Lecture critique d'articles scientifiques

Pr. Hirtz Christophe & Dr. Coppens Salomé

Programme

- Rappel sur la structure d'un papier et les marqueurs de référence
- Initiation à la lecture critique d'article
- Pratique: Lecture critique d’un article

Objectifs

- Pouvoir critiquer un article
- *Afin de ne pas perdre de temps*
- *D'en tirer le plus important*

- Proposer un plan expérimental alternatif

Qu'est-ce qu'un Article Scientifique

- **L’article de recherche** présente les résultats originaux (*a priori* ou *a posteriori*) d’une recherche.
- **L’article de synthèse** est une synthèse bibliographique présentant un état de l’art sur un problème ou un sujet donné.

But ?

Permet au chercheur de partager ses travaux et résultats avec ses pairs et d’autres experts dans son domaine.

Ou trouve-t-on les articles scientifiques ?

- **Pubmed**
- **Google Scholar**
- **Research Gate**
- **Nature et autres revues**
- *Des sources fiables ?* ***Chartre Hon*** *(Health on the Net)*
- Le HONcode est un code de déontologie guidant les responsables de sites Web dans la mise en place de mécanismes fondamentaux permettant de mettre à disposition une information médicale de qualité, objective et transparente adaptée à la mission et à l'audience du site. La transparence d'un site améliore l'utilité et l'objectivité de l'information et la publication de données correctes.

https://www.hon.ch/fr/recherche.html

Comment sélectionner un article ?

- **La pertinence** : ce document va-t-il permettre de répondre à la question que l'on se pose ?
- **La source** : le document est-il fiable ?
- **Les auteurs** : leur affiliation et la date de parution sont aussi à prendre en compte

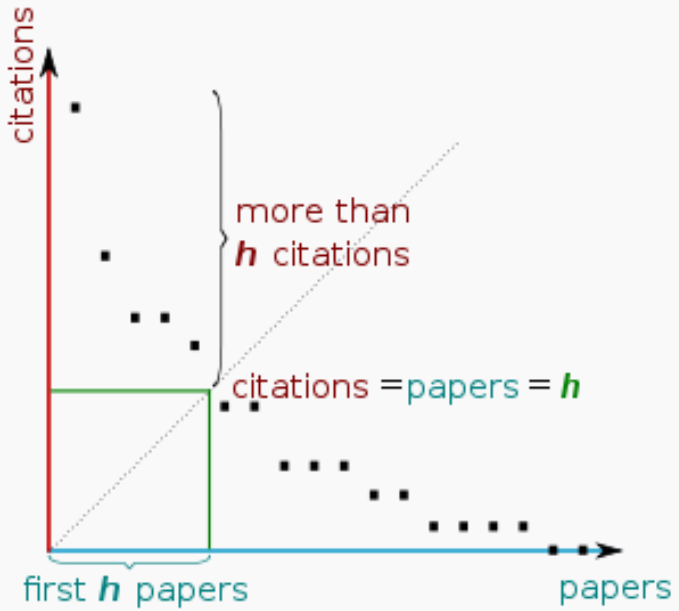
- *Attention aux vieilles données*

Le facteur d'impact

Impact factor d'une revue

Qu'est-ce que c'est ? Google scholar

Le principe : Plus les revues ont publié d'articles qui sont cités un nombre élevé de fois par les pairs, plus leur impact factor est important.

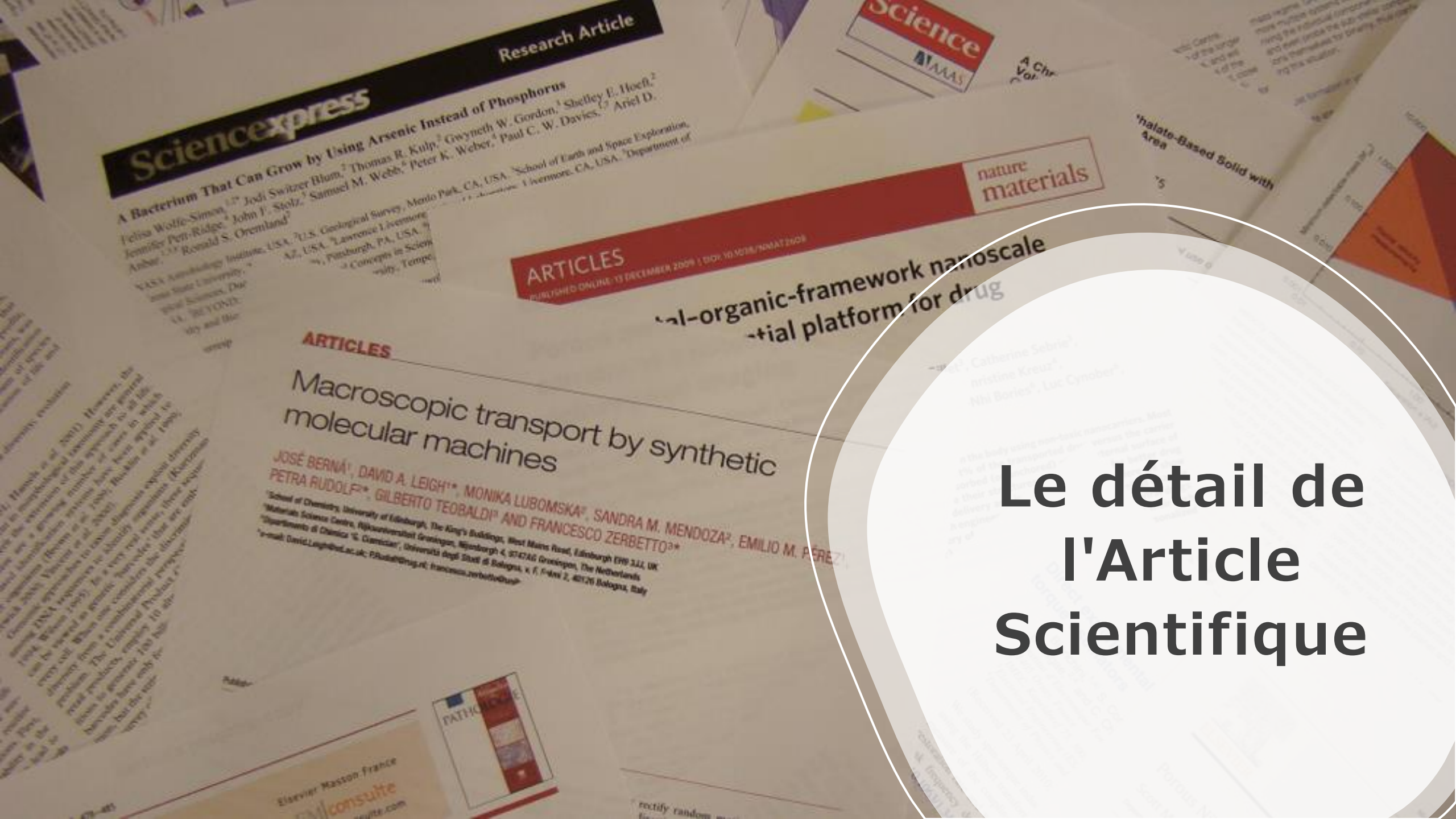


Et pour les auteurs ?

Pour les auteurs, le H index est une valeur qui classe les auteurs en fonction de leur nombre de publications et de leur importance pour la communauté, c'est-à-dire le nombre de fois où elles vont être cités.

Le H index peut-être influencer par plein de chose. Lesquelles ?

A ce titre est-il un bon indicateur de la qualité d'un chercheur ?



Le détail de l'Article Scientifique

Comment est construit l'article scientifique ?

Structure IMRAD

Suit une démarche scientifique :

- Observation
- Hypothèse
- Expérimentation
- Résultats
- Conclusion

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Pattern Recognition

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Fuzzy multilevel graph embedding

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ABSTRACT

Structural pattern recognition approaches offer the most expressive, convenient, powerful but computational expensive representations of underlying relational information. To benefit from mature, less expensive and efficient state-of-the-art machine learning models of statistical pattern recognition they must be mapped to a low-dimensional vector space. Our method of explicit graph embedding bridges the gap between structural and statistical pattern recognition. We extract the topological, structural and attribute information from a graph and encode numeric details by fuzzy histograms and symbolic details by crisp histograms. The histograms are concatenated to achieve a simple and straightforward embedding of graph into a low-dimensional numeric feature vector. Experimentation on standard public graph datasets shows that our method outperforms the state-of-the-art methods of graph embedding for richly attributed graphs.

1. Introduction

Pattern recognition has emerged as an important research domain and has supported the development of numerous applications in many different areas of activity. For a general introduction to former we refer the interested reader to [1,2]. The methods for pattern recognition are broadly categorized as statistical, structural or syntactic approaches [3]. In this paper we address the problem of lack of computational tools for structural pattern recognition and propose to exploit the computational efficiency of statistical pattern recognition. This permits a pattern recognition application to benefit from representational power of structural methods and computational efficiency of statistical methods, while avoiding the limitations of both. The next two paragraphs briefly introduce the main advantages and limitations of structural and statistical pattern recognition.

Structural pattern recognition is characterized by the use of symbolic data structures i.e. graphs, strings and trees. Graphs are widely used in structural pattern recognition and can safely be termed as representative of symbolic data structures (strings and trees are special instances of graphs [4]). Graphs provide a convenient and powerful representation of relational information. They are able to represent not only the values of both symbolic and numeric properties of an object, but can also explicitly model the spatial, temporal and conceptual relations that exist between its parts. Moreover, graphs do not suffer from the constraint of fixed dimensionality. For example, the number of nodes and edges in a graph is not limited a priori and depends on the size and the complexity of the actual object to be modeled [5]. And above all, graphs have foundations in strong mathematical formulation and have a mature theory at their basis. However two serious drawbacks of graph based representations are that these representations are sensitive to noise and that the algorithmic tools for performing different operations on them are computational expensive. For instance the much needed operations of graph matching and graph isomorphism are NP-complete. For further reading on structural pattern recognition we refer the interested reader to [4–8].

Statistical pattern recognition is characterized by the use of numeric feature vectors. A very important advantage of these representations is that because of their simple structure, the basic operations that are used in machine learning can easily be executed on them. This makes a large number of mature algorithms for pattern analysis and classification immediately available to statistical pattern recognition. And, as a result of this fact, the statistical pattern recognition offers state-of-the art computational efficient tools of learning, classification and clustering. However, feature vector based representations have associated representational limitations, which arise from their simple structure and the fact that they have same length and structure regardless of the complexity of object to be modeled [9]. For further reading on statistical pattern recognition and classification we refer the interested reader to [10].

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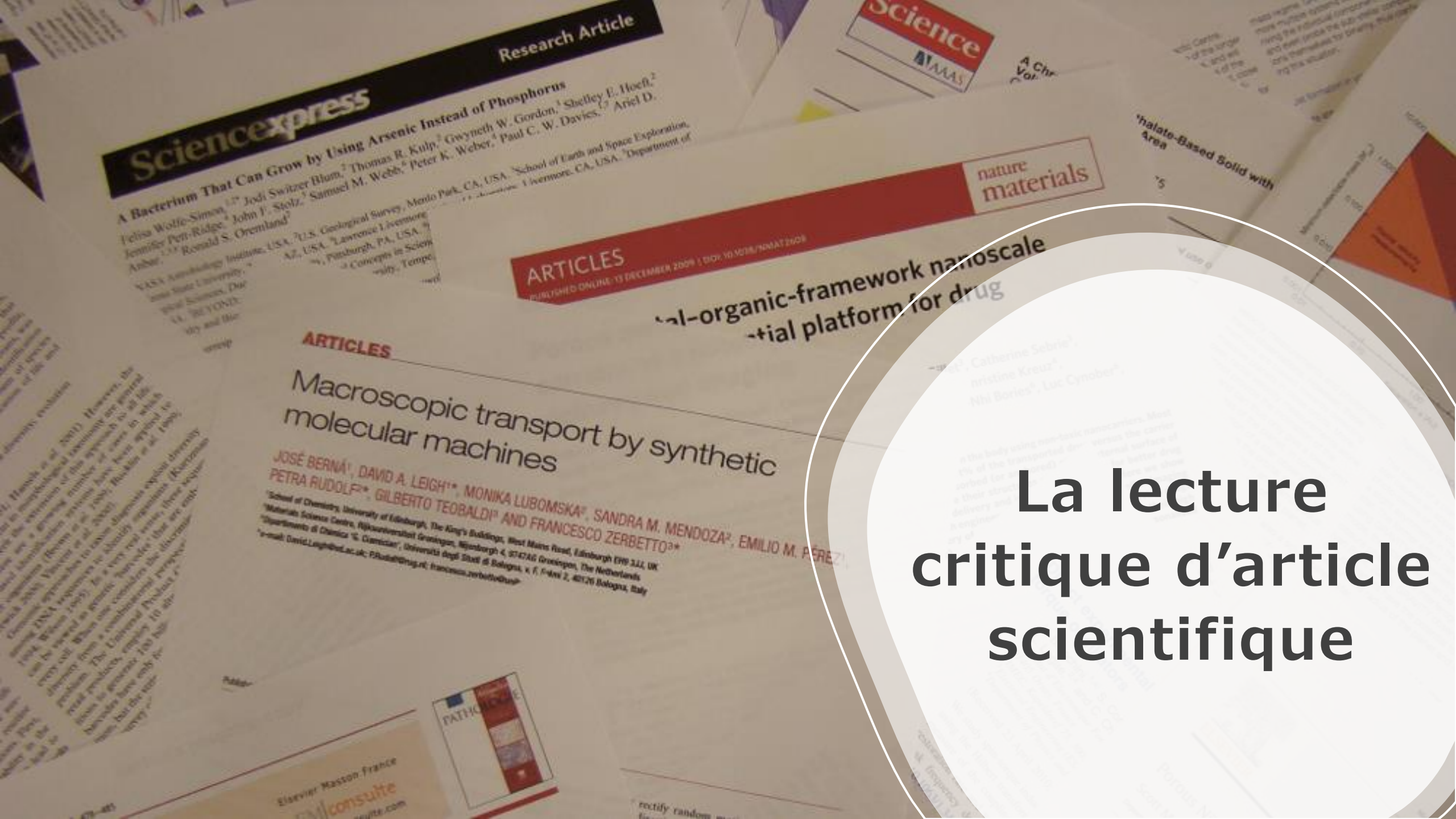
Comment est construit l'article scientifique ?

Structure IMRAD

- Introduction → contexte, problématique
- Matériels & Méthodes → type d’échantillon, nombre de patients, pré-analytique, sample prep, type d’analyse, post-analytique (ex. test statistique, logiciel de retraitement, etc.)
- Résultats →
- Discussion →



La lecture critique d'article scientifique

Qu'est-ce que la lecture critique d'article ?

La lecture critique d'Article scientifique permet de sélectionner les articles pour en faire une lecture critique et en retirer, à partir des résultats produits, les éléments pertinents et crédibles pouvant être transférés dans la pratique clinique du fait de la qualité de la méthodologie utilisée pour répondre à la question posée.

Quelques questions à se poser

Pouvez-vous trouver cette information dans l'article ?	**Problème de méthodologie ?**	**Impact de ce problème sur la validité de l'étude ?**
Quelle est la question posée par les auteurs ?	S'agit-il de l'évaluation de l'impact d'une intervention? De l'importance d'un problème de santé?...	**Impact de ce problème sur la validité de l'étude?**
Quel est le schéma de l'étude?	Est-il approprié à la recherche?	**Si non, les résultats sont-ils utiles?**
Quelles sont les variables étudiées et comment sont-elles mesurées?	Les variables sont-elles pertinentes?	**Biais et erreurs de mesures?**
Y a-t-il des facteurs de confusion potentiels?	Erreurs de mesures? Ces facteurs ont-ils été contrôlés?	**Impact de l'importance du problème sur les résultats?**
Quelle est la méthode d'échantillonnage?	Biais de sélection?	**Impact de l'importance du biais sur les résultats?**
Des tests statistiques ont-ils été utilisés?	Les tests sont-ils appropriés aux données? Les intervalles de confiances sont-ils fournis?	**Les test sont-ils appropriés aux données?** **Les intervalles de confiances sont ils donnés?** **Puissance?**
Les résultats ont-ils un intérêt clinique ou « social »?	La taille de l'échantillon était-elle adaptée pour détecter cet intérêt (puissance)?	**Le résultat est-il utile ou non concluant?**
Quelles sont les conclusions des auteurs?	**Ces résultats sont-ils intéressants pour la population qui vous intéresse?**	

Quelques questions à se poser

Est-ce que je vais lire cet article ?

TITRE

- Le titre reflète-t-il une question pertinente?

RESUME (format IMRaD)

- Le résumé apporte-t-il un objectif pertinent? Des résultats informatifs?

INTRODUCTION

- les auteurs connaissent-ils leur sujet?
- Ont-ils pris compte des études antérieures?
- Se termine-t-elle par l'énoncé d'un objectif concret?

➔ A cette étape, une idée claire de l'information donnée par l'article doit être extraite facilement.

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ORIGINAL ARTICLE

Journal of PERIODONTAL RESEARCH WILEY

Multiplexed LC-MS/MS quantification of salivary RNA modifications in periodontitis

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Abstract

Objective: To analyse the salivary epitranscriptomic profiles as periodontitis biomarkers using multiplexed mass spectrometry (MS).

Background: The field of epitranscriptomics, which relates to RNA chemical modifications, opens new perspectives in the discovery of diagnostic biomarkers, especially in periodontitis. Recently, the modified ribonucleoside N6-methyladenosine (m6A) was revealed as a crucial player in the etiopathogenesis of periodontitis. However, no epitranscriptomic biomarker has been identified in saliva to date.

Materials and Methods: Twenty-four saliva samples were collected from periodontitis patients ($n=16$) and from control subjects ($n=8$). Periodontitis patients were stratified according to stage and grade. Salivary nucleosides were directly extracted and, in parallel, salivary RNA was digested into its constituent nucleosides. Nucleoside samples were then quantified by multiplexed MS.

Results: Twenty-seven free nucleosides were detected and an overlapping set of 12 nucleotides were detected in digested RNA. Among the free nucleosides, cytidine and three other modified nucleosides (inosine, queuosine and m6Am) were significantly altered in periodontitis patients. In digested RNA, only uridine was significantly higher in periodontitis patients. Importantly there was no correlation between free salivary nucleoside levels and the levels of those same nucleotides in digested salivary RNA, except for cytidine, m5C and uridine. This statement implies that the two detection methods are complementary.

Conclusion: The high specificity and sensitivity of MS allowed the detection and quantification of multiple nucleosides from RNA and free nucleosides in saliva. Some ribonucleosides appear to be promising biomarkers of periodontitis. Our analytic pipeline opens new perspectives for diagnostic periodontitis biomarkers.

KEYWORDS
biomarker, epitranscriptomics, mass spectrometry, periodontitis, saliva

Margaux Vignon and Amandine Bastide these authors contributed equally to this work.

Lecture critique – résumé & introduction

1) Introduction rapide à l'épitranscriptomique

2) Identifier:

   - l'aspect novateur / ce qui fait que vous allez lire l'article

   - les zones d'ombres (cliniques, techniques, technologiques)

   - les études existantes ?

   - l'hypothèse et/ou la problématique de recherche

3) Evaluer la qualité (journal, auteur, affiliations…)

Lecture critique – résumé & introduction

1) Aspect novateur

- *Identification de potentiel biomarqueurs épitranscriptomique dans la salive par LC-MS/MS*
- *Approche de diagnostic précoce de la parodontite*

2) Les zones d'ombres

- *Clinique : méthodes actuelles ne permettent pas un diagnostic précoce et/ou pronostic fiable*
- *Technique : besoin de méthodes sensibles, spécifiques et multiplexes pour l'étude du profil épitranscripto*

3) Etudes existantes

- *Réf 22, 23 & 24*

4) Hypothèse / Problématique

- *Utilité du profilage épitranscriptomique pour la recherche de biomarqueur de la parodontite par LC-MS/MS*

Quelques questions à se poser

Est-ce que le plan expérimental est adapté à la question posée ?

MATÉRIELS ET MÉTHODES

- Le Mat & Meth est conçu selon les objectifs et le temps de l'étude.
- Plusieurs paramètres doivent être présenté tels que: la méthode d'analyse utilisée, le type d'échantillon et/ou la population étudiée, les critères d'évaluation et les tests statistiques.

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Lecture critique – matériels & méthodes

1) Introduction rapide à la spectrométrie de masse

2) Identifier:

- Quelle méthode d'analyse est utilisée? S'agit-il du gold standard ?
- Quelle population est étudiée ? Nombre de sujets ? Critères d'inclusion ? Présence de contrôles ?
- Quels sont les critères d'évaluation ? Sont ils trop permissifs ou restrictifs ?
- Quels tests statistiques sont utilisés ? Sont ils adaptés ?

Lecture critique – matériels et méthodes

1) Méthode d'analyse

- *Analyse ciblée par LC-MS/MS avec quantification absolue des nucléosides après extraction et potentiellement digestion des ARN*

2) Populations

- *24 échantillons de salive issue de patients sains (n=8) et avec parodontite (n=16)*
- *Critère d'inclusion: présenter ou non une parodontite, fumer moins de 15 cig/jour si fumeur.*

3) Critères d'évaluation

- *Présence d'une différence significative entre les conditions*

4) Tests statistiques

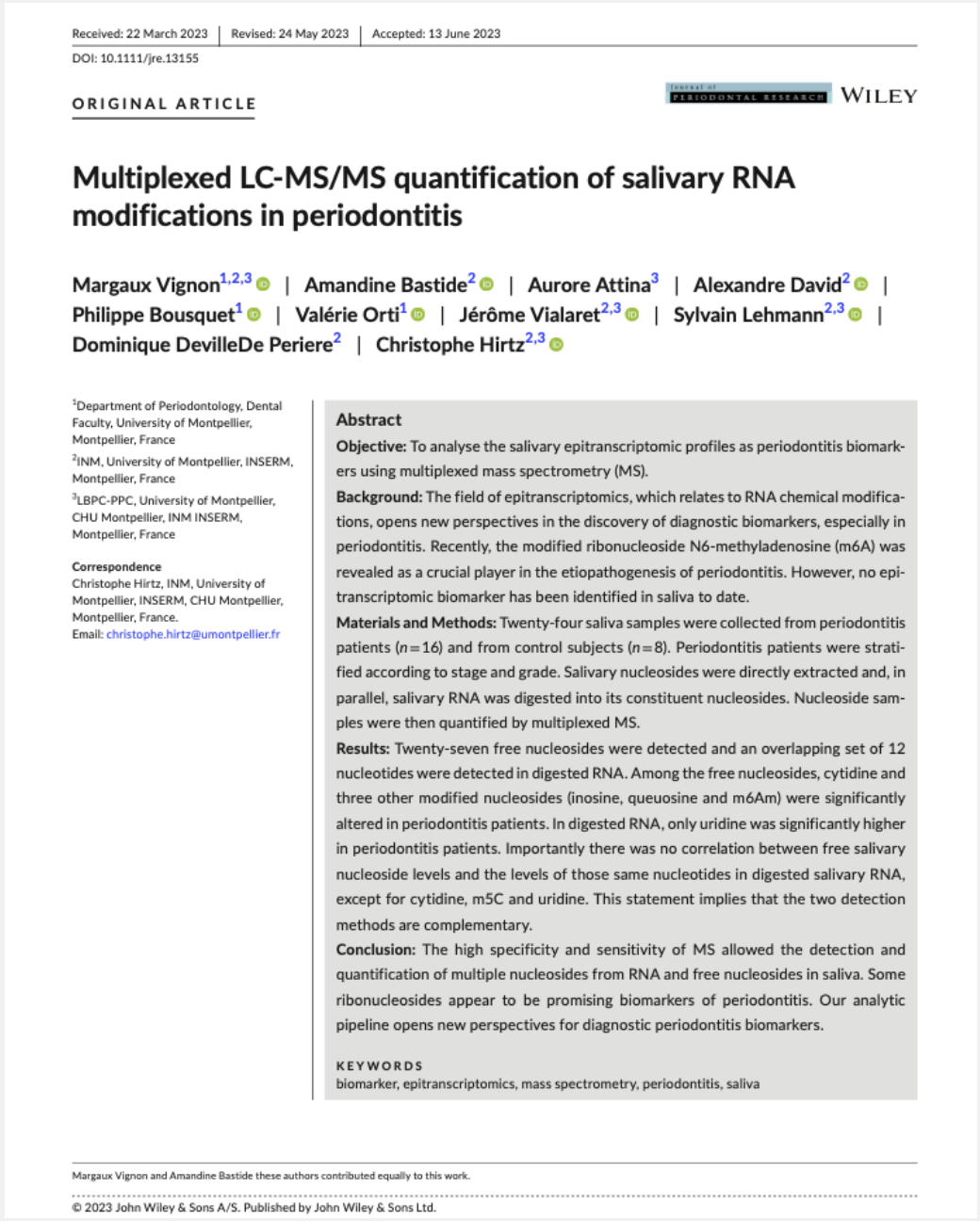
- *Mann-Whitney, test non paramétrique (ne suit pas de loi normale) comparant la somme des rangs*

Quelques questions à se poser

Les auteurs répondent-ils à la question posée ?

RÉSULTATS

- Les résultats doivent répondre uniquement à l'objectif de l'étude.
- Les résultats sont-ils présentés de façon compréhensible (type, titre des graphs, légendes) ?



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Lecture critique – résultats

Analyser et commenter les résultats

- Les graphs et légendes sont-ils compréhensibles ?
- Identifiez les résultats intéressants
- Y a-t-il une réponse à la question de recherche ?

Lecture critique – résultats

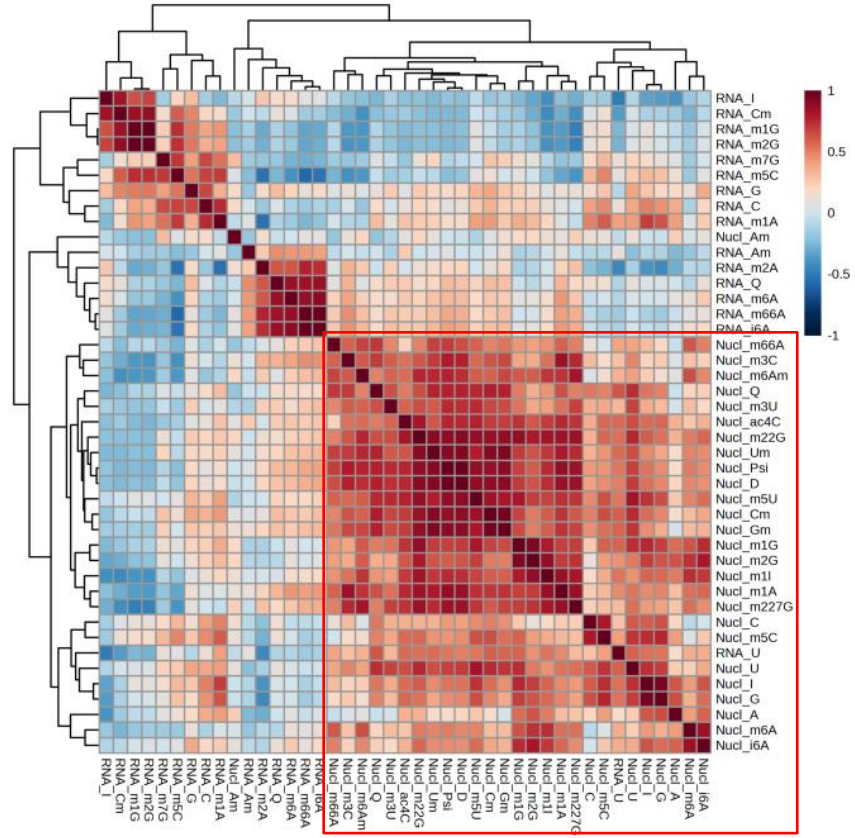

FIGURE 2 Correlogram of salivary nucleosides from digested RNA (RNA) and free nucleosides (Nucl). Data of the peak area intensity (log10 transformed) were analysed using Pearson rank correlation within MetaboAnalyst (v 5.0). The heatmap represents clusters of nucleosides covarying positively or negatively. Colour scale of correlation coefficient is shown (red and blue colours mean positive and negative correlations, respectively).

- 16 ribonucléosides identifiés dont 12 modifiés
- 27 nucléosides libres identifiés
- Forte corrélation entre les nucléosides libres

Lecture critique – résultats

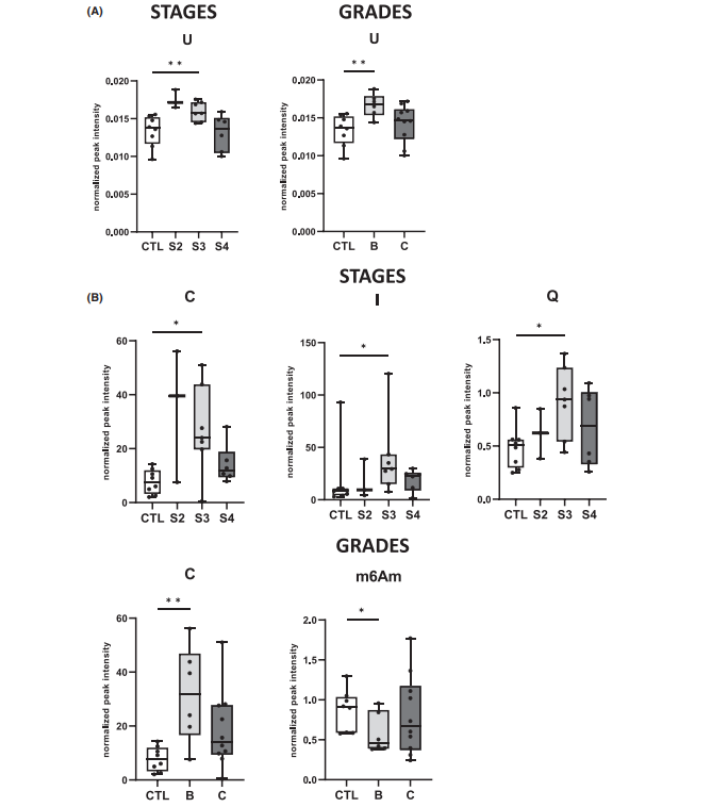

FIGURE 3 Box and whisker plots of the most significant salivary nucleosides between periodontitis and healthy subjects. (A) Nucleosides from digested salivary RNA comparison results regarding periodontitis stages and grade. (B) Free salivary nucleoside comparison results according to periodontitis stages or grade. The y-axis shows the normalized peak intensity. The box extends from the 25th to 75th percentiles. Medians are indicated by horizontal lines within each box. The minimum and maximum values are indicated as whiskers. Single data points are indicated by black dots. Mann–Whitney *p*-values: $^{*}p < .05$, $^{**}p < .01$. CTL, control; B, Grade B; C, Grade C; S2, Stage 2; S3, Stage 3; S4, Stage 4.

- RNA U significativement augmenté chez les sujets stade 3 et grade B
- Nucl C, I et Q significativement augmenté chez les sujets stade 3 et Nucl C chez les grades B
- Nucl m6Am significativement diminué chez les sujets stade 3 et grade B

Quelques questions à se poser

Y a-t-il des limites et/ou de nouvelles pistes ?

DISCUSSION

- Il s'agit d'un résumé des données. Elle contient les conclusions et limites de l'étude.
- Les conclusions répondent-elles à la problématique énoncée ?
- Quelles ont été les limites ?
- Y a-t-il des perspectives ?

- Attention aux hors sujet, extrapolations, imprécisions.

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KEYWORDS
biomarker, epitranscriptomics, mass spectrometry, periodontitis, saliva

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Lecture critique – discussion

Analyser et commenter la discussion

- Quels sont les conclusions ? Y en a-t-il d'autres selon vous ?
- Quels sont les limites et perspectives (clinique, technique) ? D'autres approches auraient-elles pu être utilisées ?

Lecture critique – discussion

Plan expérimental alternatif

Qu’auriez vous fait ?