INTRODUCTION

- Malaria is one of the most impactful INFECTIOUS diseases affecting 219 million people and reporting 435,000 deaths in 2017 [1].
- Current treatments are based on artemisinin-based combination therapies (ACTs), but the emergence of drug resistance is compromising their effectiveness.
- Several single nucleotide polymorphism (SNPs) within the gene kelch 13 of Plasmodium falciparum are associated to the development of artemisinin-resistant malaria [2].

Detecting rapid and specifically the presence of the mutant (MT) allele from a blood sample will enable early rapid diagnostics at the point-of-care (PoC), and will preserve the effectiveness of current therapies.

OBJECTIVES

- Low-cost, portable, scalable, real-time signal transduction without the need of any post-amplification analysis [5,6] → CMOS-based ISFET biosensing platform.

EXPERIMENTAL METHODS

- Two reactions were performed using the MT specific primer set [4,7]:
  - Specific reaction: mutant synthetic DNA + pH-LAMP_MT
  - Unspecific reaction: wild type synthetic DNA + pH-LAMP_WT

- ISFET sensors were fabricated in UNMODIFIED CMOS technology using the top passivation layer (Si3N4) for pH sensing.
- Variations in pH were sensed by an array of 4096 SENSORS (total silicon area of 0.57 mm²) and converted into an electronic (voltage) signal which was recorded (0.3 fps) and interfaced to a PC [6].
- A microfluidic reaction chamber was assembled on top of the sensing platform.

RESULTS - ISFET platform vs qPCR

<table>
<thead>
<tr>
<th>Reaction</th>
<th>qPCR (Light Cycler 96)</th>
<th>ISFET platform</th>
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<tbody>
<tr>
<td><strong>TTP</strong> (min ± SD)</td>
<td>ΔpH (pH units)</td>
<td><strong>TTP</strong> (min ± SD)</td>
</tr>
<tr>
<td>MT allele</td>
<td>18.65 ± 0.29</td>
<td>1.32</td>
</tr>
<tr>
<td>WT allele</td>
<td>-</td>
<td>0.24</td>
</tr>
</tbody>
</table>

CONCLUSIONS

- High allele specificity (ONLY MT allele amplified)
- High speed (less than 25 min)
- Real-time detection
- High sensitivity

REFERENCES