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Miniaturized and battery-free temperature and humidity sensor for smart pharmaceutical packaging

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***Abstract*—Temperature and humidity levels inside pharmaceutical packaging can significantly affect the shelf life of the enclosed medications. The RFID technology in the UHF band is promising to address this issue as it permits to wirelessly monitor the inner environment at the item level. This work presents the design and experimental characterization of a miniaturized battery-less RFID sensor, able to simultaneously measure temperature and humidity. The proposed sensor includes a helical antenna and is compatible with the insertion into a capsule, similar to common drugs. A first prototype of the miniaturized sensor was realized and tested in terms of both communication and sensing performance. Despite variable boundary conditions, a reading distance greater than 40 cm was demonstrated. A realistic readability analysis under uncontrolled conditions estimated a probability of 65% to read the sensor from more than 20 cm. Furthermore, the humidity sensor performance was extensively characterized in a climate chamber through several tests, resulting in an accuracy of ±5% in the RH range 40-80% that is compliant with the requirements of several pharma applications.**

***Index Terms*—Smart packaging, wireless sensor, pharmaceutical, RFID, Industry 4.0, E-Health, vaccines, humidity and temperature sensors.**

I. Introduction

PHARMA is a highly regulated industry where the capillary control of temperature and humidity and more generally other factors (e.g. UV light and oxygens) inside the pharmaceutical packaging can be of utmost importance throughout the pharmaceutical's lifecycle, from production to distribution [1]. For instance, recent studies have investigated the impact of temperature exposure on the stability and efficacy of emergency medical service (EMC) drugs, such as Lorazepam, and found that excipients can significantly decrease in just a few weeks when stored outside recommended conditions, e.g. in emergency transport vehicles, thus becoming unstable over a short period [2]. Recently, the outbreak of the global COVID-19 pandemic has highlighted the importance of managing the integrity of the cold-chain to ensure the effectiveness and safety of vaccines [2], [3]. It is similarly crucial to control and monitor relative humidity (RH) for most pharmaceutical products, all the way from pre-production through to delivery to the patient. This has recently been exemplified by recent developments in understanding the relationship between a pharmaceutical product's shelf life and its storage temperature and RH. Quantitative models can now be developed for the effects of temperature and RH on the degradation processes of pharmaceutical products. Typically, these quantities models are obtained through Accelerated Predictive Stability (APS) studies in which the rates of degradation are monitored at elevated temperatures and over a range of humidity conditions (50-80 °C and 10-75 % RH). Accurate modelling of pharmaceutical stability requires accurate laboratory measurements of temperature and humidity inside packaging and containers; opening the packaging and containers to take RH measurements can compromise the measurement and in some cases requires breaking the packaging seal. Similarly, outside the testing laboratory, monitoring the RH inside packaging (i.e. the product's in-situ water activity) over the product's lifetime would enable much more accurate calculation of the long-term stability of solid packaged products [4] and could help to further improve product quality and patient safety. The control of the micro-environment at the item-level opens to new procedures for designing high-performance packaging tailored to sensitive products and certifying their quality [5]. In summary, measuring environmental conditions inside containers, bottles, vials and blisters ensure product stability, efficacy and safety throughout its lifecycle.

Currently, the parameters inside the packaging are mostly acquired by means of wired devices and invasive destructive procedures that cannot be carried out on many samples. For these reasons, indirect methods resorting to the measurement of external ambient parameters to estimate the conditions inside the packaging are sometimes preferred, despite of their limited accuracy. Several data-loggers provided with multi-parametric sensing systems are available on the market. However, these devices are often bulky, due to the presence of onboard batteries and require wired interface for off-line data retrieval at the end of the measurement session.

The new paradigm of Pharma 4.0 exploiting the RFID technology [3], [6], [7] open to new solutions for the wireless measurements of ambient parameters, in addition to the consolidated identification, anti-counterfeiting, traceability [8] and anti-tampering features of pharmaceutical products,

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resulting in reduced costs, waste and distribution times. Early examples of passive RF device for the non-destructive quality controls exploiting sensor-less [9] or even chip-less [10] approaches have been proposed in literature. However, the achievable accuracy of these devices may be insufficient for pharmaceutical applications. A HF RFID sensor tag for food traceability and cold chain monitoring was proposed in [11]. However, the short-reading range of HF standard requires supervised procedure for data retrieval, thus limiting its usability in automatic industrial systems. The work [12] introduces a low power RFID logger operating in the UHF band for pharmaceutical cold-chain but the overall size and the complexity are still not suitable for integration inside small packaging. In [13] the authors demonstrated the feasibility of integrating a multi-sensing RFID passive transponder inside a plastic bottle. The resulting electronics exploiting an external MUX is still too complex and power-demanding to guarantee a robust communication link in the real conditions involving random tag position and variable drugs' content.

Starting from the preliminary conference paper [14], this work aims at further corroborating the applicability of passive RFID technology in the context of smart packaging for pharma, by proposing the design of a fully-passive transponder for simultaneous temperature and relative humidity monitoring down to very small packaging microenvironments. The miniature size allows for integration into a capsule or tablet, thus ensuring high-fidelity monitoring of the medications under test due to the cohabitation within the same bottle.

In particular, additional results are discussed w.r.t. the conference paper, namely:

i. Deepened characterization of communications performances under controlled conditions, considering different pharmaceutical packaging and types of tablets;

ii. A statistical analysis of the reading distance obtained in a real scenario of use;

iii. An extensive relative humidity sensor characterization of 20 different sensors prototypes, including accuracy and statistical analysis.

Starting from the design of a miniaturized tag layout fitting with a typical tablet dimensions (Section II), a first prototype is manufactured (Section III) and fully characterized in operative conditions in terms of robustness of the communication link (Section IV) and relative humidity sensor performance (Section V).

II. DESIGN AND OPTIMIZATION

The concept of the miniaturized RFID sensor is shown in Fig. 1, where *i*) the RFID microchip, *ii*) the copper wire helicoidal antenna to be optimized, wrapped around a Polyammide substrate ($\varepsilon_r = 3.4$, $tan\delta = 0.03$), and *iii*) a polymeric capsule ($\varepsilon_r = 40$, $\sigma = 0.5$ S/m) used as a coating to protect the overall device are highlighted. The overall size of the miniaturized RFID sensor is a cylinder of 15.4 mm – height and 7 mm – diameter, including the external coating. The RFID microchip is the AS3213 IC by Asygn ($Z_{chip} = (23 - j213)\Omega$, IC sensitivity $p_C = -13$ dBm) [15], which embeds both temperature (range $-40°C < T < 125°C$, accuracy $\pm 1°C$, resolution $\pm 0.35°C$) and humidity (range $0\% < RH < 100\%$, accuracy $\pm 5\%$, resolution $\pm 0.2 - 0.4\%$) sensors. The 3D model design of the RFID sensor and the simulations for the antenna layout optimization were performed using the Electromagnetic solver CST Microwave Studio.

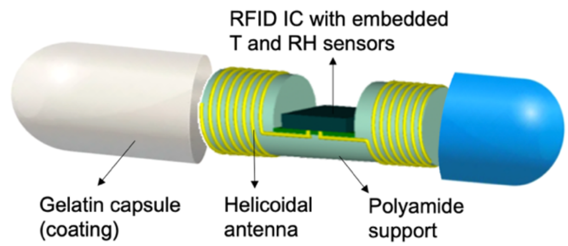

Fig. 1. 3D numerical model of the miniaturized sensor

The Normal-Mode Helical Antenna (NMHA) can be modeled as *n* loops, with diameter *d*, in series with *n* dipoles of length *s* [16]. The overall radiation pattern is the superposition effect of the radiation patterns of each element; thus, it is expected to be maximized over the plane normal to the helix axis. The resonant frequency of the antenna in free space depends on the overall length of the wire L_{wire}:

$$L_{wire} = L_b + L_{helix} \quad (1)$$

$$L_{wire} = L_b + nL_0 \quad (2)$$

Where

$$L_0 = \sqrt{s^2 + (\pi d)^2} \quad (3)$$

The diameter and the step of turns were fixed at $d = 4$ mm and $s = 0.7$ mm respectively for manufacturing reasons and for guaranteeing the miniaturization of the device. Moreover, the length of the central segment L_b was imposed by the footprint of the chip and set to 6 mm. The tuning parameters are the overall length of the wire antenna L_{wire}, which can be defined by the number of turns (n), and the position of the chip on the y-axis $d_{y,feed} = |\Delta n| \cdot s$ (Fig. 2), where Δn is the difference between the number of turns on the top and bottom side.

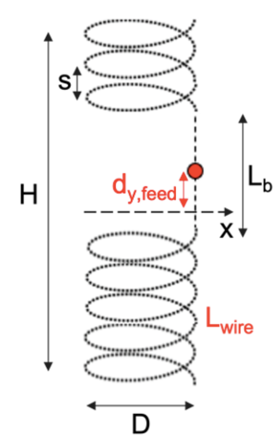

Fig. 2. Antenna geometrical parametrization. Sizes (in mm) of the fixed parameters: $S = 0.7, D = 4, L_b = 6$.

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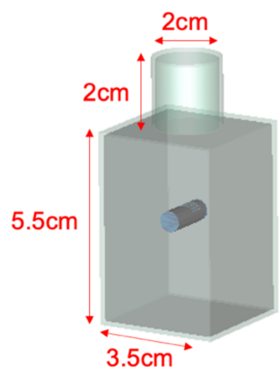


Fig. 3. 3D numerical model of the pharma package in PTFE with a homogeneous material emulating the drug content.

The antenna layout (Fig. 2) is optimized to maximize the communication performance in terms of realized gain $G \cdot \tau$, which takes into account the antenna gain and the antenna-chip impedance matching (τ) [16]. Simulations were performed considering the miniaturized sensor inserted into a pharmaceutical packaging, represented in Fig. 3, made in PTFE ($\varepsilon_r = 2.1$, $tan\delta = 0.0002$). The drug content is emulated by a homogenous material with an equivalent $\varepsilon_r = 2$ and $tan\delta = 0.0002$. Fig. 4 shows the isolines of the power transmission coefficient τ by varying the control parameters $\{L_{wire}, d_{y,feed}\}$ at the working frequency of 866 MHz (EU frequency band). The maximum value of $\tau = 0.8$ is obtained for $L_{wire} = 174.7$ mm and $d_{y,feed} = 3.0$ mm. The optimized realized gain results $G\tau = -17.5$ dB at 866 MHz, so that a theoretical read distance up to 70 cm can be achieved with 3.2 W transmitted EIRP and 0.5 as polarization factor (since in the real architecture a circularly polarized interrogation antenna will be used as opposed to the linear polarization of the sensor's antenna). The read range is hence significantly greater than similar solutions based on HF/NFC technology [17].

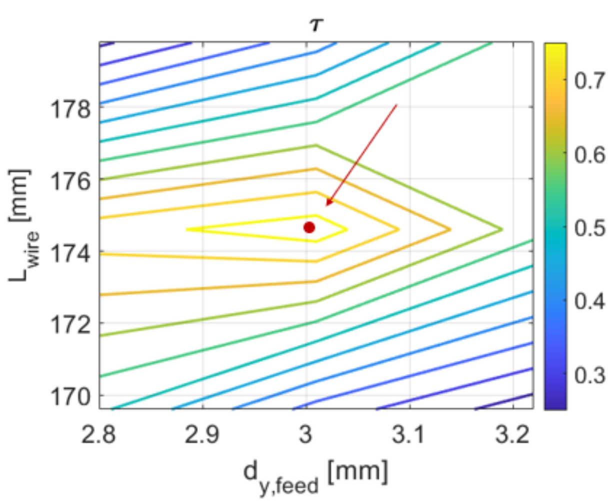


Fig. 4. Electromagnetic performance: isolines of the power transmission coefficient τ at 866 MHz, by varying the control parameters L_{wire} and $d_{y,feed}$.

III. PROTOTYPE MANUFACTURING

The prototype of the RFID sensor was manufactured by manually winding a copper wire (200 µm – diameter) (Fig. 5a) over the body of two M4 screws (4 mm – diameter, 15 mm – overall length) made of polyamide (PA) (Fig. 5b). The screws were pasted to each other and a notch was cut to host the RFID microchip (QFN24 4 mm x 4 mm x 0.5 mm) in the proper position (Fig. 5c). The chip was then soldered over a Duroid RT5880 PCB of 0.5 mm – thickness. The helicoidal antenna was finally inserted into a polymeric capsule (Fig. 5d). The capsule was provided with three holes (of 0.3 mm diameter) in correspondence of the IC to guarantee the exposure of the probe to the temperature and humidity of the environment (Fig. 5e).

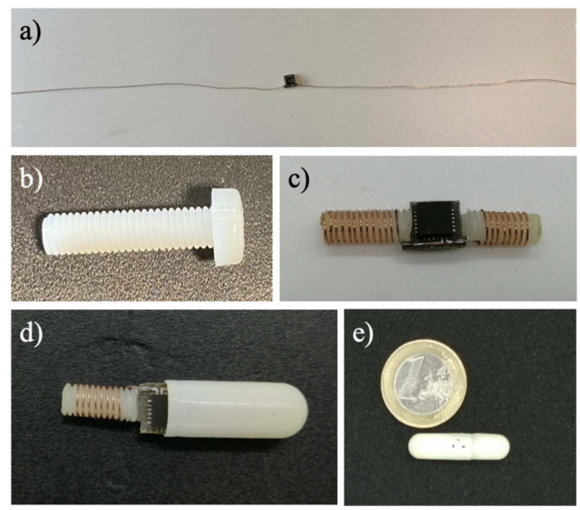


Fig. 5. Manufacturing procedure of the prototype: a) the copper wire antenna is wrapped around the b) body of the M4 screw. c) The resulting tag with a helicoidal antenna is then d) inserted in a polymeric capsule for insulating reasons. e) The final prototype of the miniaturized sensor.

IV. COMMUNICATION PERFORMANCE

A. Electromagnetic characterization

The setup for the electromagnetic validation of the simulated model includes the Voyantic TagFormance measurement station, which returns the turn-on power, that is the minimum power P_{in}^{TO} that the transmitter must emit to make the RFID sensor tag responding [18]. The realized gain can be accordingly calculated from the Friis formula by imposing that, at the turn-on, the power $P_{R\to T}$ delivered to the tag equals the chip sensitivity p_c:

$$\tilde{G}_\tau^{meas} = \left(\frac{4\pi d}{\lambda}\right)^2 \frac{p_c}{P_{in}^{TO} G_R \eta_P}$$

where λ is the wavelength, d is the reader-tag distance, G_R is the gain of the reader antenna, and η_P the polarization factor.

To perform the testing, the RFID sensor was inserted into a pharmaceutical bottle filled with reference inactive drug capsules (Fig. 6) and positioned at a distance of 25 cm from the interrogating antenna, which was a log-periodic array with a gain of 4 dBi.

The comparison between the measured and simulated realized gain is shown in Fig. 7. The gray band of the simulated realized gain in broadside (Fig. 7a) is obtained by varying the losses of the drug capsules between $0.0002 < tan\delta < 0.05$, thus accounting for the uncertainty of their realistic properties. The narrower bandwidth of the measured gain w.r.t. the simulated one is probably due to the change of the chip impedance over frequency, while it is considered constant in the simulation for the sake of simplicity. The radiation patterns at 866 MHz were also measured and compared with the simulation (Fig. 7b). Overall, good agreement between measured and simulated antenna performance was obtained in the UHF band, with a maximum difference of 0.3 dB.

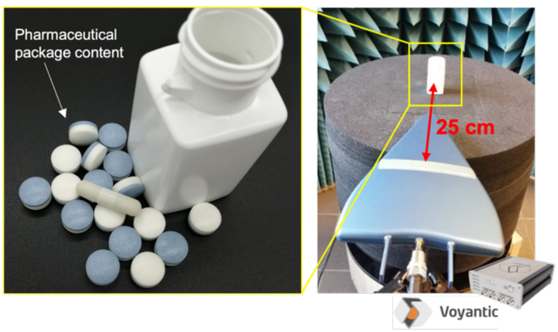
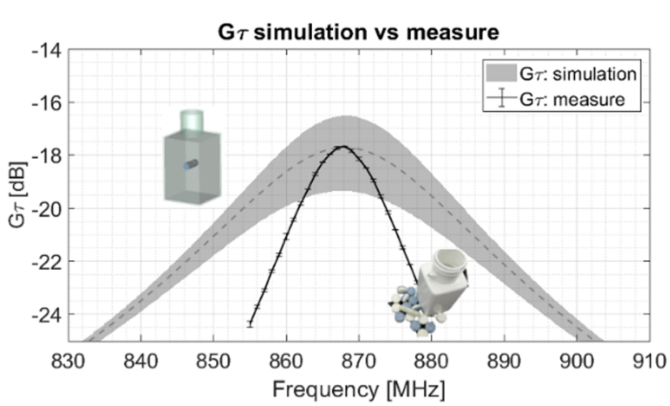
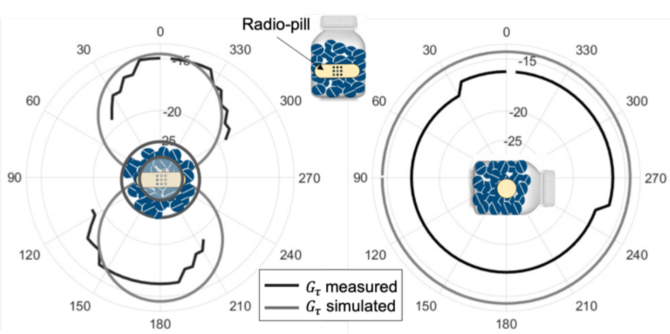


Fig. 6. Measurement setup includes the TagFormance Station with a rotation platform for the radiation pattern analysis and the pharma package filled with reference drug capsules and the prototype of the RFID miniaturized sensor.



(a)



(b)

Fig. 7. Comparison between measured and simulated results: (a) broadside realized gain over frequency and (b) radiation patterns at 866 MHz.

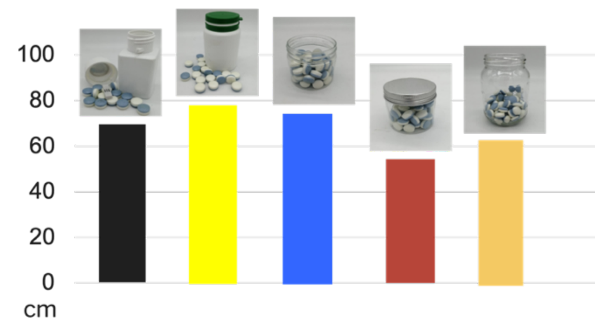
B. Sensitivity of the communication link

Typically used materials for primary pharma packaging, i.e. the one that comes into direct contact with the drugs, include aluminum, glass and plastic while the types of tablets can be categorized into hard capsules and gelatin capsules containing powders, granules or liquids. The sensitivity of the communication link is evaluated by considering it against:

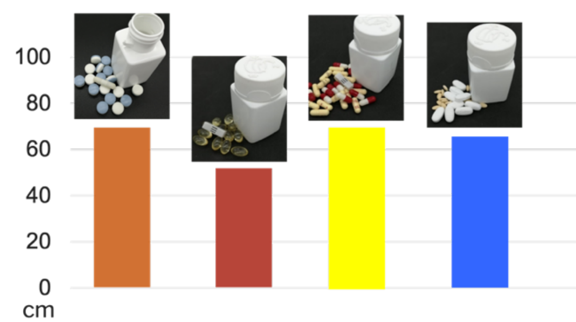
i. The variability of the packaging material, including glass or plastic cases with and without plastic or aluminum caps

ii. The variability of the dielectric properties of the pharmaceutical product which are closely related to the chemical and physical composition of the pharmaceutical mix, and in particular soft capsules filled with liquid medicine, hard capsules and tablets

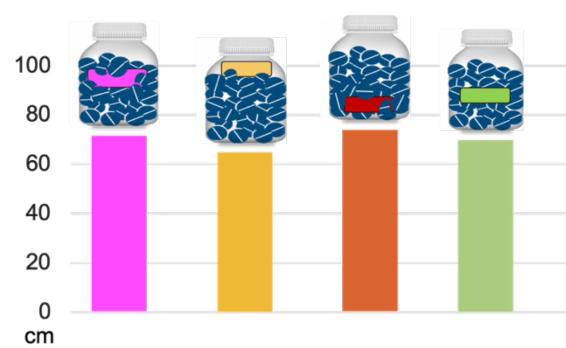
iii. The uncertainty of the position and orientation of the sensor inside the bottle by considering four possible depths of the RFID sensor w.r.t. the pharmaceutical product.



(a)



(b)



(c)

Fig. 8. Theoretical read distances obtained from the measurements of (a) five different packaging materials, (b) four types of pharmaceutical product, and (c) four different positions of the miniaturized RFID sensor.

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Fig. 8 shows the sensitivity of the communication link due to these three effects, by evaluating the theoretical read distances calculated at 866 MHz, with 3.2 W EIRP, and 0.5 polarization factor. Despite some variations, a read range of at least 40 cm is always guaranteed, even in the worst case.

C. Readability under operative conditions

The readability of the RFID sensor with a more realistic setup is evaluated under operative conditions, within a scenario that emulates a laboratory bench, through statistical analysis. The setup includes the USB Pro ThingMagic handheld reader, a circularly polarized interrogation antenna (gain 7.5dBi), and a customized software for real-time data visualization and collection (Fig. 9). We evaluated readability from three different positions of the interrogating antenna w.r.t. the pharma bottle containing real tablets and the miniaturized sensor, i.e. on the bottom and on two sides. For 80 random orientations of the RFID sensor inside the realistic pharmaceutical package filled with pharmaceutical product, obtained by shaking the bottle of tablets each time, we measured both temperature and relative humidity, and progressively moved the pharma package away from the reader antenna. We recorded the maximum distance at which the sensor data could be read using a roll meter. Fig. 10 shows the Complementary Cumulative Distribution Functions (CCDF) for each antenna positioning and reveals that the RFID-sensor can be read from a distance greater than 15 cm in the 80% of the configurations, regardless of the tag position or antenna orientation. The helical antenna has indeed two regions of null in one direction, each of approximately 70 degrees, as properly represented by the radiation pattern (Fig. 7), which can cause missed readings under uncontrolled conditions. The random variation in the orientation angle of the sensor relative to the interrogating antenna explains the high probability of such short reading distances, as the gain exhibits significant variations with the orientation angle (approximately 5 dB for 60 degree variation). However, this issue can be solved by using a second interrogation antenna, orthogonal to the first.

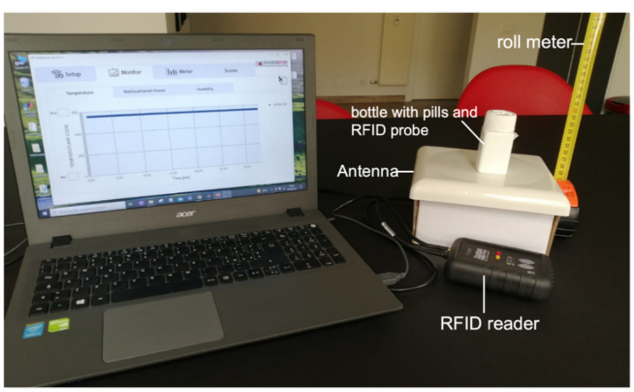

Fig. 9. Realistic interrogation infrastructure includes an RFID reader, a reader antenna (here placed at the bottom of the pharma bottle containing the miniaturized sensor), a roll meter and a PC with customized software for data collection and visualization.

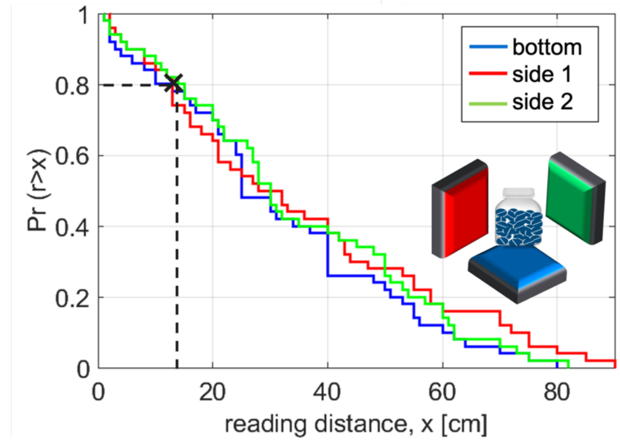

Fig. 10. Complementary Cumulative Distribution Functions of the achievable reading distances of the miniaturized RFID sensor with a realistic interrogation architecture, for three different antenna positioning.

This solution would significantly decrease the chances of missed readings and substantially improve the probability of achieving greater reading distances. It is important to note that increasing the overall length of the helical antenna is not a viable option due to the application constraints on the dimension.Therefore, suggesting a reading architecture that incorporates two interrogating antennas results in a highly feasible and practical solution for real-world scenarios.

V. CHARACTERIZATION OF HUMIDITY SENSOR

The experimental characterization of the internal humidity sensor integrated into the AS3213 IC involved the evaluation of achievable accuracy, hysteresis and reproducibility errors. This was conducted on 20 prototypes of the miniaturized RFID sensor in order to ensure robustness and consistency across the design. The characterization process involved placing the RFID sensors under test inside a climate chamber (Binder MK56), which is capable of controlling both humidity and temperature (Fig. 11). The transponders were placed on polymeric foam substrate and interrogated in real-time by a patch antenna

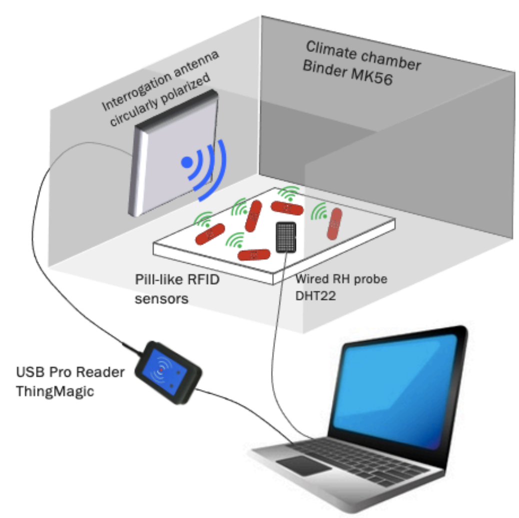

Fig. 11. Measurement set up for sensing performance characterization inside a climate chamber.

placed inside the metal cavity of the chamber and connected to an external RFID reader. The setup includes also a reference wired probe DHT22 in the close proximity of the RFID sensors for comparison.

A. Humidity sensing at fixed temperature

The first session focused on evaluating the response of the RH sensors at a fixed temperature T=20 °C. The typical humidity range required for solid pharmaceutical products is 25% - 60% while for RH > 60% there is a high risk of microbial growth or product degradation. To assess the sensors' performance in real application conditions, the relative humidity was raised in the range of 20% - 80 % with a step of 20%, with each level being maintained for 20 minutes to ensure stationary conditions. The 20 miniaturized sensors were divided into five groups and characterized in consecutive sessions. An example of the measurement results is shown in Fig. 12. The trends in the figure were obtained by processing the raw data, which involved removing outliers and applying a moving average on 100 samples.

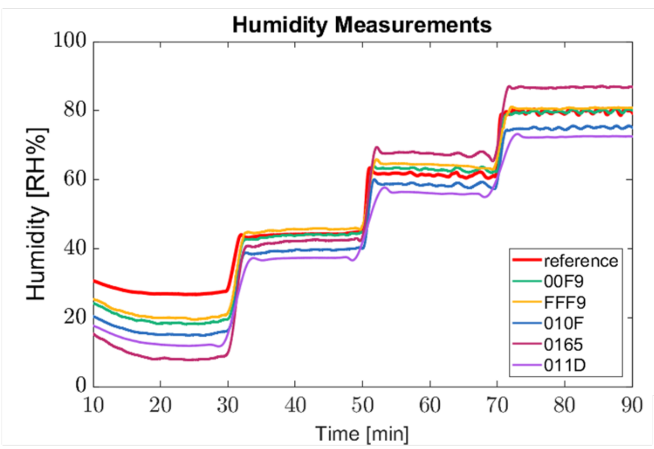

Fig. 12. Example of measurement in the climatic chamber: humidity measurement with 20% RH steps in the range 20% -80%, keeping the temperature constant. The trends were obtained with a group of five different sensors indicated in the legend, while the red curve is the measurement of the wired reference probe.

To determine the accuracy of the sensors, the average measured RH values were calculated for both the RFID sensors and the reference wired probe DHT22 at each plateau level, i.e. for each set RH value. The plateau regions were defined to start 2 minutes after each jump in humidity level.

Fig. 13 displays the accuracy of the 20 miniaturized probes (gray dots), w.r.t. the reference wired probe DHT22. The averaged accuracy (red dots) calculated for the overall set of probes is within the acceptable range of ±5% within the 40% - 80% interval of relative humidity. At lower values, the average error is significantly higher (about 10%), with the worst-performing probes returning an error of 15%-18%.

The probability of having an accuracy that falls within the acceptable range of ±5% is calculated through the Cumulative

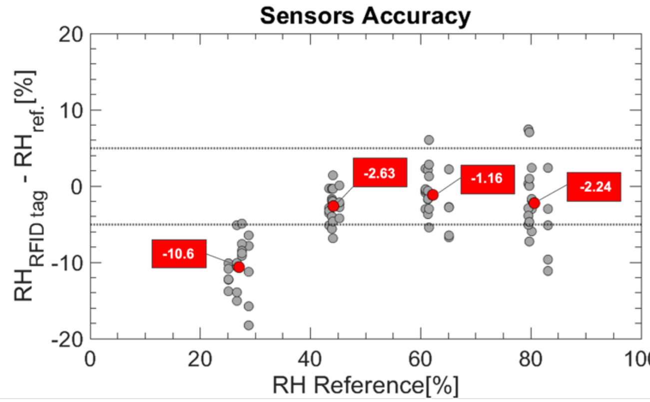

Fig. 13. Accuracy of the 20 RFID probes humidity sensors (gray dots) w.r.t. a reference probe and its average values (red dots) for each humidity level.

Distribution Function (CDF) (Fig. 14) evaluated considering all the miniaturized sensors under test.

If the whole humidity range [20% - 80%] is considered, the miniaturized probes return an RH level with an average difference of less than 5% w.r.t. the reference probe in the 60% of the considered measures. The above percentage rises to 80% for a reduced range of humidity, namely 40% - 80%.

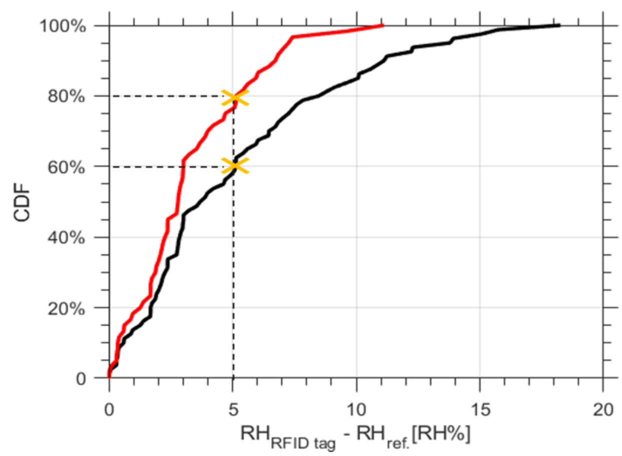

Fig. 14. Cumulative distribution function of the relative humidity accuracy of the RFID probes under test.

B. Humidity sensing at variable temperature

The impact of the temperature on the humidity sensing accuracy was evaluated by testing 5 probes at three different temperature values {20°C, 40°C, 60°C}. For each temperature level, the humidity was increased in the range 20% - 80% with a step of 20%, each lasting 20 minutes. Fig. 15 shows the regression lines calculated for each RFID probe at the different considered temperatures. Each point represents the measured humidity level averaged over 20 minutes interval. As the temperature increases the regression lines of each RFID probe remain roughly parallel. However, the measured values of relative humidity increase despite the temperature compensation already being accounted for by the conversion formula provided by the IC manufacturer [15]. This phenomenon should be taken into account for future calibration efforts.

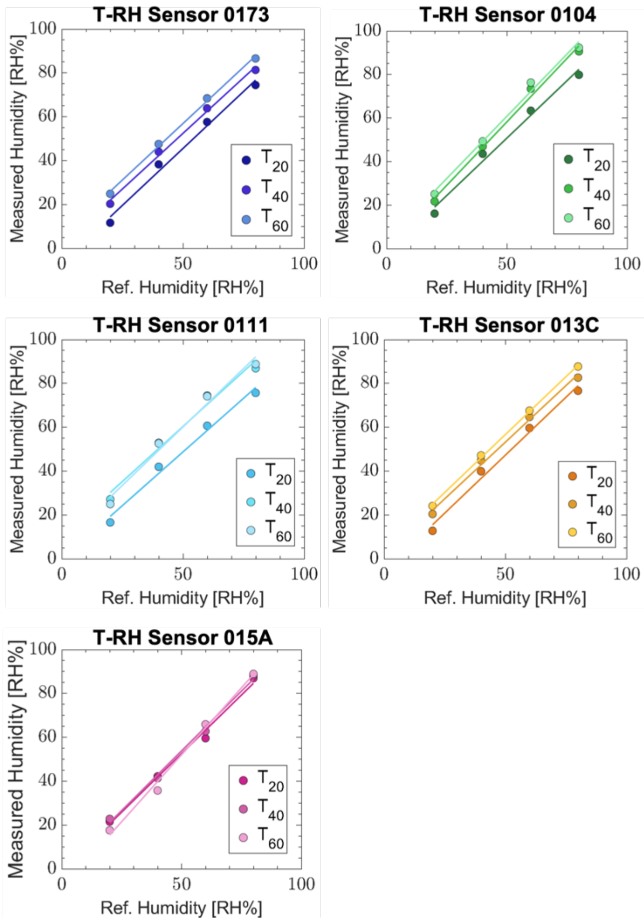

Fig. 15. Humidity regression lines of five RFID sensors at 20°C, 40°C and 60°C.

C. Hysteresis

To investigate the reliability of the miniaturized sensors' measurements, a hysteresis characterization was performed on a subset of five RFID sensors. The objective was to evaluate whether the sensors' output, i.e. the target RH level, differs when the relative humidity is increased compared to when it is decreased. During the session, the temperature was set constant at 40°C while the humidity was first increased and then decreased by 10% RH step within the range of 20% - 60%. The regression lines calculated for each probe are reported in Fig. 16, where the black lines correspond to the increasing phase of humidity and the gray lines to the decreasing one. The nearly coincident pair of lines for all tested sensors demonstrates that the RFID sensors are not affected by hysteresis. Any small discrepancies observed are mostly due to the climate chamber's inability to reach and/or maintain the set humidity level.

D. Reproducibility

The reproducibility of the RFID miniaturized sensors was evaluated by testing a subset of 5 in two separated sessions, repeated in consecutive days, with slight variations in the spatial arrangement of the testing setup and initial conditions of the environment inside the climate chamber. The temperature was set at 20 °C and the humidity was raised in the range of 20 % -80 % with a step of 20%. Fig. 17 displays the average humidity levels over 20 minutes intervals, grouped by sensor, obtained during the two sessions (distinguished by color intensity). The reproducibility error, defined as the overall difference between the values collected in different tests, was found to be within ±2% (with the exception of sensor FFF9 at 20% humidity).

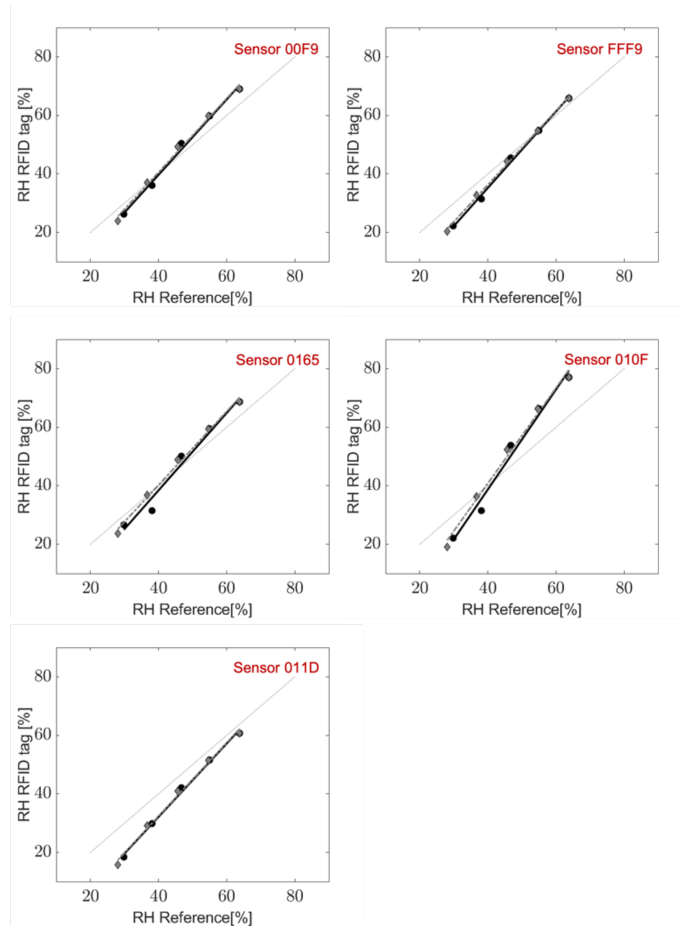

Fig. 16. Humidity regression lines of the hysteresis cycle for five RFID probes.

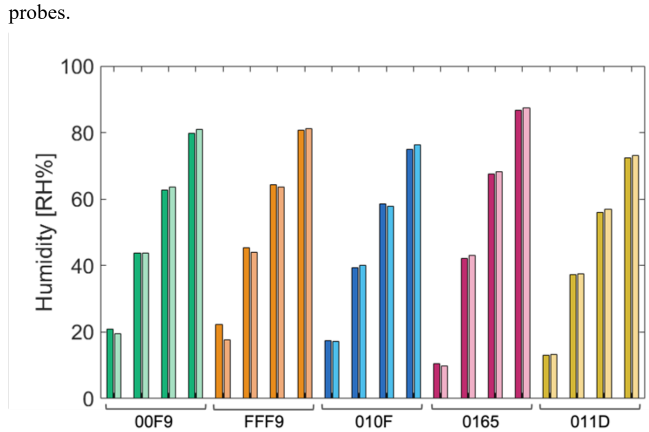

Fig. 17. Reproducibility: RH measurements measured during the two different test sessions (represented by the same color of different intensity) for each RFID probe.

VI. CONCLUSIONS

A miniaturized RFID sensor with similar dimensions to a typical pharmaceutical tablet or capsule was designed and optimized for passive and wireless monitoring of micro-environments within pharmaceutical packaging. The first prototype was realized and tested in realistic conditions. The variability of the boundary conditions of the miniaturized sensor inside the pharmaceutical package was then evaluated, by considering different types of packaging, types of pharmaceutical product, and positions of the sensor inside the bottle. In all cases, the sensor exhibited a read range of over 40 cm, even in the worst case condition. Furthermore, the sensor's readability was also evaluated through statistical analysis, demonstrating an 80% probability of successfully reading the sensor from a distance greater than 15 cm under operative uncontrolled conditions. Furthermore, the relative humidity sensor performance was characterized through several tests in the climate chamber. An accuracy of ±5% was demonstrated in the range of 40%-80% RH with a reproducibility error of ±2%. Overall, the presented miniaturized RFID sensor is promising for enabling direct environmental control at the item level, which could help monitor and prevent pharmaceutical product damage caused by temperature and humidity fluctuations within pharmaceutical packaging.

REFERENCES

[1] Jaffer, G. Pharma's Almanac. Keys to Successful Storage, Management and Transport of Biological Materials. Available online: (Accessed on Apr. 2023).

[2] De Winter S, Vanbrabant P, Vi NT, Deng X, Spriet I, Van Schepdael A, Gillet JB. Impact of temperature exposure on stability of drugs in a real-world out-of-hospital setting. Ann Emerg Med. 2013 Oct;62(4):380-387.

[3] Ramakanth, D., Singh, S., Maji, P.K. *et al.* Advanced packaging for distribution and storage of COVID-19 vaccines: a review. *Environ Chem Lett* 19, 3597–3608 (2021).

[4] Scrivens, Garry, Donald Clancy, and Paul Gerst. "Theory and fundamentals of accelerated predictive stability (APS) studies." Accelerated Predictive Stability. Academic Press, 2018. 33-7.

[5] McKeen, Laurence W. Permeability properties of plastics and elastomers. William Andrew, 2016.

[6] D. K. Sharma, P. Gupta, Priety, Chapter 9 - Internet of Things: the new Rx for pharmaceutical manufacturing and supply chains, *An Industrial IoT Approach for Pharmaceutical Industry Growth*, Academic Press, 2020, Pages 257-288.

[7] E. Saha, P. Rathore, R. Parida, N. P. Rana, *The interplay of emerging technologies in pharmaceutical supply chain performance: An empirical investigation for the rise of Pharma 4.0*, Technological Forecasting and Social Change, Volume 181, 2022.

[8] K. M. Botcha, V. V. Chakravarthy and Anurag, "Enhancing Traceability in Pharmaceutical Supply Chain using Internet of Things (IoT) and Blockchain," *2019 IEEE International Conference on Intelligent Systems and Green Technology (ICISGT)*, Visakhapatnam, India, 2019, pp. 45-453.

[9] S. Manzari, C. Occhiuzzi, S. Nawale, A. Catini, C. Di Natale and G. Marrocco, "Polymer-doped UHF RFID tag for wireless-sensing of humidity," *2012 IEEE International Conference on RFID (RFID)*, 2012, pp. 124-129.

[10] Y. Feng, L. Xie, Q. Chen and L. -R. Zheng, "Low-Cost Printed Chipless RFID Humidity Sensor Tag for Intelligent Packaging," in *IEEE Sensors Journal*, vol. 15, no. 6, pp. 3201-3208, June 2015.

[11] E. Abad, F. Palacio, M. Nuin, A. González de Zárate, A. Juarros, J.M. Gómez, S. Marco, RFID smart tag for traceability and cold chain monitoring of foods: Demonstration in an intercontinental fresh fish logistic chain, Journal of Food Engineering, Volume 93, Issue 4, 2009, Pages 394-399.

[12] J. C. S. dos Santos *et al*., "Optimized ultra-low power sensor-enabled RFID data logger for pharmaceutical cold chain," *2015 IEEE Brasil RFID*, 2015, pp. 1-5.

[13] N. D'Uva *et al*., "Batteryless Wireless Temperature/Humidity Sensor for Item-level Smart Pharma Packaging," *2021 IEEE International Workshop on Metrology for Industry 4.0 & IoT (MetroInd4.0&IoT)*, 2021, pp. 145-149.

[14] D. Masi *et al*., "Radio-pill: RFID miniaturized and battery-free humidity probe for pharmaceutical moisture analysis," *2022 IEEE 12th International Conference on RFID Technology and Applications (RFID-TA)*, Cagliari, Italy, 2022, pp. 153-156.

[15] Datasheet. Online [Available]: https://asygn.com/as321x/. May, 2022.

[16] *Balanis*, Constantine A. *Antenna Theory*: Analysis and Design. 3rd ed. Hoboken, NJ: John Wiley, 2005.

[17] Boada, M., Lazaro, A., Villarino, R., & Girbau, D. (2018). Battery-less soil moisture measurement system based on a NFC device with energy harvesting capability. IEEE Sensors Journal, 18(13), 5541-5549.

[18] P.V. Nikitin and K.V.S. Rao. "Theory and measurement of backscattering from RFID tags". In: *IEEE Antennas and Propagation Magazine* 48.6 (2006), pp. 212–218.

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