Accelerated Raman hyperspectral imaging for cancer diagnosis

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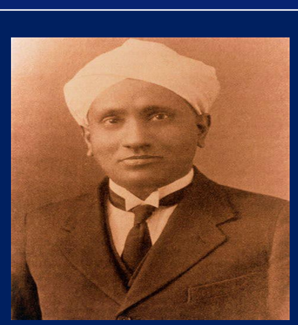
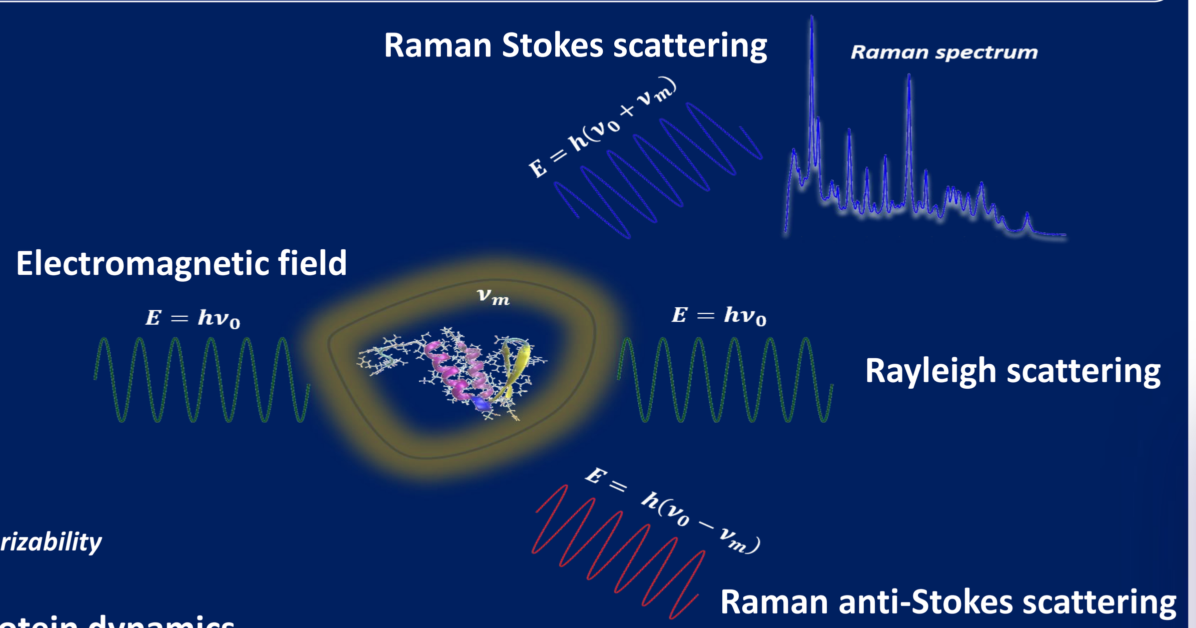
Raman spectroscopy, a label free vibrational spectroscopy which exploits the non-elastic diffusion property of light matter interaction, is becoming a popular technique to explore the biological world at different scales, from single molecule detection to tissue analysis. Indeed, in the last ten years, the advances in Raman confocal microscopy make possible to sense chemical information of constituents present in biological samples with a high spatial resolution, rending this technology highly promising to get new insights in cancer biology. Nevertheless, the Raman diffusion is a rare event, and getting a spatio-spectral map of biological sample can be time consuming. To overcome this difficulty, we have developed a novel kind of microscope based on the compress sensing ideas, which senses and compresses the information at the same time. The challenge is then to recover the original spatio-spectral information by solving an advanced optimization problem with a primal-dual splitting approach.

Raman scattering



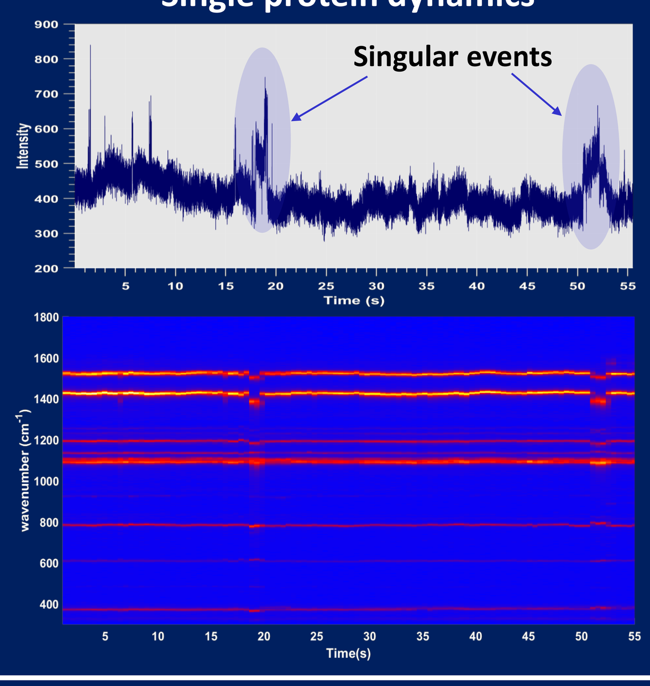
C.V RAMAN 1928

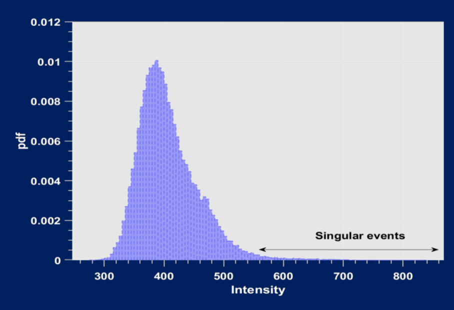


$P = [\alpha]E$

Induced dipole moment *Polarizability*

Single protein dynamics



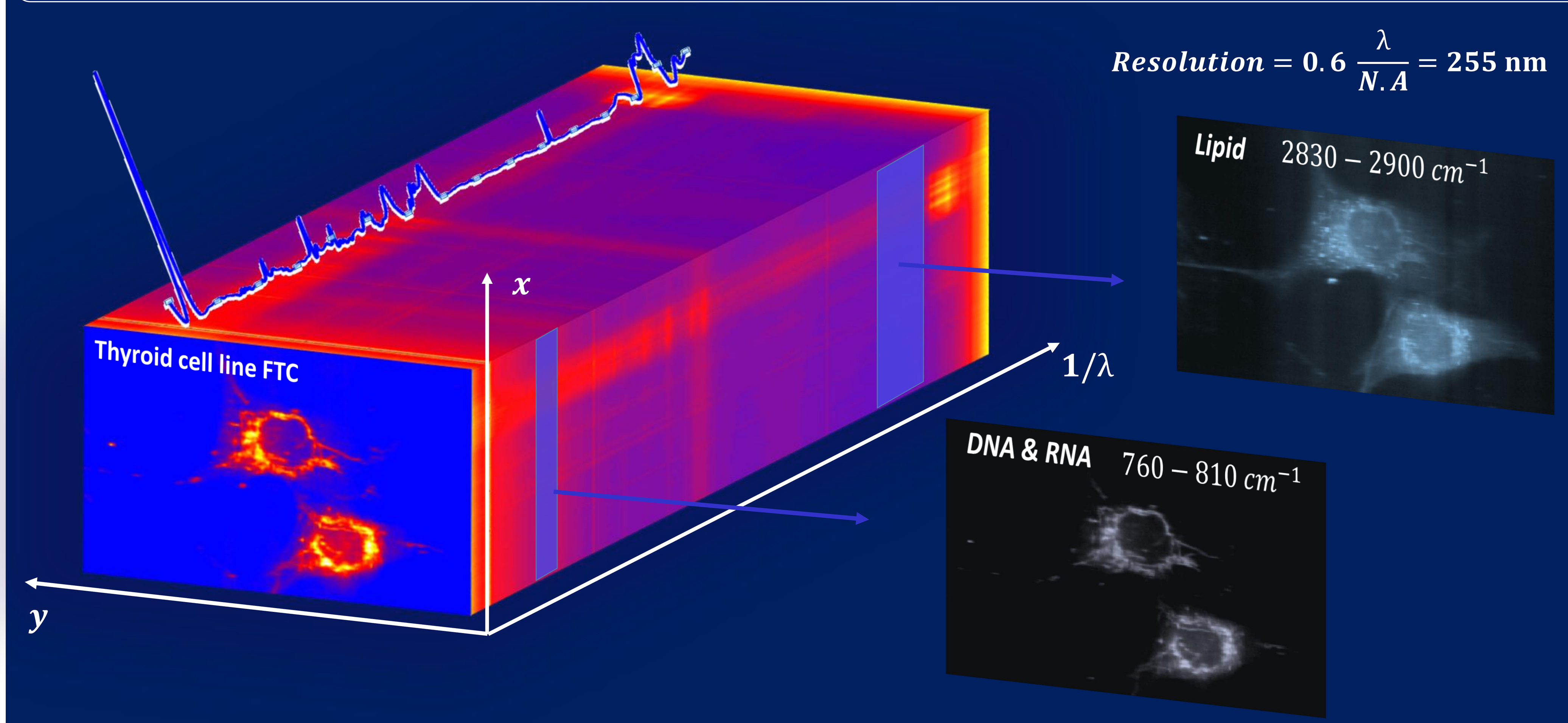


Enhanced Raman spectroscopy is an outstanding technology to explore biological system dynamics such as protein-protein interactions or protein conformational changes at the single level.

This spectroscopy which is highly sensitive to subtle molecular changes is a good candidate to detect singular events.

Raman Hyperspectral imaging

$$Resolution = 0.6\,\frac{\lambda}{N.A} = 255\text{ nm}$$



Hyperspectral imaging has emerged as an new technique to examine with high-resolution biological complex systems such as cells . This instrumentation provides with high fidelity comprehensive information about the biochemical composition of biological samples. In that way, it is then possible to appreciate sub-cellular changes which can happen inside the cell body under disease conditions. Raman hyperspectral imaging is then a new promising approach to understand the early mechanism of pathology development. Nevertheless to acquire such hyperspectral images is time-consuming and we need to find solutions to reduce data time acquisition. One solution is to build a microscope that exploits the original idea of *Compress Sensing.*

This accelerated Raman information measurement gives hope it will be possible to have access to the dynamics of tumor progression from a molecular point of view, allowing to better understand the emergence of these singular events.

Compress Sensing framework

Sensing matrix

$$\mathrm{v} = \phi u \quad [1]$$

measurement original signal

General problem of reconstructing a vector $u \in R^N$ from few linear non-adaptative measurements $v \in R^K$ ($\phi \in R^{KxN}$)

Mysterious case : Undetermined scenario K<<N

Is it hopeless to recover u in this situation?

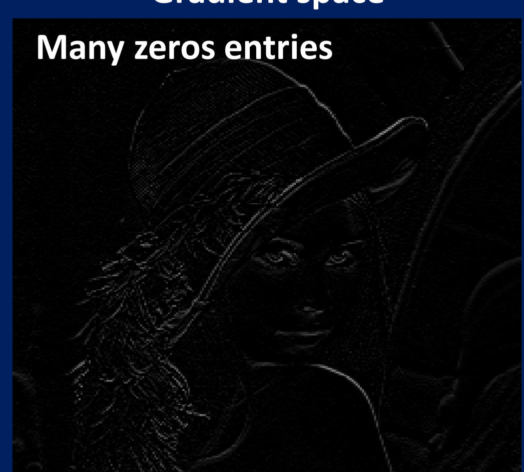
Sparsity is the key

Original space

Horizontal finite differences

$$Du_{i,j} = u_{i+1,j} - u_{i,j}$$

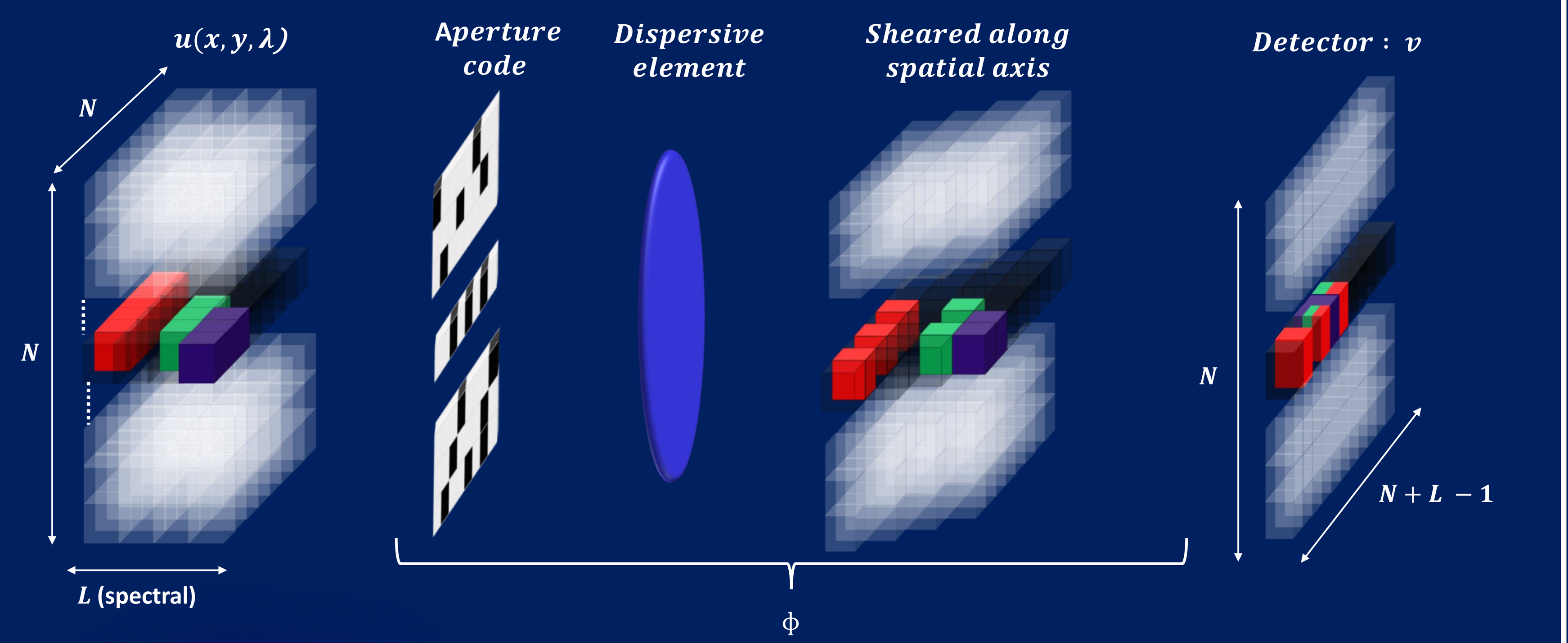
Gradient space

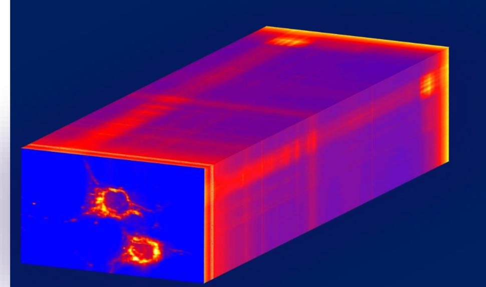


Recovering u from v [1], can be done by solving the following optimization problem :

$$\min_{u \in R^N} \|\psi \boldsymbol{u}\|_1 \quad st\ \|\phi u - v\| < \varepsilon,$$ where ψ is a sparsifying transform

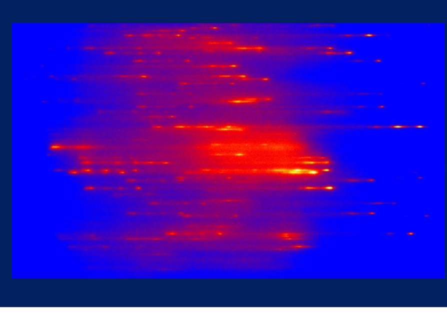
Code Aperture Spectral Snapshot





Random projection of high dimensional data onto a lower dimensional space while preserving as much information as possible

The challenge is then to recover the original hyperspectral image by solving an optimization problem



Primal-Dual Splitting algorithm

Many problems to solve in image processing can be expressed as the general optimization problem of the form:

Notations

Γ_0 : set of all proper semicontinuous convex functions on R^n

$prox$: proximal operator defined as

$$prox_{\gamma_1 f} = \underset{y \in R^n}{argmin}\ f(y) + \frac{1}{\gamma}\|x - y\|_2^2$$

Primal formulation

$$\min_{x \in R^n}\ g(x) + h(Lx) \quad [2]$$

where $g \in \Gamma_0(R^n), h \in \Gamma_0(R^n)$, and L is a linear operator

Dual formulation

$$\min_{y \in R^k}\ h^*(-L^T y) + g^*(y) \quad [3]$$

h^* is the convex conjugate function of h

The strategy is to solve problem [2] and [3] jointly

More precisely the goal is to find a *Kuhn Tucker point* $(\hat{x}, \hat{y}) \in R^k \times R^n$ which satisfies the following optimal conditions

$$0 \in \partial g(\hat{x}) + L^T\hat{y}$$
$$0 \in \partial h^*(\widehat{y}) - L\hat{x}$$

The following iterative procedure solves this inclusion problem

$$\hat{x} = prox_{\gamma_1 g}(\hat{x} - \gamma_1 L^T\hat{y})$$
$$\hat{y} \leftarrow \hat{y} - \gamma_2 \mathrm{L}(2\hat{x} - \hat{x}) \quad [4]$$
$$\hat{y} = \hat{y} - \gamma_2 prox_{h/\gamma_2}(\tfrac{1}{\gamma_2}\hat{y})$$

Proposed framework to recover hyperspectral images

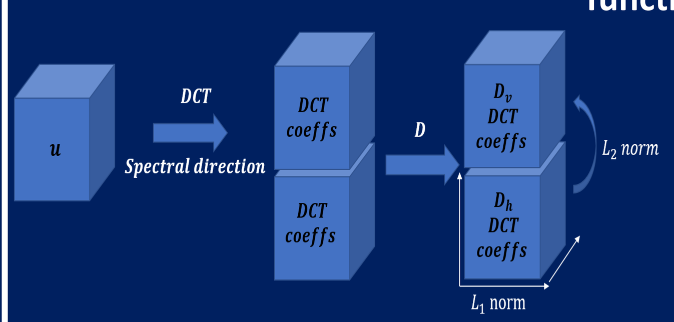
Properties of Hyperspectral images → Smoothness in both spatial and spectral directions

Transformed domain → Hyperspectral total variation

$$\min_{u \in R^n} \|DCu\|_{1,2} \quad st\ \|\phi u - v\| < \varepsilon, u \in [0,\mu]^N \quad [5]$$

where $D = (D_h, D_v)$ *stands for local difference, and C for discrete cosine transform*

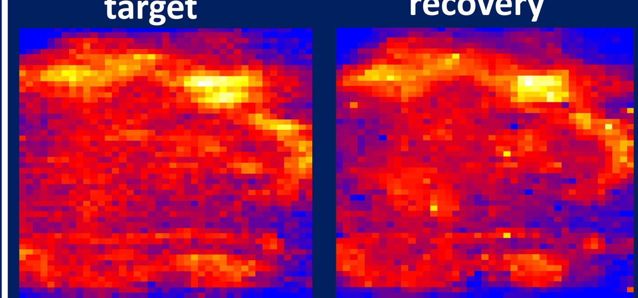
Reformulation of problem [5] to an unconstrainted form, by introducing an indicator function, $i_C(x)$



$$\min_{u \in R^n}\ \|DCu\|_{1,2} + i_{[0,\mu]^N}(u) + i_{B_{v,\varepsilon}}(\phi u) \quad [6]$$

$$\begin{cases} i_C(x) = 0\ if\ x \in \mathrm{C} \\ i_C(x) = +\infty\ if\ x \notin \mathrm{C} \end{cases}$$

target recovery



Splitting variables

$$\min_{u, y_1, y_2}\ \|y_1\|_{1,2} + i_{[0,\mu]^N}(u) + i_{B_{v,\varepsilon}}(y_2) \quad st\ \begin{bmatrix} y_1 \\ y_2 \end{bmatrix} = \begin{bmatrix} DC \\ \phi \end{bmatrix}[u]$$

$$g(u) = i_{[0,\mu]^N}(u)$$
$$h(y_1, y_2) = \|y_1\|_{1,2} + i_{B_{v,\varepsilon}}(y_2)$$
$$L = \begin{bmatrix} DC \\ \phi \end{bmatrix}$$

Primal dual splitting algorithm

$$u^{(k+1)} = P_{[0,\mu]^N}(u^{(k)} - \gamma_1(DC^T y_1^{(k)} + \phi^T y_2^{(k)}))$$
$$y_1^{(k)} \leftarrow y_1^{(k)} + \gamma_2 DC(2u^{(k+1)} - u^{(k)})$$
$$y_2^{(k)} \leftarrow y_2^{(k)} + \gamma_2\phi(2u^{(k+1)} - u^{(k)})$$
$$y_1^{(k+1)} = y_1^{(k)} - \gamma_2\, prox_{\frac{1}{\gamma_2}\|\cdot\|_{1,2}}(1/\gamma_2\, y_1^{(k)})$$
$$y2^{(k+1)} = y2^{(k)} - \gamma_2\, prox_{P_{B_{v,\varepsilon}}}(1/\gamma_2\, y_2^{(k)})$$

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