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Wireless light-emitting device for the determination of chirality in real samples

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28 **Keywords**

29 Bipolar electrochemistry, chirality, light emitting diodes, enantiomeric excess, real sample
30 analysis.

31 **1. Introduction**

32 Amino acids are one of the most important types of natural compounds due to their
33 involvement in essential and well-known physiological processes. For example, in biology,
34 commonly the L-form of amino acids largely dominates, thus, high levels of certain D-
35 amino acids have been attributed to bacterial activity in food or to different pathologies,
36 such as chronic kidney disease and neurological disorders, like schizophrenia and
37 Alzheimer's disease. Therefore, simultaneous monitoring and quantification of D- and L-
38 amino acids for biomedical applications, as a marker of quality, authenticity and food
39 safety, is highly needed [1]. Commonly, simultaneous detection of both enantiomers of
40 amino acids has been carried out mainly through high performance liquid chromatography,
41 which requires time-consuming protocols and expensive instrumentation. In addition,
42 alternative procedures such as capillary electrophoresis [2], reactive extraction [3], or
43 ultrafiltration through an enantioselective membrane have been developed [4]. Recently a
44 different approach to distinguish the enantiomers of two classes of amino acids in blood
45 and plasma has been proposed, involving "on the fly" bio-detection [5]. However, such thus
46 type of detection was only possible by analyzing the enantiomers in separate solutions,
47 limiting the analysis of mixtures, often present in real samples. An interesting alternative is
48 the development of fast and straightforward optical read-outs of different electroactive
49 analytes [6-9]. Recently electrochemistry-based light emitting systems have gained
50 considerable attention due to the possible direct visualization of chemical information.

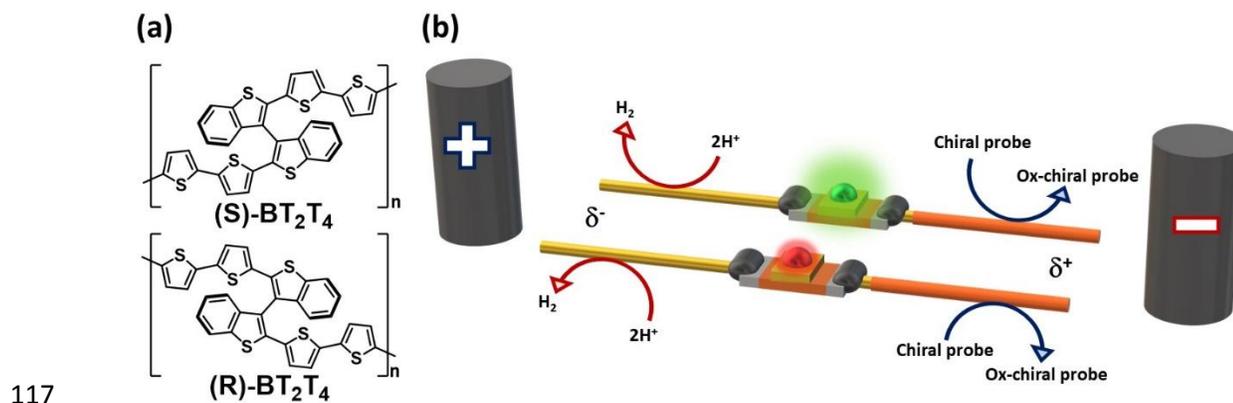
51 Different light emitting systems, based on electroluminescence [10] or fluorescence [11]
52 have been exploited for the quantification of different analytes of interest [12-16].
53 However, these methods require the use of additional chemicals, such as luminophores, co-
54 reactants, fluorescent dyes, and often the light emission is triggered by complex reactions
55 pathways. A promising alternative is the use of light emitting diodes (LEDs) for the direct
56 visualization of electrochemical processes. In such devices, the analytical information is
57 directly encoded by the electric current passing through the LED and the concomitant light
58 emission. Although light emission can be triggered by a direct electrical connection [17], an
59 interesting approach is to power these devices in a wireless manner, via coupling
60 thermodynamically spontaneous reactions to the terminals of the LED [18,19] or by using
61 bipolar electrochemistry (BPE) [20,21]. The wireless nature of the BPE approach has been
62 proven to be very convenient for materials science and analytical applications [22-28].
63 Recently BPE has been used for the electroanalytical determination of chiral information
64 coupled with mechanical actuation or light emission [29-31]. These systems are based on
65 the enantioselective oxidation of a chiral probe on the surface of an inherently chiral
66 oligomer, coupled with the reduction of a pristine polypyrrole strip, leading to a selective
67 electron-flow. The selectivity of these systems is based on the diastereomeric interactions
68 between the inherently chiral oligomer and the antipodes dissolved in solution. Therefore,
69 the actuation of the polypyrrole strip or the light emission occurs only in the presence of the
70 right enantiomer. Herein, we take advantage of such a highly enantioselective light
71 emission to design a double light-emitting bipolar recognition device for the simultaneous
72 analysis of enantiomeric mixtures of amino acids in real samples. The light emitting bipolar
73 device is designed by combining three main ingredients; (i) an inherently chiral oligomer,
74 which is the site of enantioselective oxidation; (ii) pristine gold wires, where the reduction

75 reaction occurs; and (iii) a micro-LED for the light emission (Scheme 1). This hybrid
76 device is placed in a solution containing enantiomers of two different chiral model analytes;
77 Tryptophan (Tryp) and Ascorbic Acid (AA). Tryp is an essential amino acid used
78 commonly to balance the nitrogen content in adults and also involved in the growth of
79 infants. Tryp antipodes were chosen to be simultaneously detected and quantified by using
80 the double LEDs bipolar device. Finally, AA was chosen for its high abundance in fresh
81 fruit juice, especially blackcurrants, citrus fruit and strawberries. In addition, L-ascorbic
82 acid is one of the most important water-soluble vitamins, since it acts as a free-radical
83 scavenger of reactive oxygen and nitrogen species [32,33]. Due to its relatively low
84 oxidation potential, different classic electrochemical methods have been used for ascorbic
85 acid quantification in complex media [34]. However, a straightforward visual readout of the
86 enantio-recognition of such a chiral probe has not been explored so far.

87 **2. Experimental**

88 LiClO₄ (Aldrich, 99%), anhydrous acetonitrile (Aldrich, 99.9%), Au wires ($d = 0.25$ mm,
89 Alfa Aesar, 99.9%), L-ascorbic acid (ACS reagent, $\geq 99\%$), L- and D-Tryptophan (Aldrich,
90 $\geq 99\%$), agar silver paint (Agar scientific Ltd.) and miniaturized red (0603 SMD diode,
91 Wurth Elektronik, 1.60 mm \times 0.8 mm) and green light-emitting diodes (LED, 0603 SMD
92 diode, OSRAM Opto Semiconductors, 1.70 mm \times 0.8 mm) were used as received.
93 Enantiopure (*R*)- or (*S*)-2,2'-bis(2-(5,2'-bithienyl))-3,3'-bithianaphthene ((*R*)-BT₂T₄ and (*S*)-
94 BT₂T₄, scheme 1a) were synthesized following a published methodology [35]. All solutions
95 were prepared with deionized water (MilliQ Direct-Q[®]).

96 Enantiopure oligo-(*R*) and oligo-(*S*)-BT₂T₄ films were obtained according to previous
97 reports [29-31]. Electrodeposition was carried out in a 0.1 M LiClO₄/ACN solution,
98 containing 1 mM of monomer by chronopotentiometry applying 1.5 mA for 25 minutes. A
99 gold wire was used as working electrode together with a platinum mesh and Ag/AgCl as
100 counter and reference electrodes, respectively. The double bipolar devices were assembled
101 by connecting a wire modified with the corresponding oligo-BT₂T₄ film and an unmodified
102 Au wire to the anode and the cathode of the LEDs, respectively (Scheme 1b). In brief, the
103 Au electrodes with the desired dimensions and the LED were attached to a glass support
104 using double-sided adhesive tape. A small volume of agar silver paint was employed to
105 establish an electric connection between the electrodes and the LED. The total length of the
106 final bipolar electrode is 1.8 cm. For the bipolar recognition, the enantiopure oligo-(*R*)- and
107 oligo-(*S*)-BT₂T₄-LED-Au devices were fixed in parallel at the center of a bipolar cell. Two
108 graphite feeder electrodes were positioned at the extremities of the cell at a distance of 5
109 cm. The first recognition experiments were carried out in an aqueous 5 mM LiClO₄
110 solution in the presence of different ratios of the Tryp enantiomers (90:10 and 10:90) by
111 varying the electric field from 0 V cm⁻¹ to 3.6 V cm⁻¹. The experiments with different
112 concentrations of L-AA (2, 4, 6, 8 and 10 mM) were carried out at a constant electric field
113 (2 V cm⁻¹). The standard addition method (from 2 to 10 mM) was used to carry out the
114 quantification of L-AA in a commercial lemon juice sample, at a constant electric field (2 V
115 cm⁻¹). Experiments were monitored by using a CCD camera (CANON EOS 70D, Objective
116 Canon Macro Lens 100 mm 1:2.8). Images were processed with Image J software.



118 Scheme 1. (a) Chemical structures of the two enantiomers of BT_2T_4 oligomers. (b)

119 Schematic illustration of the bipolar set-up used for the wireless quantification of chiral

120 probes based on the double light emission with a representation of the associated chemical

121 reactions. The orange part stands for the BT_2T_4 oligomer. The distance between the feeder

122 electrodes is 5 cm and the length of the bipolar object is 1.8 cm.

123 3. Results and Discussion

124 In order to evaluate the electric field required to switch on the LED integrated in each

125 bipolar electrode, a non-enantioselective green and red Au-LED-Au system was tested first.

126 The double LED device was placed at the center of a bipolar cell, containing an aqueous 5

127 mM LiClO_4 solution. To induce redox reactions in such a set-up, an electric field, high

128 enough to sufficiently polarize the bipolar electrode at its extremities, was applied. Under

129 these conditions, the oxidation and reduction of water at the anode and cathode of the LED,

130 respectively, trigger the light emission of the diode. At low electric field values (below 2 V

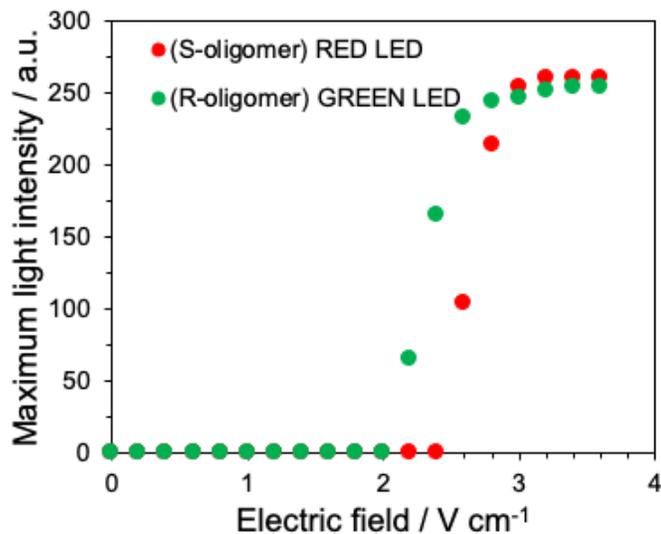
131 cm^{-1}), there is not enough driving force to induce these redox reactions, thus both LEDs

132 remains in the off-state (Figure S1). Once the electric field reaches a threshold value

133 (around 2 and 2.4 V cm^{-1} for the green and red LED, respectively) the polarization potential

134 difference, with respect to the surrounding solution, induces the oxidation and reduction of
135 water at the extremities of both Au-LED-Au bipolar electrodes. This creates an electron
136 flow from the anodic to the cathodic side of the LED and thus a concomitant light emission.
137 As it can be seen from Figure S1, the emitted light intensity is a function of the electric
138 field value. However, the difference of threshold value (0.4 V cm^{-1}) between the green and
139 red LED is attributed to the intrinsic resistance of the diode.

140 After the evaluation of the threshold potential of a non-enantioselective set up, the
141 influence of the inherently chiral oligomer on the threshold potential of the same system, in
142 the absence of chiral probe, was studied. At first, a device combining a red oligo-(*S*)-
143 BT₂T₄-LED-Au and green oligo-(*R*)-BT₂T₄-LED-Au system was placed at the center of a
144 bipolar cell containing only an aqueous 5 mM LiClO₄ solution. In the absence of the chiral
145 probe, water oxidation and reduction remain the redox reactions occurring at the
146 extremities of the bipolar electrode. Thus, a similar behavior of the light intensity as a
147 function of the applied electric field was observed for the double functionalized device
148 (Figure 1) in comparison with the non-enantioselective system (Figure S1).



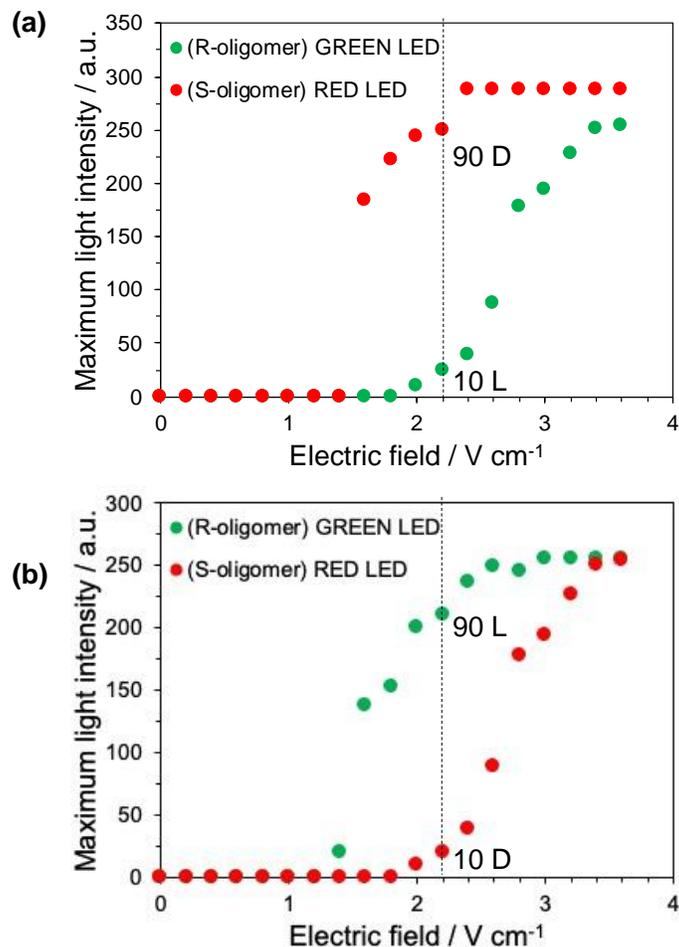
149

150 Figure 1. Maximum light intensity as a function of the applied electric field for the
 151 combination of a red oligo-(*S*)-BT₂T₄-LED-Au and green oligo-(*R*)-BT₂T₄-LED-Au system
 152 in an aqueous solution of 5 mM LiClO₄.

153 Below 2 V cm⁻¹ both LEDs remains switched-off, whereas, around 2 and 2.4 V cm⁻¹ (for
 154 the green and red LED, respectively) the electric field reaches the threshold value inducing
 155 the light emission. An identical response was observed for the inverted configuration,
 156 combining a red oligo-(*R*)-BT₂T₄-LED-Au and green oligo-(*S*)-BT₂T₄-LED-Au (Figure
 157 S2), with a similar difference of threshold potential (0.4 V cm⁻¹) between the green and red
 158 device. Thus, in the presence of the inherently chiral oligomers and in the absence of a
 159 chiral probe, the threshold potential is governed by the intrinsic resistance of the LED.

160 The first step, before testing the device in the presence of a chiral probe, was to verify by
 161 differential pulse voltammetry (DPV) the enantioselectivity of (*R*)- and (*S*)-BT₂T₄
 162 oligomers deposited on a gold wire with respect to the enantiomers of Tryptophan, L-Tryp

163 and D-Tryp, in separate solutions (4.5 mM). The DPV shows a peak-to-peak separation of
164 approximately 700 mV on (*S*)-oligomer modified electrodes for the electrooxidation of the
165 Tryp enantiomers (Figure S3). This very high thermodynamic differentiation allows the
166 simultaneous detection of both Tryp enantiomers with a double light-emitting device. The
167 red oligo-(*S*) and green oligo-(*R*)-BT₂T₄-LED-Au system was placed in the center of a
168 bipolar cell containing an aqueous 0.5 mM LiClO₄ solution. Theoretically, in the presence
169 of both chiral probes, by varying the electric field, both LEDs will switch on, and their light
170 intensity should correlate with the concentration of the corresponding enantiomer. For these
171 measurements, a ratio of 90:10 D:L-Tryp (4.5, 0.5 mM, respectively), and the specular one
172 10:90, have been chosen.



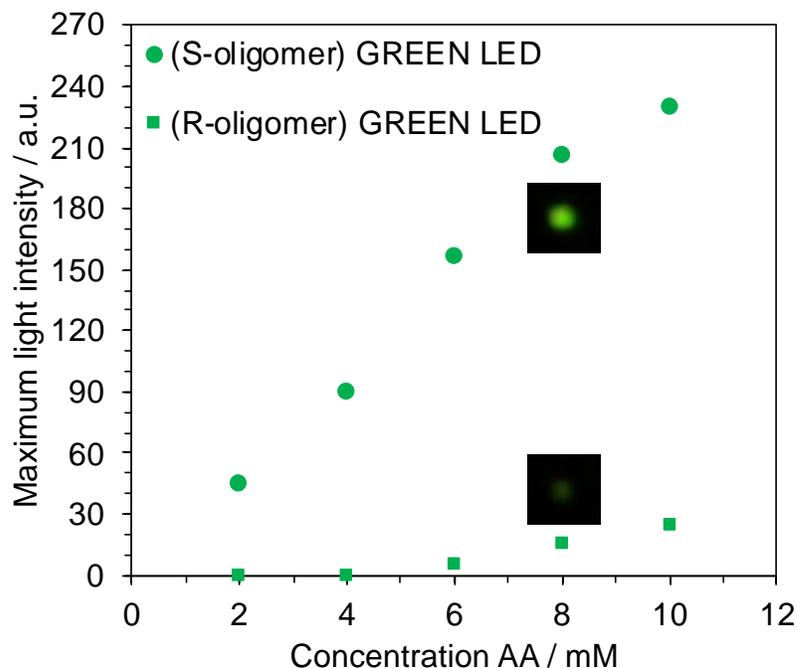
173

174 Figure 2. Maximum light intensity as a function of the applied electric field for a red oligo-
 175 (*S*)-BT₂T₄-LED-Au and green oligo-(*R*)-BT₂T₄-LED-Au system in (a) an aqueous solution
 176 of 5 mM LiClO₄ containing 4.5 mM D-Tryp and 0.5 mM L-Tryp and (b) an aqueous
 177 solution of 5 mM LiClO₄ containing 0.5 mM D-Tryp and 4.5 mM L-Tryp.

178 Under these conditions, the light intensity for the oligo-(*S*)-BT₂T₄-LED-Au device is higher
 179 than the one related to the oligo-(*R*)- BT₂T₄-LED-Au when the double recognition device is
 180 placed in the 90 D : 10 L solution (Figure 2a). The specular response was obtained by
 181 placing the same device in the 10 D : 90 L solution (Figure 2b). This is coherent with the

182 DPV measurements (Figure S3) showing a preferential oxidation of D-Tryp on the (*S*)-
183 oligomer modified wire. When comparing the light intensity for the oxidation of D- (250
184 a.u.) and L-Tryp (25 a.u.) at 2.2 V cm^{-1} , the values correlate with the 90:10 D-Tryp/L-Tryp
185 ratio present in solution. Similar results were obtained with the opposite ratio, D- (10 a.u.)
186 and L-Tryp (210 a.u.) at 2.2 V cm^{-1} ,

187 In the next step, the threshold potential of the device in the presence of L-AA was
188 evaluated. The diastereomeric interaction between the (*S*)-oligomer and L-AA is more
189 favorable from a thermodynamic point of view. Differential pulse voltammograms show a
190 peak-to-peak separation of approximately 100 mV for the electrooxidation of L-AA on (*S*)-
191 and the (*R*)-oligomer modified electrodes, respectively (Figure S4). Although, this peak
192 separation is smaller in comparison with those observed for other chiral probes (e.g. 600
193 mV for DOPA enantiomers) [29-31], it is still high enough for bipolar recognition
194 experiments. Since for this set of experiments the enantiomeric probe was available in only
195 one configuration, the double device was built with only the green LEDs that are the ones
196 having a lower intrinsic resistance (Figure S5a). The green oligo-(*S*) and oligo-(*R*)-BT₂T₄-
197 LED-Au system was placed at the center of a bipolar cell containing an aqueous 5 mM
198 LiClO₄ solution in the presence of 10 mM L-AA. Under these conditions, the threshold
199 potential for generating light at the (*S*) bipolar electrode is lower (1.4 V cm^{-1}), than the one
200 needed for the (*R*) device to switch on (1.8 V cm^{-1}), thus allowing chiral discrimination. An
201 analog light emission behavior was observed when the red oligo-(*S*) and oligo-(*R*)-BT₂T₄-
202 LED-Au system was used (Figure S5b), with a similar difference in threshold values (0.4 V
203 cm^{-1}) between the enantiopure electrodes.



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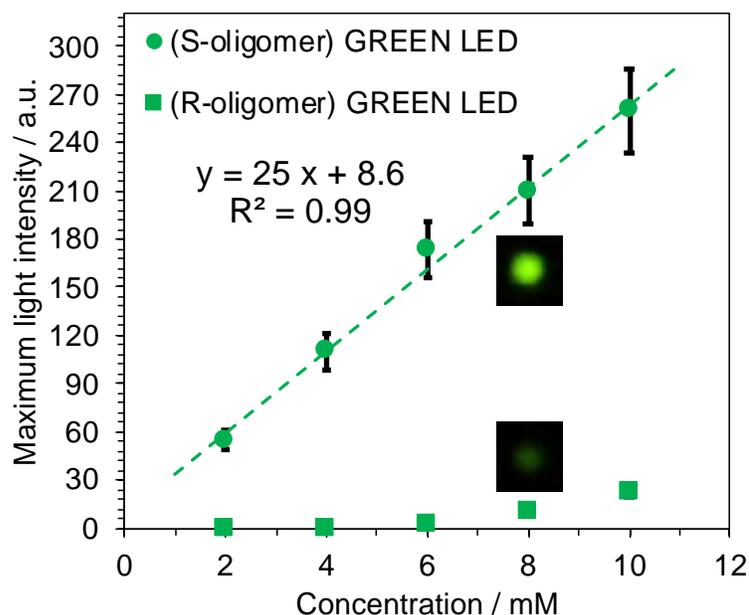
205 Figure 3. Maximum light emission as a function of L-AA concentration measured by the
 206 enantioselective oxidation of L-AA on a double green oligo-(*R*)- and oligo-(*S*)-BT₂T₄-LED-
 207 Au bipolar device, in a 5 mM LiClO₄ solution at a constant applied electric field (2 V cm⁻¹).
 208 Inset: optical pictures of the (*S*)- and (*R*)-BT₂T₄-LED-Au bipolar device at a given L-AA
 209 concentration of 8mM.

210 After demonstrating chiral discrimination through an on-off light emission, the next step
 211 was to evaluate the possibility of using the concept for the quantitative analysis of L-AA.
 212 The light intensity was measured as a function of the enantiomer concentration. Five L-AA
 213 samples were analyzed (2, 4, 6, 8 mM and 10 mM) with a green oligo-(*R*)- and oligo-(*S*)-
 214 BT₂T₄-LED-Au bipolar device by applying a constant electric field (2 V cm⁻¹). For each
 215 concentration, the average light intensity over a period of 10 sec has been used, in order to
 216 eliminate small fluctuations of the light intensity during the experiment caused by the fast

217 consumption of the analyte. A plot of the light intensity as a function of L-AA
218 concentration reveals a linear correlation ($R^2 = 0.983$) for the oligo-(*S*)-BT₂T₄-LED-Au
219 with a high sensitivity ($m_{(S)} = 24.3$ a.u./mM), in contrast to the oligo-(*R*)-BT₂T₄-LED-Au,
220 which shows, as expected, almost no signal (Figure 3). This sensitivity and linearity is
221 comparable to the one obtained with classic electrochemical systems that require
222 sophisticated electrode materials [36,37]. This illustrates the possible use of such a light
223 emitting bipolar device as an analytical tool for the qualitative and quantitative
224 measurement of enantiomers with relatively close oxidation potential.

225 Finally, in order to test the reliability of the results in real samples, the quantification of L-
226 AA in commercial lemon juice was performed. Recently, different bipolar electrochemical
227 light emitting systems, based on electrochemiluminescence, have been developed for the
228 quantification of AA in aqueous solution [38,39]. However, the light response is based on
229 indirect electrochemical mechanisms, without the possibility to directly distinguish between
230 the enantiomers of the analyte.

231 Before starting the experiments, the sample had to be diluted (12.5%) due to the turbidity of
232 the medium, which might interfere with the light response. First of all, light emission of the
233 diluted juice was measured using a green oligo-(*S*)- and oligo-(*R*)-BT₂T₄-LED-Au bipolar
234 device, at constant electric field (2 V cm^{-1}). Results show, as expected, enantioselective on-
235 off recognition of L-AA, with the green LED switching on only if connected to the (*S*)-
236 enantiomer of the oligomer (Figure 4).



237

238 Figure 4. Maximum light emission as a function of L-AA concentration measured by the
 239 enantioselective oxidation of L-AA on a double green oligo-(*R*)- and oligo-(*S*)-BT₂T₄-LED-
 240 Au bipolar device, in 12.5% commercial lemon juice at a constant electric field (2 V cm⁻¹).
 241 Error bars refer to measurements carried out three times on the same bipolar device. Inset:
 242 optical pictures of the (*S*)- and (*R*)-BT₂T₄-LED-Au bipolar device at a given L-AA
 243 concentration.

244 The standard addition method was selected for the quantification of L-AA in commercial
 245 lemon juice. Five solutions with different standard concentrations, from 2 to 10 mM, were
 246 prepared. Plotting the maximum light intensity as a function of concentration leads to a
 247 linear correlation ($R^2 = 0.99$) for the oligo-(*S*)-BT₂T₄-LED-Au, and again hardly any
 248 emission is recorded for the oligo-(*R*)-BT₂T₄-LED-Au (Figure 4). By using the regression
 249 equation $y = 25x + 8.6$, with y being the light intensity and x the concentration, a L-AA

250 concentration of 2.7 mmol L^{-1} was calculated, which is in very good agreement with the L-
251 AA content reported in the lemon juice specifications and in the literature (2.5 mmol L^{-1})
252 [40].

253 4. Conclusions

254 A bipolar electrochemical device, modified with inherently chiral oligomers has been
255 designed for the simultaneous optical determination of the enantiomers of Tryptophan,
256 present in solution, and for the quantification of L-ascorbic acid in real samples. The
257 concept of wireless light emission was successfully used for the determination of the
258 enantiomeric ratio between the two configurations of Tryp, both present in the same
259 solution. The average light intensity was found to be directly proportional to the analyte
260 concentration and used for the direct quantification of L-ascorbic acid in commercial lemon
261 juice through the standard addition technique. The calculated values are in perfect
262 agreement with those found in the literature and with the ones indicated on the lemon juice
263 specifications. The sensitivity and linearity achieved for L-AA quantification is comparable
264 to those obtained with classic electrochemical systems, that require sophisticated electrode
265 materials. The presented approach can thus be considered as an efficient and
266 complementary alternative for chiral discrimination with respect to the common
267 spectroscopic methods. Moreover, since the same device has been employed for all the
268 experiments presented herein, it can be used for multiple determinations without noticeable
269 fouling effects which might interfere with the measure of light emission. These results open
270 up the possibility to use such double light emitting bipolar devices as straightforward
271 analytical tools for the qualitative and quantitative discrimination of enantiomers, even
272 when they have relatively close oxidation potentials on a given chiral selector layer.

273 5. Acknowledgments

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