measurements.

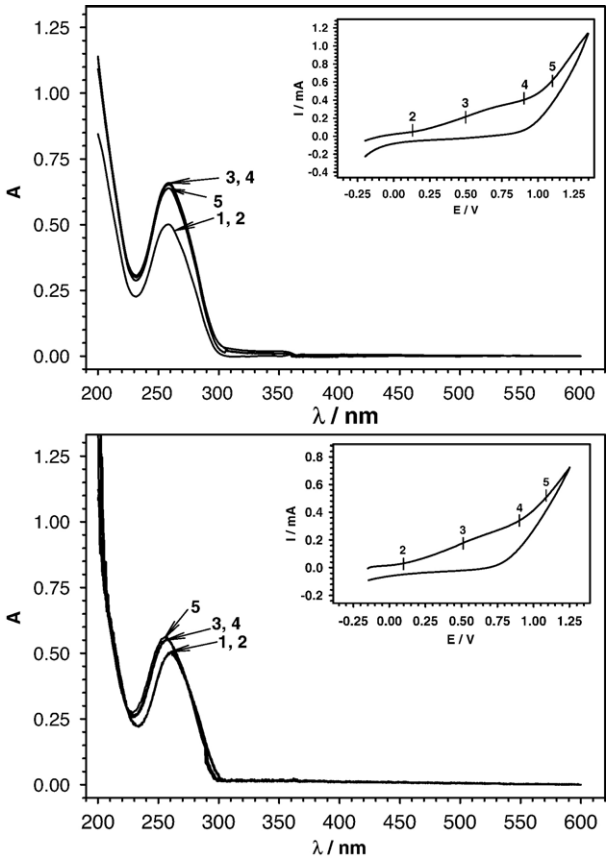

Fig. 4. *In situ* UV–Vis spectra of dsDNA obtained at different potentials applied to mesh Pt electrode: bare (A), carbon vapor deposited (B). Electrode potential during spectral measurements: no potential (1), 0.1 (2), 0.5 (3), 0.9 (4), and 1.1 V (5).

4. Conclusions

The chemical/biological purity that was attained by a procedure that consisted of, among others, the water-vapor cleaning allowed us to obtain the anodic dsDNA signal at glassy carbon and platinum electrodes without the necessity of accumulation of dsDNA at the electrode surface and of adding a mediator. The carbon surface worked better than Pt, since in the anodic scans obtained with GC electrode, 2 peak-shaped signals appear; they mark well the oxidation of guanine and adenine. This is promising, since by measuring the direct

current and charge, conclusions of more quantitative character may be drawn on the interactions between dsDNA and drugs.

The UV–Vis spectra, which were recorded during chronoamperometric electrooxidation of dsDNA at mesh electrodes, indicate that the absorbance increases upon electrooxidation. Certainly this cannot be explained in terms of just an increase in dsDNA concentration. The spectra rather suggest that some conformational changes take place (local loosening of the helix may be a part of it) as a result of dsDNA electrooxidation and correspondingly the chromophoric area of the dsDNA molecules is changed. The absorbance increases more for the Pt mesh electrode compared to the carbon covered mesh, which may be due to the adsorption of dsDNA chains at the platinum surface. At carbon electrodes no adsorption of dsDNA was detected at short time experiments.

Interesting are the differences between the peak wavelengths in the spectra taken with Pt and C mesh. The hipsochromic shift obtained with C mesh is identical to that reported for the reduction of dsDNA at a GC electrode modified with methylene green [40], and may mean that the configuration change of dsDNA is identical upon electroreduction and electrooxidation at the GC surface. No absorbance peak shift was obtained with the Pt mesh, and this may indicate that there is no configuration change of dsDNA upon electrooxidation at Pt surface. The more extensive oxidation of dsDNA chains at Pt surface may be responsible for different post-oxidation behavior of the helix.

We believe that from biological point of view the results presented in this paper are noteworthy, since they show that the use of various electrode materials in the electrochemical investigation of electrooxidation of dsDNA may lead to different conclusions. Especially important is the fact that better results, i.e. closer to natural conditions, should be obtained with soluble and not adsorbed dsDNA. Under such conditions the interactions of dsDNA examined in a laboratory should be better related to those in biological reality.

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