12TH GALENUS INTERNATIONAL WORKSHOP:

Bioengineering the future of drug delivery

Biocatalytic Nanobots

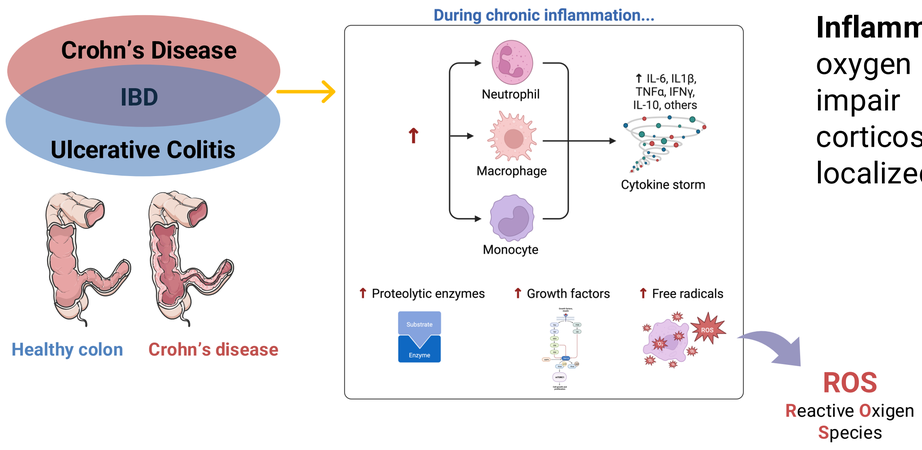
Enhancing Reactive Oxygen Species Neutralisation for Targeted Therapy in Inflammatory Bowel Disease

Ana Sofia Sousa[1,2,3], André Mayer[1], Celso A. Reis[2,3,4,5], Maria Manuela Pintado[1] & Ezequiel R. Coscueta[1]

[1] Universidade Católica Portuguesa, CBQF - Centro de Biotecnologia e Química Fina – Laboratório Associado, Escola Superior de Biotecnologia, Rua Diogo Botelho 1327, 4169-005 Porto, Portugal [2] i3S—Instituto de Investigação e Inovação em Saúde, Universidade do Porto, 4200-135 Porto, Portugal; [3] Institute of Molecular Pathology and Immunology of University of Porto, Ipatimup, 4200-135 Porto, Portugal; [4] ICBAS – Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, 4050-313 Porto, Portugal; [5] Medical Faculty, University of Porto, Al. Prof. Hernâni Monteiro, 4200-319 Porto, Portugal.

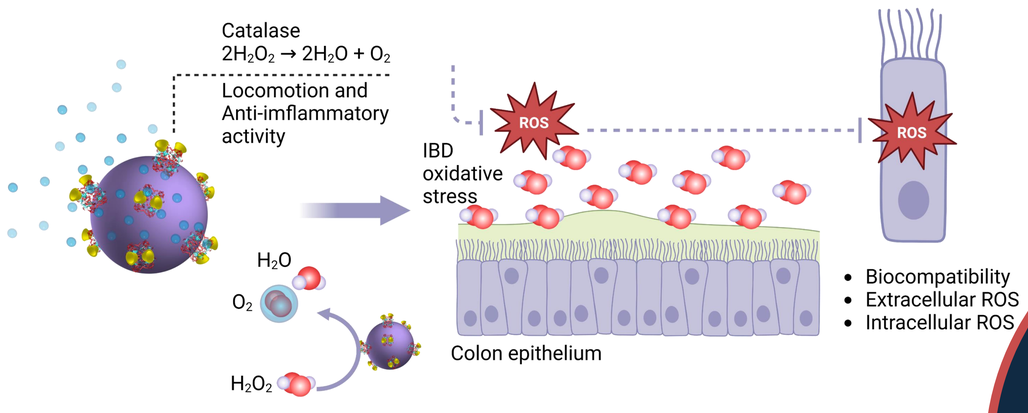
ecoscueta@ucp.pt ecoscueta

BACKGROUND & IDEA



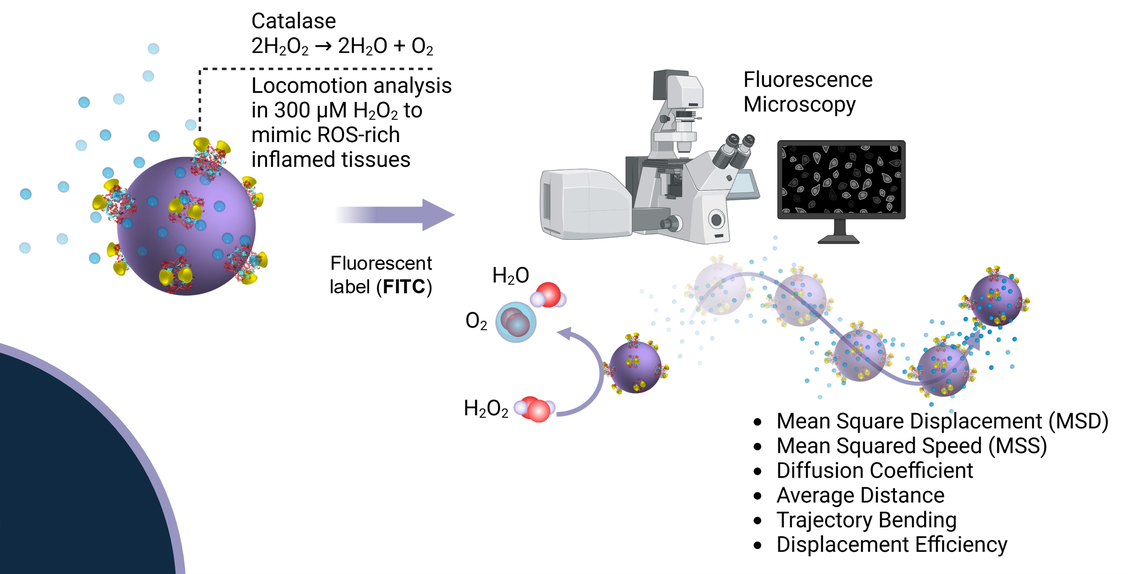
Inflammatory bowel disease (IBD) is marked by chronic intestinal inflammation and an overproduction of reactive oxygen species (ROS) within the gastrointestinal mucosa [1]. Elevated ROS levels contribute to tissue damage and impair mucosal healing, thereby intensifying the inflammatory process. Conventional treatments, such as corticosteroids and immunosuppressants, primarily target systemic inflammation but are limited in addressing the localized oxidative stress characteristic of IBD.

To overcome these limitations, our study introduces a **polymeric biocatalytic nanobot (NB)** system designed to combine efficient propulsion with ROS neutralisation. The NB is built around a chitosan core with mucoadhesive properties [2], which promotes prolonged retention at inflamed mucosal surfaces and may also enhance the delivery of bioactive compounds [3].



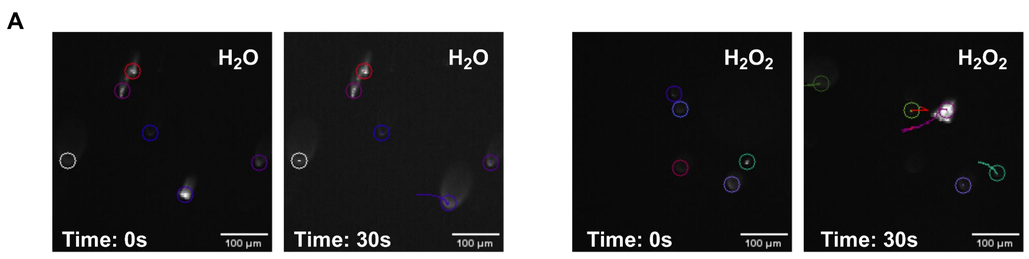
OBJECTIVE & METHODOLOGY

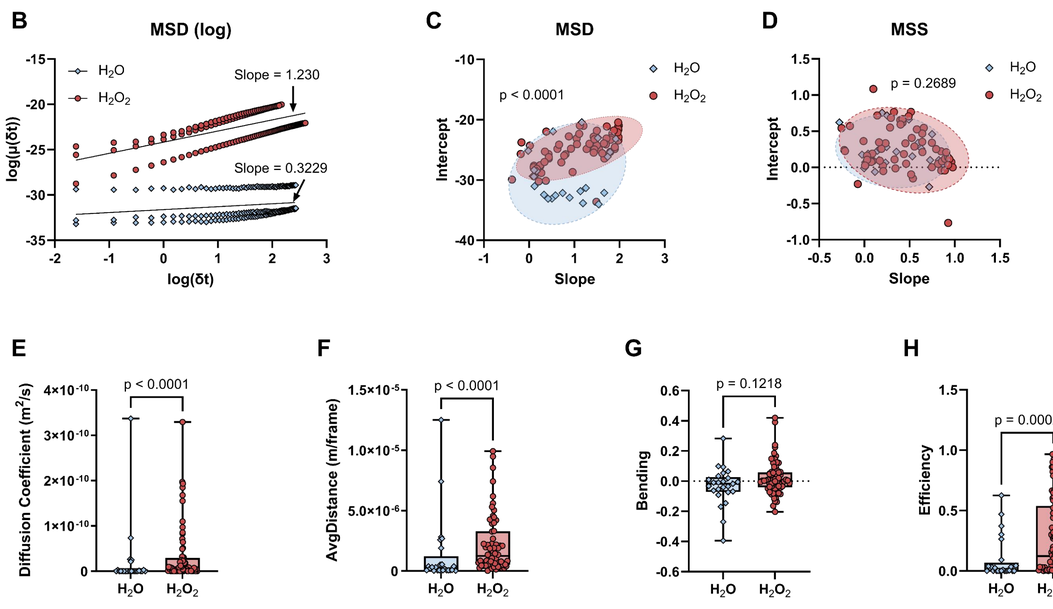
The **specific objective** of this work is to evaluate the locomotion performance of the designed NBs under basal conditions and in environments enriched with ROS [3], thereby simulating the inflamed state typical of IBD.



gBiOT

RESULTS





Figures: Analysis of NB's propulsion mechanism powered by hydrogen peroxide (H_2O_2) using fluorescence microscopy: **A)** the **trajectories of NB** in H_2O and 300 µM H_2O_2 at 0 and 30 seconds; **B)** the **MSD** as a function of time, highlighting a significant difference ($p < 0.0001$) in **mobility favouring H_2O_2**; **C)** comparison of the intersection and slope of the MSD, reinforcing the **improved mobility under H_2O_2 conditions**; **D)** the Mean Squared Speed (MSS) does not indicate significant differences between H_2O and H_2O_2 ($p = 0.2689$); **E)** a noteworthy **increase in the diffusion coefficient** in H_2O_2; **F)** the particles travelled a markedly greater distance in H_2O_2 ($p < 0.0001$), confirming **better directional movement** in this medium; **G)** analyses trajectory curvature, showing no significant differences ($p = 0.1218$), suggesting **similar randomness in movement patterns** across both media; **H)** the displacement efficiency is significantly greater in H_2O_2 ($p = 0.0002$), indicating more direct movement from the origin. Statistical analyses were carried out using the MANOVA test for Figures 1C and 1D and the Mann-Whitney test for Figures 1E-1H, with $p \leq 0.05$ considered statistically significant.

Discussion

The behaviour of the NB under ROS-enriched conditions supports their **potential for targeted navigation in inflamed environments**, as encountered in IBD. The distinct propulsion observed in the presence of ROS—contrasting with the random motion under basal conditions—underscores the efficacy of the H_2O_2 decomposition mechanism to trigger NB movement.

This ROS-responsive locomotion highlights a key advantage of the NB system, which may be harnessed to enhance retention and accumulation at inflamed mucosal sites.

From a broader perspective, these findings encourage further exploration into optimising NB design for improved performance in the complex milieu of the gastrointestinal tract. **Future work** will focus on further **refining the NB system** by investigating its **protective mechanisms under gastrointestinal conditions**, such as resistance to proteolytic enzymes and acidic pH. This will be essential for ensuring effective retention and function within the inflamed colon, thereby advancing the application of NB as a precision tool for IBD management.

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