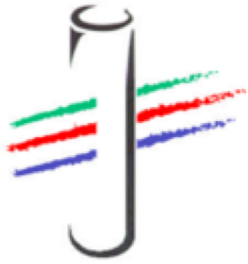


# SPECTR

Serum Protein Electrophoresis Computer-assisted Recognition

**Intelligence artificielle d'interprétation automatisée  
des électrophorèses des protéines sériques**

Floris Chabrun, Xavier Dieu, Marc Ferré, Olivier Gaillard,  
Anthony Mery, Juan Manuel Chao de la Barca, Audrey Taisne,  
Geoffrey Urbanski, Pascal Reynier, Delphine Mirebeau-Prunier



COLLEGE NATIONAL DE BIOCHIMIE DES HÔPITAUX

30<sup>èmes</sup> Journées Nationales

Jeudi 27 et vendredi 28 janvier 2022

SAINT-MALO

PALAIS DU GRAND LARGE

**DECLARATION D'INTERET  
DANS LE CADRE DE MISSIONS DE FORMATION  
RÉALISÉES POUR LE CNBH**

Dr CHABRUN Floris, Dr DIEU Xavier

Exerçant au CHU Angers – Laboratoire de Biochimie et Biologie Moléculaire  
déclarent sur l'honneur

Avoir un intérêt direct ou indirect (financier), avec des entreprises pharmaceutiques, du diagnostic ou d'édition de logiciels susceptible de modifier notre jugement ou nos propos, concernant le sujet et les DMDIV présentés.

Motif : collaboration en cours avec l'entreprise SEBIA (Lisses, France)

Contexte : pourquoi SPECTR ?

# Limites de l'électrophorèse des protéines sériques

- ▶ Temps d'interprétation important :
  - ▶ Partie analytique :  $\approx 100$  échantillons / heure
  - ▶ Interprétation :  $\approx 2-4$  heures / 100 échantillons
- ▶ Interprétation manuelle :
  - ▶ Opérateur-dépendant
  - ▶ Nécessité d'une expérience technique et d'une expertise biologique
  - ▶ Difficulté d'harmonisation inter-opérateurs et inter-laboratoires

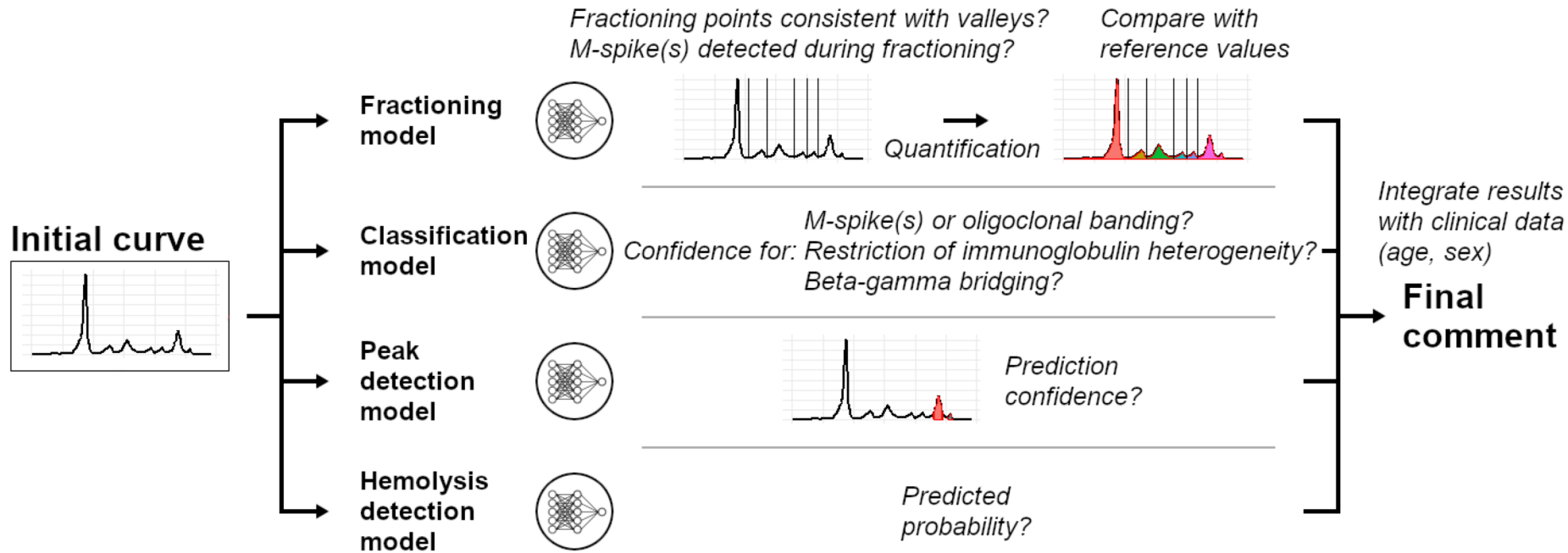
# Objectifs

- ▶ Automatiser **intégralement** l'étape d'interprétation des électrophorèses des protéines sériques via une **intelligence artificielle**
- ▶ Conserver une **complète transparence** et permettre au biologiste de **reprendre la main** sur toutes les étapes de l'interprétation
- ▶ Objectifs à long terme :
  - ▶ **Economie de temps** (limiter l'intervention humaine à la validation et la correction si besoin) afin de se concentrer sur les profils les plus atypiques
  - ▶ **Assistance à la validation** pour les cas rares/particuliers grâce à une IA entraînée sur la base d'avis de différents biologistes
  - ▶ **Harmonisation inter-opérateurs et inter-laboratoires** dans un processus d'accréditation

# Matériels et méthodes

The background features abstract, overlapping geometric shapes in various shades of blue, ranging from light sky blue to dark navy blue. These shapes are primarily located on the right side of the slide, creating a modern, layered effect. The text 'Matériels et méthodes' is positioned on the left side of the slide in a clean, sans-serif font.

# Construction de SPECTR



# Systeme expert

A. Order checked	B. Priority (sort order)	C. Criteria (conditions) checked	D. Comment if left criteria are verified	E. Refined comment criteria	F. Refined comment according to left criteria
c1	7	Hypoprotidemia, major hypoalbuminemia, decreased alpha-1, increased alpha-2	Nephrotic syndrome comment		
c5	5	Increased alpha-1 or alpha-2 <u>without nephrotic syndrome (c1)</u>	Inflammatory syndrome comment	Associated hypoalbuminemia?	Chronic inflammatory syndrome pattern
				Associated hypergammaglobulinemia, without m-spike/OB/RH/bridging*	Inflammatory syndrome associated with immune response comment

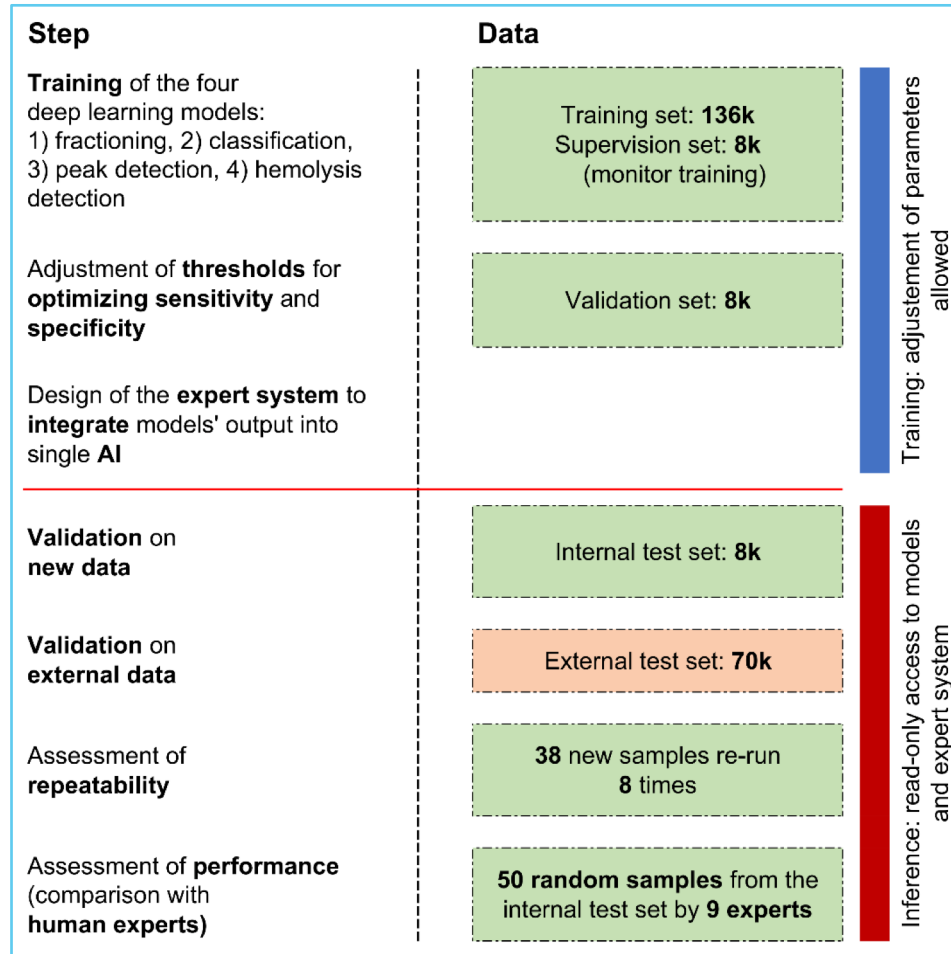


# Processus et données utilisées

159,969 échantillons du CHU d'Angers entre 2008 et 2018

70,362 échantillons du CH du Mans entre 2011 et 2019

- Analysés sur automate **Capillarys 2 (SEBIA)**, interprétation selon **Szymanowicz et al. (2006)**
- Tous les patients ont été inclus, sans restriction d'âge, de sexe ou de pathologie
- Echantillons **normaux**, ainsi que tous types d'anomalies incluant notamment : **pics d'aspect monoclonal**, aspect **oligoclonaux** ou de restriction d'hétérogénéité, **blocs bêta-gamma**, **syndromes néphrotiques**, **inflammatoires**, **dénutrition**, **produits de contraste iodés** ou profils avec **hémolyse in-vitro**



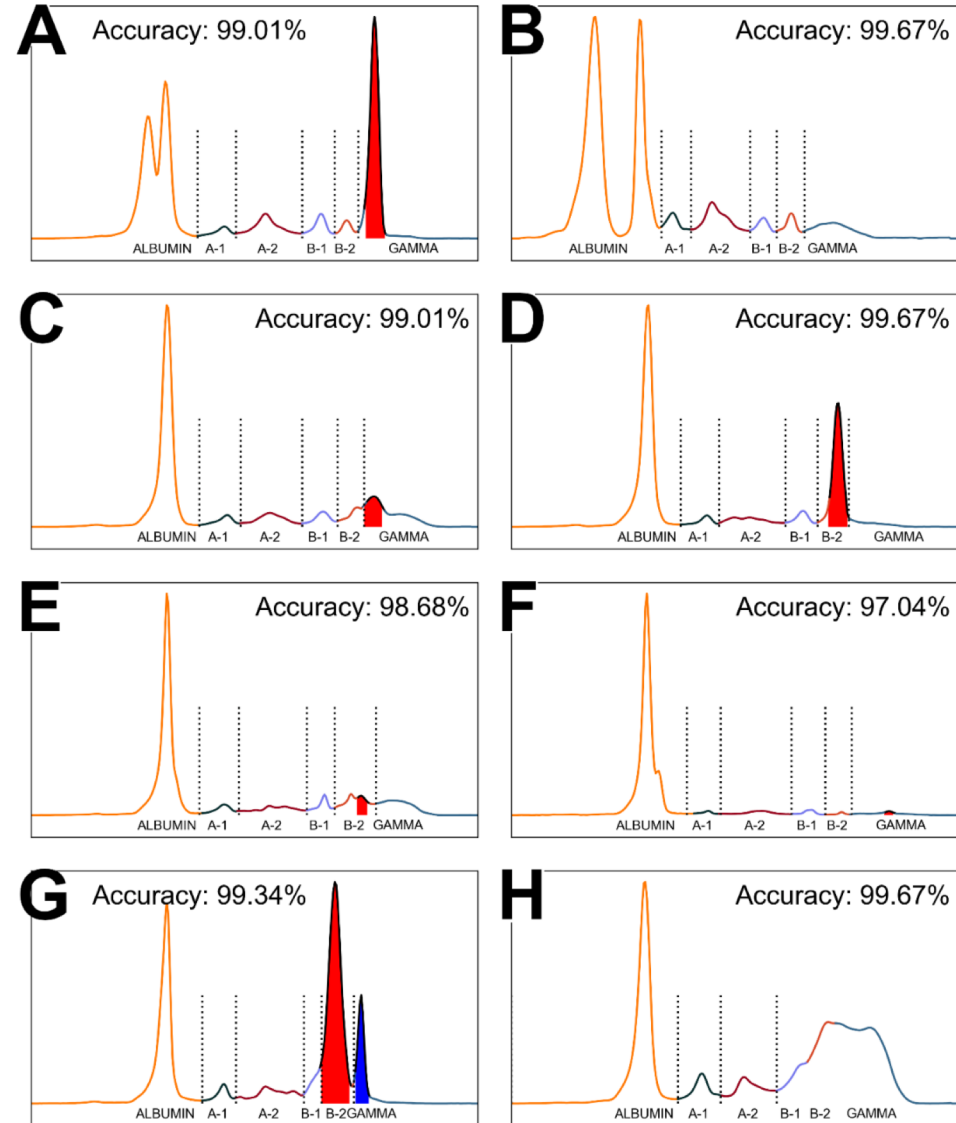
# Résultats

The background features abstract, overlapping geometric shapes in various shades of blue, ranging from light sky blue to deep navy blue. These shapes are primarily located on the right side of the page, creating a modern, dynamic aesthetic.

# Modèle de fractionnement

- IoU moyenne :
  - 99%
- Erreur de quantification moyenne :
  - $< 0.01 \pm 1.00$  g/L

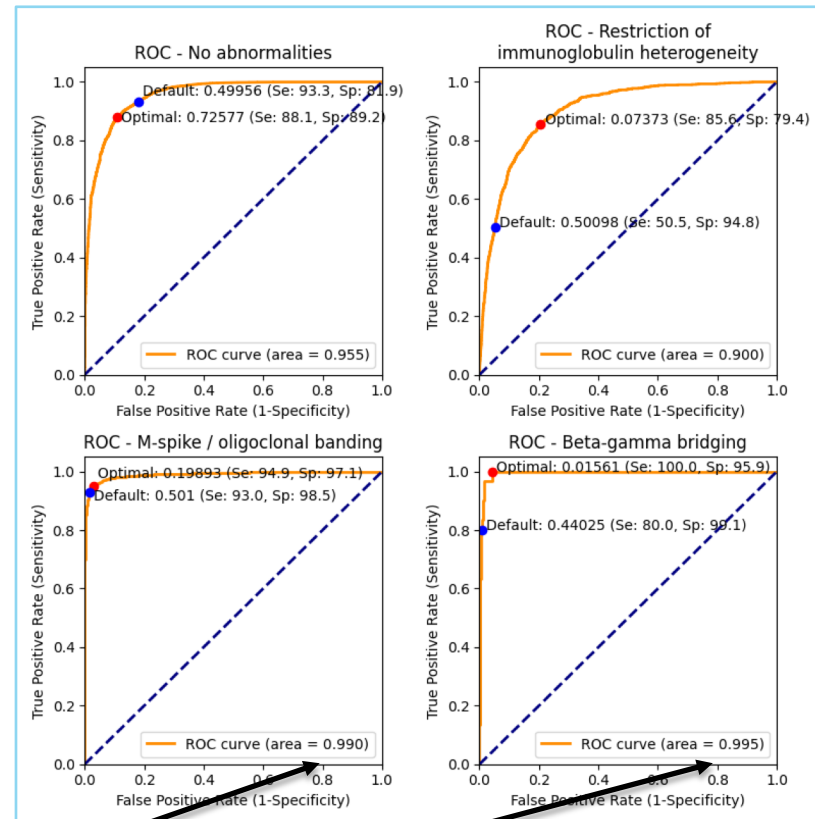
- Robustesse aux anomalies fréquentes gênant le fractionnement automatique
- Préviend d'autres erreurs en aval du pipeline d'IA



# Modèle de classification

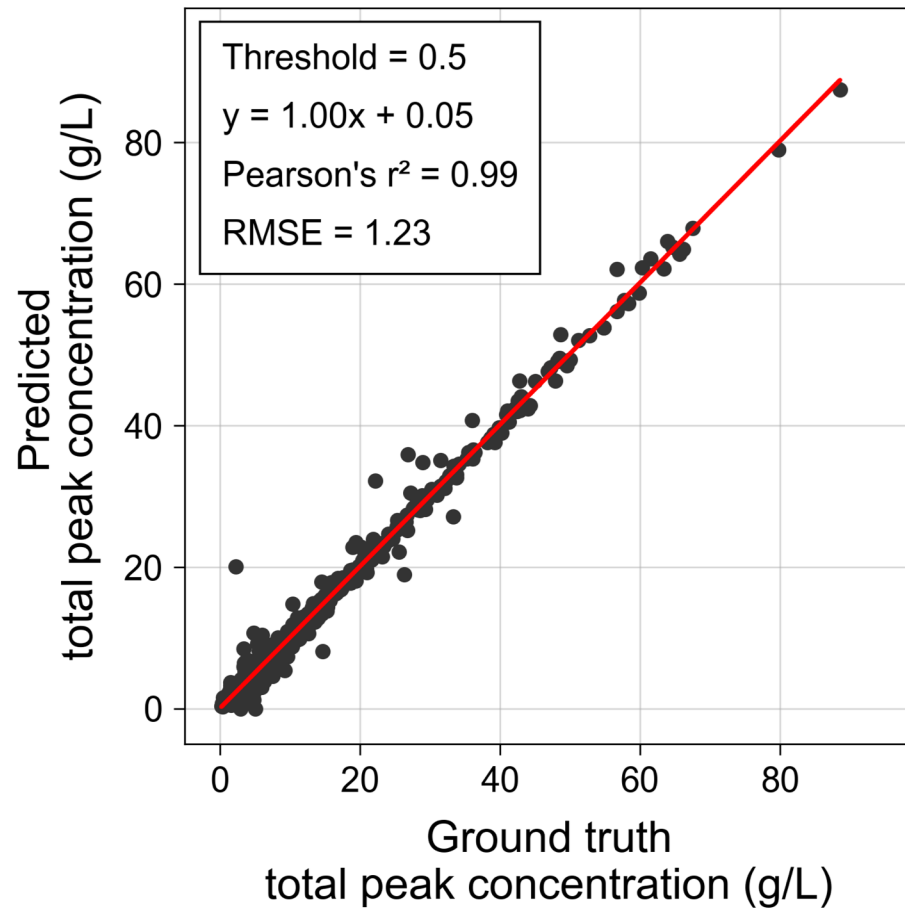
Echantillons	Précision
Normaux	92.0 %
Aspect de restriction	73.2 %
Pic(s) / oligoclonaux	87.8 %
Blocs bêta-gamma	83.3 %
Tous	89.4 %

- AUC-ROC (0,99) >>> précision globale
- Possibilité de renvoyer une alerte avec une haute sensibilité (> 95%) quand une anomalie cliniquement significative est suspectée

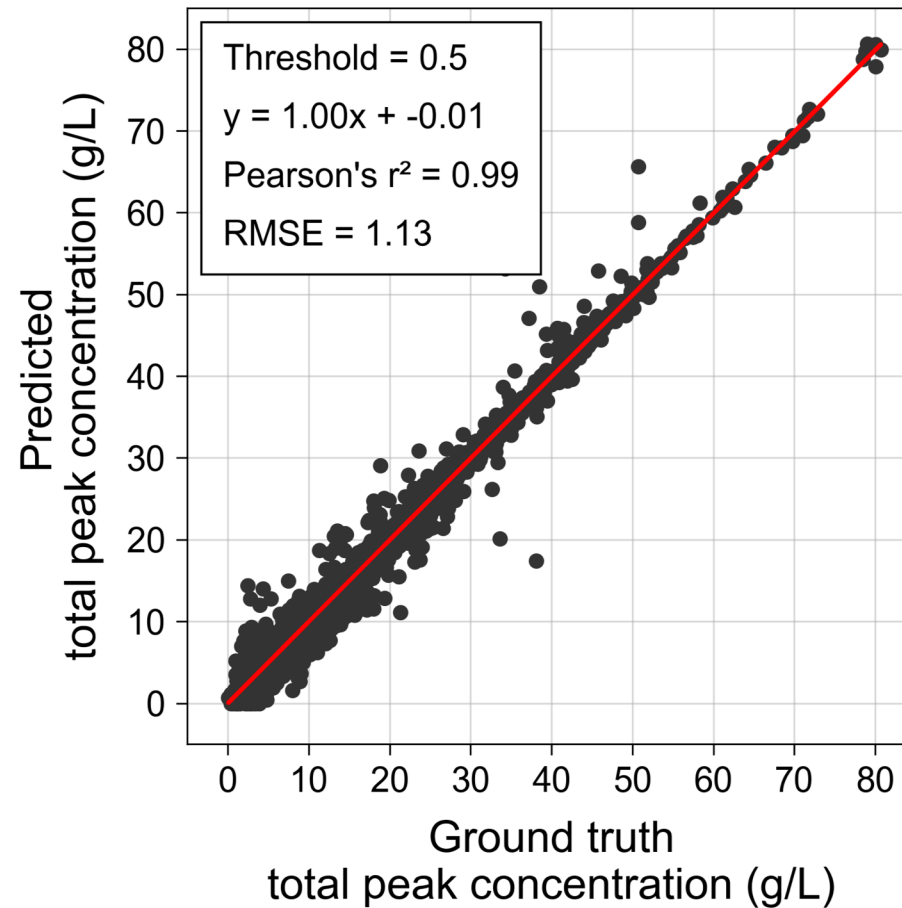


# Modèle de localisation des pics

## A. Internal test set



## B. External test set



# Validation de l'IA globale

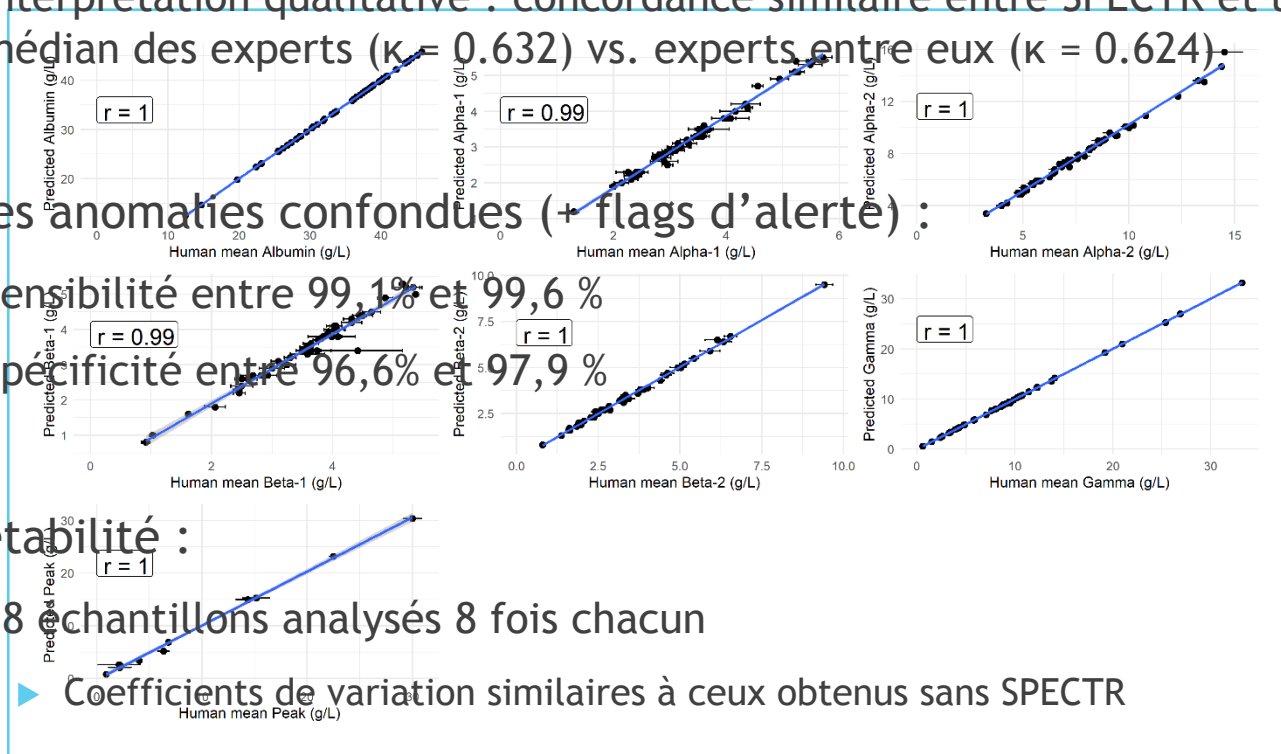
- ▶ Confrontation à 9 experts indépendants de divers centres hospitaliers :
  - ▶ Quantification :  $r^2$  entre 0,99 et 1 pour toutes les fractions/pics d'aspect monoclonal
  - ▶ Interprétation qualitative : concordance similaire entre SPECTR et le choix médian des experts ( $\kappa = 0.632$ ) vs. experts entre eux ( $\kappa = 0.624$ )

- ▶ Toutes anomalies confondues (+ flags d'alerte) :

- ▶ Sensibilité entre 99,1% et 99,6 %
- ▶ Spécificité entre 96,6% et 97,9 %

- ▶ Répétabilité :

- ▶ 38 échantillons analysés 8 fois chacun
- ▶ Coefficients de variation similaires à ceux obtenus sans SPECTR



Application : SPECTR

# SPECTR

Using recommendations from **Szymanowicz et al., 2006**. **For research use only.**  
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**CNN map visualization:**  
None ▾

**4/8: peak-6983 (M, 58)**  
<< < 4 > >> Reset

**Qualitative abnormality:**  
Normal (0%) ▾

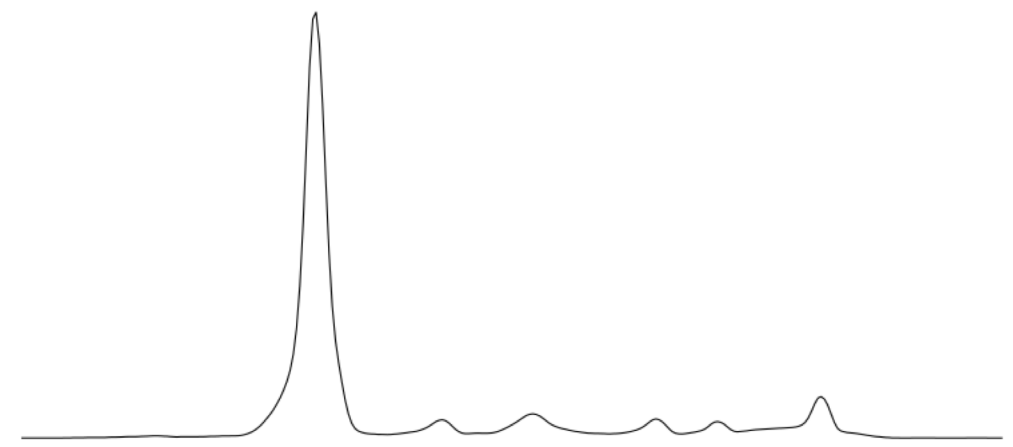
Hemolyzed serum

**Automated analysis output:**  
**Analysis flags:**

Batch Sample

**Sample ID:** peak-6983  
**Age:** 58  
**Sex:** M  
**Total protein:** 48 g/L

Fraction	Pct.	Ref. (%)	Conc.	Ref. (g/L)
?	100.0 %	-	48.0 g/L	-



Not fractionned yet

**Automatic interpretation:**

- Interpretation impossible.



# SPECTR

Using recommendations from [Szymanowicz et al., 2006](#). **For research use only.**  
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[E-mail the corresponding author](#)

## CNN map visualization:

None

4/8: peak-6983 (M, 58)

<< < 4 > >> Reset

## Qualitative abnormality:

Clonal anomaly (100%)

Hemolyzed serum

## Automated analysis output:

- Fractioning confidence: 100.00%
- Classified as: **Clonal anomaly (100%)**
- Monoclonal spike? (96.72 %)

## Analysis flags:

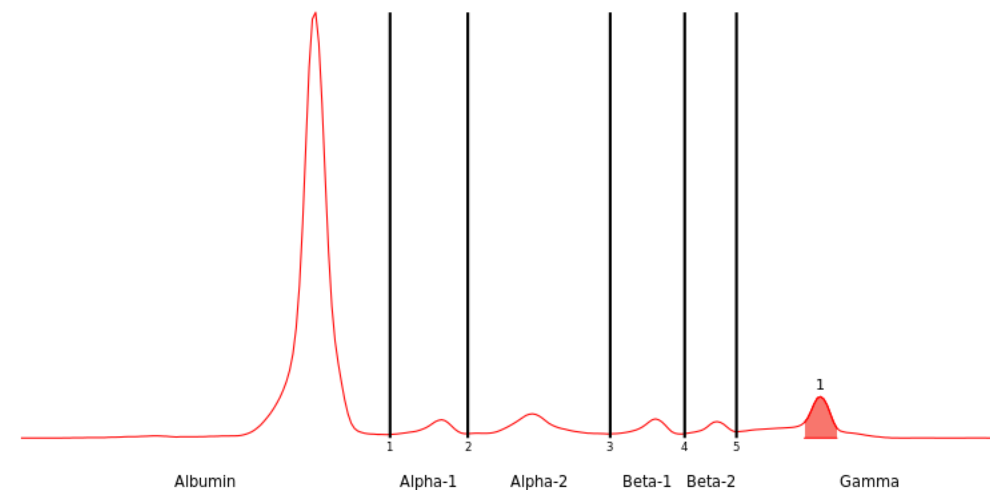
- Clonal anomaly
- Age > 45
- Male
- Plasmapheresis?
- Total protein < 55 g/l
- Albumin < 35 g/l
- Beta-2-globulins < 2 g/l
- Gamma (res.) < 8 g/l
- 1 spike(s) in gamma

Batch Sample

Sample ID: peak-6983  
 Age: 58  
 Sex: M  
 Total protein: 48 g/L

Fraction	Pct.	Ref. (%)	Conc.	Ref. (g/L)
Albumin	72.5 %	55.8-66.1	34.8 g/L	40.2-47.6
Alpha-1	3.8 %	2.9-4.9	1.8 g/L	2.1-3.5
Alpha-2	7.8 %	7.1-11.8	3.8 g/L	5.1-8.5
Beta-1	3.7 %	4.7-7.2	1.8 g/L	3.4-5.2
Beta-2	2.7 %	3.2-6.5	1.3 g/L	2.3-4.7
Gamma	9.4 %	11.1-18.8	4.5 g/L	8-13.5
Gamma (res.)	4.5 %	11.1-18.8	2.1 g/L	8-13.5

Spike	Pct.	Conc.
1	5.0 %	2.4 g/L



## Automatic interpretation:

- Suspected M-spike in gammaglobulins.
- Global decrease of globulins: plasmapheresis?

# SPECTR

Using recommendations from [Szymanowicz et al., 2006](#). **For research use only.**  
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[E-mail the corresponding author](#)

## CNN map visualization:

None

4/8: peak-6983 (M, 58)

<< < 4 > >> Reset

## Qualitative abnormality:

- Clonal anomaly (100%)
- Normal (0%)
- Heterogeneity restriction aspect (0%)
- Clonal anomaly (100%)
- Beta-gamma bridge (0%)

• Monoclonal spike? (96.72 %)

## Analysis flags:

- Clonal anomaly
- Age > 45
- Male
- Plasmapheresis?
- Total protein < 55 g/l
- Albumin < 35 g/l
- Beta-2-globulins < 2 g/l
- Gamma (res) < 8 g/l
- 1 spike(s) in gamma

Batch Sample

Sample ID: peak-6983

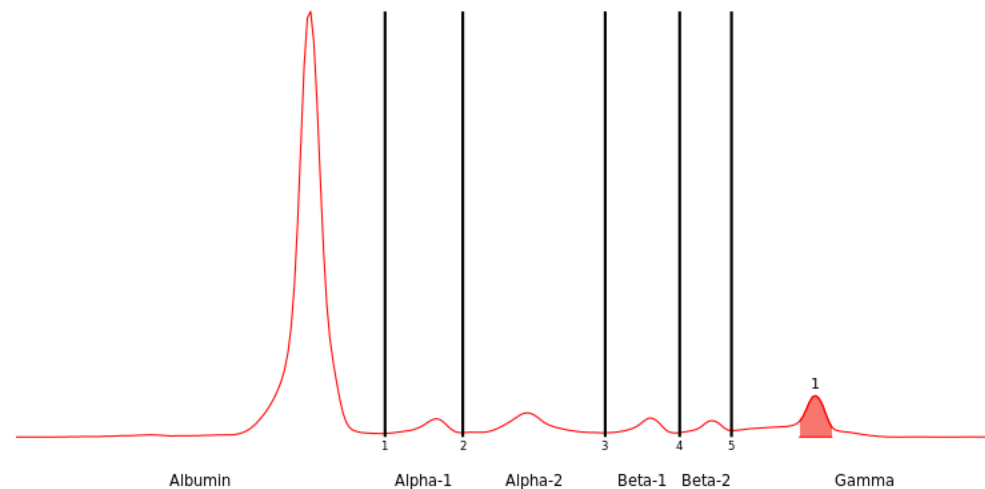
Age: 58

Sex: M

Total protein: 48 g/L

Fraction	Pct.	Ref. (%)	Conc.	Ref. (g/L)
Albumin	72.5 %	55.8-66.1	34.8 g/L	40.2-47.6
Alpha-1	3.8 %	2.9-4.9	1.8 g/L	2.1-3.5
Alpha-2	7.8 %	7.1-11.8	3.8 g/L	5.1-8.5
Beta-1	3.7 %	4.7-7.2	1.8 g/L	3.4-5.2
Beta-2	2.7 %	3.2-6.5	1.3 g/L	2.3-4.7
Gamma	9.4 %	11.1-18.8	4.5 g/L	8-13.5
Gamma (res.)	4.5 %	11.1-18.8	2.1 g/L	8-13.5

Spike	Pct.	Conc.
1	5.0 %	2.4 g/L



## Automatic interpretation:

- Suspected M-spike in gammaglobulins.
- Global decrease of globulins: plasmapheresis?

# SPECTR

Using recommendations from **Szymanowicz et al., 2006**. **For research use only.**  
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## CNN map visualization:

- Fractions
- None
- Fractions
- Spikes

## Qualitative abnormality:

Clonal anomaly (100%)

Hemolyzed serum

## Automated analysis output:

- Fractioning confidence: 100.00%
- **Classified as: Clonal anomaly (100%)**
- **Monoclonal spike? (96.72 %)**

## Analysis flags:

- **Clonal anomaly**
- Age > 45
- Male
- **Plasmapheresis?**
- Total protein < 55 g/l
- Albumin < 35 g/l
- Beta-2-globulins < 2 g/l
- **Gamma (res.) < 8 g/l**
- **1 spike(s) in gamma**

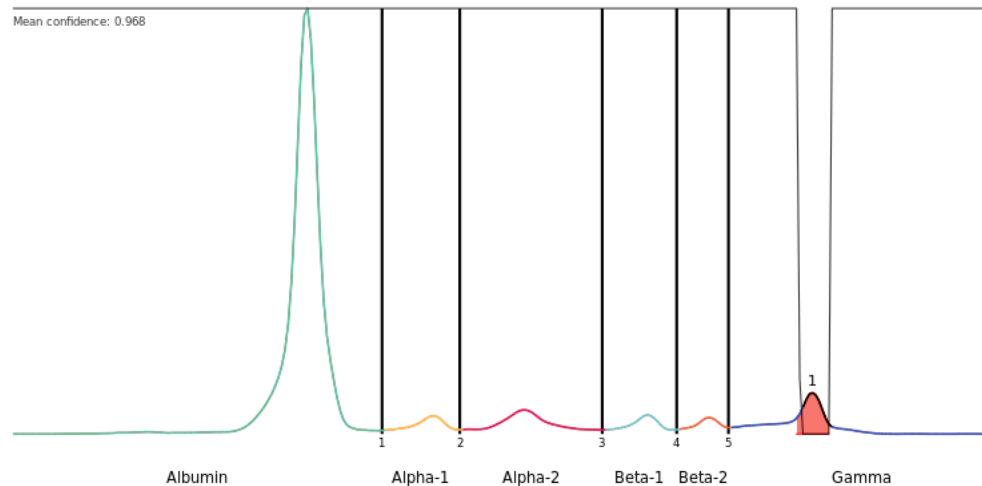
Batch Sample

**Sample ID:** peak-6983  
**Age:** 58  
**Sex:** M  
**Total protein:** 48 g/L

CNN map visualization  
 Select a model (**fractioning** model or **peak detection** model) to **overlay the output predictions on the curve**

	Ref. (%)	Conc.	Ref. (g/L)
	55.8-66.1	34.8 g/L	40.2-47.6
	2.9-4.9	1.8 g/L	2.1-3.5
Alpha-2	7.8 %	7.1-11.8	3.8 g/L
Beta-1	3.7 %	4.7-7.2	1.8 g/L
Beta-2	2.7 %	3.2-6.5	1.3 g/L
Gamma	9.4 %	11.1-18.8	4.5 g/L
Gamma (res.)	4.5 %	11.1-18.8	2.1 g/L

Spike	Pct.	Conc.
1	5.0 %	2.4 g/L



## Automatic interpretation:

- Suspected M-spike in gammaglobulins.
- Global decrease of globulins: plasmapheresis?

# SPECTR

Using recommendations from **Szymanowicz et al., 2006**. **For research use only.**  
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 E-mail the corresponding author

## CNN map visualization:

Spikes|  
 None  
 Fractions  
 Spikes

## Qualitative abnormality:

Clonal anomaly (100%)

Hemolyzed serum

## Automated analysis output:

- Fractioning confidence: 100.00%
- **Classified as: Clonal anomaly (100%)**
- **Monoclonal spike? (96.72 %)**

## Analysis flags:

- **Clonal anomaly**
- Age > 45
- Male
- **Plasmapheresis?**
- Total protein < 55 g/l
- Albumin < 35 g/l
- Beta-2-globulins < 2 g/l
- **Gamma (res.) < 8 g/l**
- **1 spike(s) in gamma**

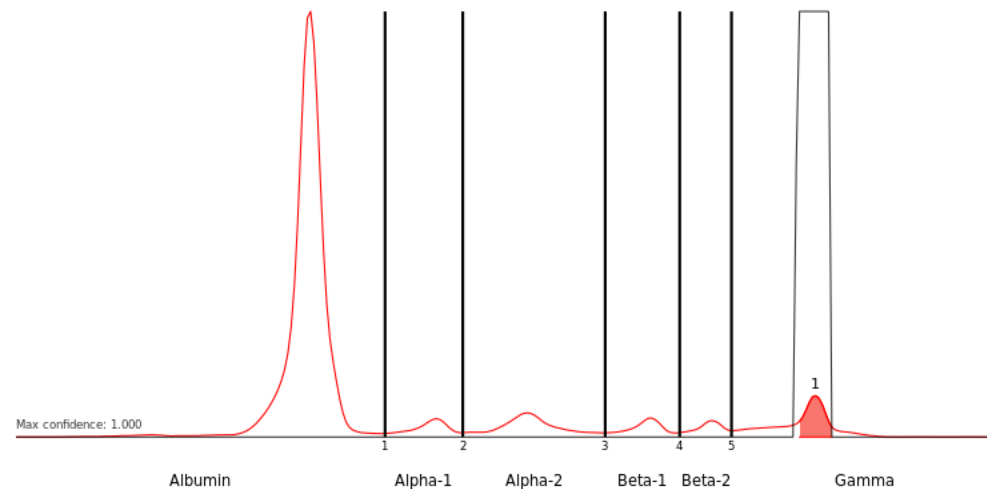
Batch | Sample

**Sample ID:** peak-6983  
**Age:** 58  
**Sex:** M  
**Total protein:** 48 g/L

CNN map visualization  
 Select a model (**fractioning** model or **peak detection** model) to **overlay the output predictions on the curve**

	Ref. (%)	Conc.	Ref. (g/L)
	55.8-66.1	<b>34.8 g/L</b>	40.2-47.6
	2.9-4.9	<b>1.8 g/L</b>	2.1-3.5
Alpha-2	7.8 %	<b>3.8 g/L</b>	5.1-8.5
Beta-1	<b>3.7 %</b>	<b>1.8 g/L</b>	3.4-5.2
Beta-2	<b>2.7 %</b>	<b>1.3 g/L</b>	2.3-4.7
Gamma	<b>9.4 %</b>	<b>4.5 g/L</b>	8-13.5
Gamma (res.)	<b>4.5 %</b>	<b>2.1 g/L</b>	8-13.5

Spike	Pct.	Conc.
1	5.0 %	2.4 g/L



## Automatic interpretation:

- Suspected M-spike in gammaglobulins.
- Global decrease of globulins: plasmapheresis?

# SPECTR

Using recommendations from [Szymanowicz et al., 2006](#). **For research use only.**  
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## CNN map visualization:

Spikes

4/8: peak-6983 (M, 58)

<< < 4 > >> Reset

## Qualitative abnormality:

Clonal anomaly (100%)

Hemolyzed serum

## Automated analysis output:

- Fractioning confidence: 100.00%
- **Classified as: Clonal anomaly (100%)**
- **Monoclonal spike? (96.72 %)**

## Analysis flags:

- **Clonal anomaly**
- Age > 45
- Male
- **Plasmapheresis?**
- Total protein < 55 g/l
- Albumin < 35 g/l
- Beta-2-globulins < 2 g/l
- **Gamma (res) < 8 g/l**
- **1 spike(s) in gamma**

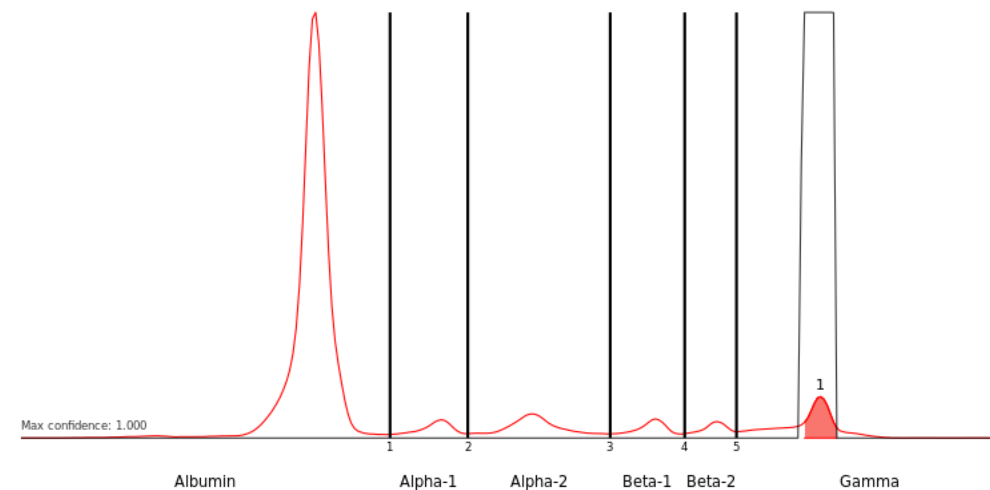
Batch Sample

Sample ID: peak-6983  
 Age: 58  
 Sex: M  
 Total protein: 48 g/L

Fraction	Pct.	Ref. (%)	Conc.	Ref. (g/L)
Albumin	72.5 %	55.8-66.1	34.8 g/L	40.2-47.6
Alpha-1	3.8 %	2.9-4.9	1.8 g/L	2.1-3.5
Alpha-2	7.8 %	7.1-11.8	3.8 g/L	5.1-8.5
Beta-1	3.7 %	4.7-7.2	1.8 g/L	3.4-5.2
Beta-2	2.7 %	3.2-6.5	1.3 g/L	2.3-4.7
Gamma	9.4 %	11.1-18.8	4.5 g/L	8-13.5
Gamma (res.)	4.5 %	11.1-18.8	2.1 g/L	8-13.5

Deep learning analysis output  
 This section lists **all abnormalities** automatically detected by **deep learning models**

Pct.	Conc.
5.0 %	2.4 g/L



## Automatic interpretation:

- Suspected M-spike in gammaglobulins.
- Global decrease of globulins: plasmapheresis?

# SPECTR

Using recommendations from **Szymanowicz et al., 2006**. **For research use only.**  
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## CNN map visualization:

Spikes

4/8: peak-6983 (M, 58)

<< < 4 > >> Reset

## Qualitative abnormality:

Clonal anomaly (100%)

Hemolyzed serum

## Automated analysis output:

- Fractioning confidence: 100.00%
- **Classified as: Clonal anomaly (100%)**
- **Monoclonal spike? (96.72 %)**

## Analysis flags:

- **Clonal anomaly**
- Age > 45
- Male
- **Plasmapheresis?**
- Total protein < 55 g/l
- Albumin < 35 g/l
- Beta-2-globulins < 2 g/l
- **Gamma (res) < 8 g/l**
- **1 spike(s) in gamma**

Batch Sample

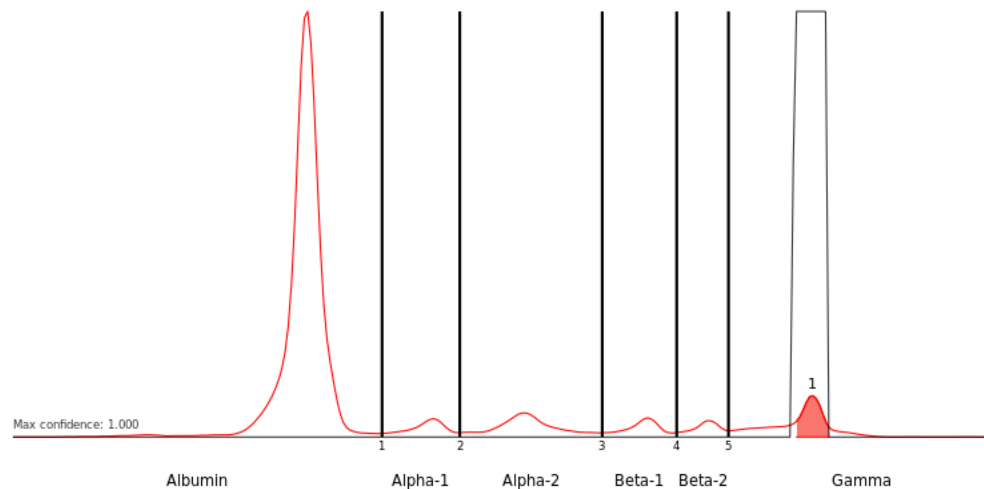
**Sample ID:** peak-6983  
**Age:** 58  
**Sex:** M  
**Total protein:** 48 g/L

Fraction	Pct.	Ref. (%)	Conc.	Ref. (g/L)
Albumin	72.5 %	55.8-66.1	34.8 g/L	40.2-47.6
Alpha-1	3.8 %	2.9-4.9	1.8 g/L	2.1-3.5
Alpha-2	7.8 %	7.1-11.8	3.8 g/L	5.1-8.5
Beta-1	3.7 %	4.7-7.2	1.8 g/L	3.4-5.2
Beta-2	2.7 %	3.2-6.5	1.3 g/L	2.3-4.7
Gamma	9.4 %	11.1-18.8	4.5 g/L	8-13.5
Gamma (res.)	4.5 %	11.1-18.8	2.1 g/L	8-13.5

Spike	Pct.	Conc.
1	5.0 %	2.4 g/L

### Automatic analysis flags

This section lists **all flags detected by the expert system** (included based on the deep learning analysis output) and **used for computing the automatic interpretation**



## Automatic interpretation:

- Suspected M-spike in gammaglobulins.
- Global decrease of globulins: plasmapheresis?

# SPECTR

Using recommendations from **Szymanowicz et al., 2006**. **For research use only.**  
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CNN map visualization:  
None

5/8: bridge-853 (F, 51)  
<< < 5 > >> Reset

Qualitative abnormality:  
Beta-gamma bridge (92.34%)

Hemolyzed serum

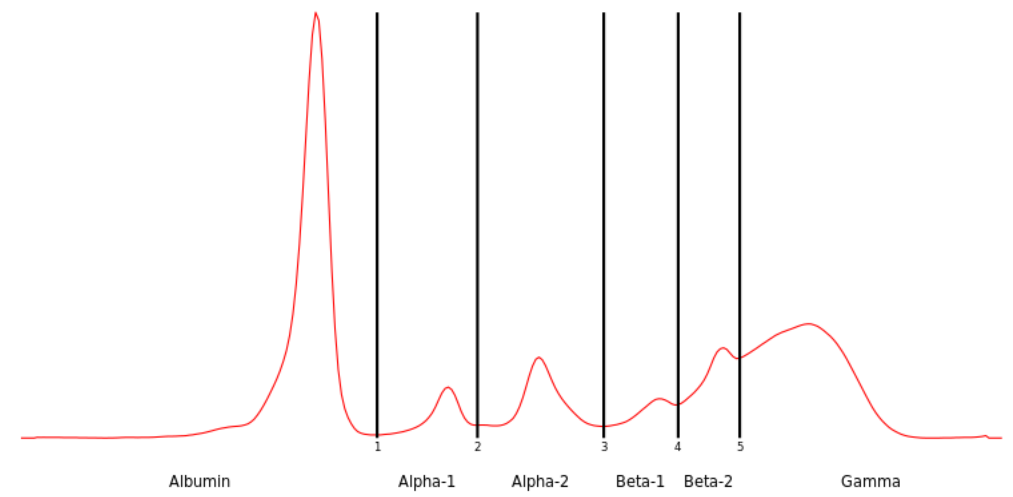
**Automated analysis output:**  
• Fractioning confidence: 100.00%  
• **Classified as: Beta-gamma bridge (92.34%)**

**Analysis flags:**  
• **Beta-gamma bridging, b2+gamma > 20g/l**  
• Age > 45  
• Female  
• Albumin < 30 g/l  
• Beta-2-globulins > 5.5 g/l  
• Beta-2-globulins > beta-1-globulins  
• **Gammaglobulins > 20 g/l**

Batch Sample

Sample ID: bridge-853  
Age: 51  
Sex: F  
Total protein: 71 g/L

Fraction	Pct.	Ref. (%)	Conc.	Ref. (g/L)
Albumin	39.2 %	55.8-66.1	27.8 g/L	40.2-47.6
Alpha-1	4.8 %	2.9-4.9	3.4 g/L	2.1-3.5
Alpha-2	10.1 %	7.1-11.8	7.1 g/L	5.1-8.5
Beta-1	4.8 %	4.7-7.2	3.4 g/L	3.4-5.2
Beta-2	9.9 %	3.2-6.5	7.0 g/L	2.3-4.7
Gamma	31.3 %	11.1-18.8	22.2 g/L	8-13.5



### Automatic interpretation:

- Major beta-gamma bridging.
- Major hypoalbuminemia.

# SPECTR

Using recommendations from **Szymanowicz et al., 2006**. **For research use only.**  
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[E-mail the corresponding author](#)

### CNN map visualization:

None

5/8: bridge-853 (F, 51)

<< < 5 > >> Reset

### Qualitative abnormality:

Heterogeneity restriction aspect (0.18%)

Hemolyzed serum

### Automated analysis output:

- Fractioning confidence: 100.00%
- **Classified as: Beta-gamma bridge (92.34%)**

### Analysis flags:

- **Heterogeneity restriction aspect**
- Age > 45
- Female
- Albumin < 30 g/l
- Beta-2-globulins > 5.5 g/l
- Beta-2-globulins > beta-1-globulins
- **Gammaglobulins > 20 g/l**

Batch

Sample

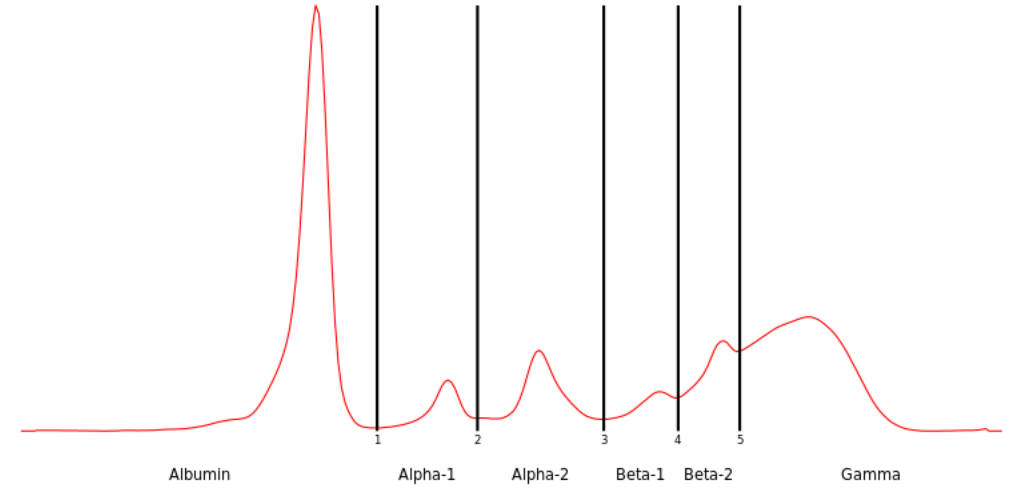
Sample ID: bridge-853

Age: 51

Sex: F

Total protein: 71 g/L

Fraction	Pct.	Ref. (%)	Conc.	Ref. (g/L)
Albumin	39.2 %	55.8-66.1	27.8 g/L	40.2-47.6
Alpha-1	4.8 %	2.9-4.9	3.4 g/L	2.1-3.5
Alpha-2	10.1 %	7.1-11.8	7.1 g/L	5.1-8.5
Beta-1	4.8 %	4.7-7.2	3.4 g/L	3.4-5.2
Beta-2	9.9 %	3.2-6.5	7.0 g/L	2.3-4.7
Gamma	31.3 %	11.1-18.8	22.2 g/L	8-13.5



### Automatic interpretation:

- Restriction of immunoglobulin heterogeneity with major hypergammaglobulinemia. Evolution to be monitored. Immunological identification is recommended as appropriate to the clinical context.
- Major hypoalbuminemia.



# Conclusion et perspectives

The background of the slide is white with abstract blue geometric shapes on the right side. These shapes include overlapping triangles and polygons in various shades of blue, from light sky blue to dark navy blue. The shapes are layered, creating a sense of depth and movement.

# Conclusion

- ▶ Extrêmement rapide : < 100 millisecondes par échantillon pour l'IA complète (sur un ordinateur portable standard)
  - ▶ Permet l'analyse en temps réel et la mise à jour automatique en cas de modification par l'opérateur
- ▶ Entièrement transparent et paramétrable par l'opérateur
  - ▶ Toutes les valeurs prédites par les modèles sont affichées à l'opérateur
  - ▶ Tous les seuils sont configurables selon les pratiques du laboratoire
  - ▶ Adaptable à différentes recommandations nationales/régionales :
    - ▶ Szymanowicz et al., 2006
    - ▶ Moss, 2016

# Perspectives

- ▶ Apport d'autres données clinico-biologiques, traitements, antécédents...
- ▶ SPECTR v1 : application en routine ?
  - ▶ Stade actuel : preuve de concept
  - ▶ **Validation prospective nécessaire** sur des populations à l'échelle nationale et internationale
  - ▶ Recommandations internationales harmonisées ?
  - ▶ **Réglementation complexe** de l'IA dans le secteur médical
- ▶ SPECTR v2 : non supervisé
  - ▶ AUC similaires après entraînement sur ~50 échantillons
  - ▶ Meilleure détection des anomalies rares
  - ▶ Vers la détection de nouvelles pathologies sans intervention humaine ?
  - ▶ Immunotypages ?

# Merci de votre attention

- ▶ Ressources supplémentaires en ligne :

- ▶ <https://SPECTRonline.fr/spectr>

- ▶ Chabrun F, Dieu X, Ferre M, Gaillard O, Mery A, Chao de la Barca JM, Taisne A, Urbanski G, Reynier P, Mirebeau-Prunier D. **Achieving Expert-Level Interpretation of Serum Protein Electrophoresis through Deep Learning Driven by Human Reasoning.** Clinical Chemistry. 2021. <https://doi.org/10.1093/clinchem/hvab133>

- ▶ Remerciements :

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# Modèle de détection d'hémolyse

