

Enhancing PathwayMapper in cBioPortal and PathwayMapper editor

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Summary

My task was to integrate PathwayMapper component to PatientView Page. Previously the PathwayMapper has been integrated to ResultsView hence I had the access to react component of PathwayMapper. Firstly, I identified what would be differently to the ResultView Page. Then I have implemented the PathwayMapper read-only version for cBioPortal PatientView Page. After the design choices were completed I finalized the PathwayMapper component for PatientView.

Design Choice

Design choices for PathwayMapper for cBioPortal PatientView Page has been changed along the way. First approach was to make an implementation similar to the PathwayMapper for ResultsView Page. However it was concluded that a different implementation was needed since the data in PatientView Page belongs to a single patient and alteration for one gene is always 100% altered. Showing alteration percentages for PatientView would not be very informative. After some deliberation, it has been concluded that the PathwayMapper should display the mutation types, fusions and copy number alterations(cna) types of the patient's genes. Displayed types are decided to be colored according to the OncoPrint color scheme.

Changes in PathwayMapper React Component

React component used resides in react-pathway-mapper.tsx and some changes have been made to this component to achieve design choices.

The interface:

```
interface IPathwayMapperProps{
  isCBioPortal: boolean;
  genes: any[];
  isCollaborative?: boolean;
  cBioAlterationData?: ICBioData[];
  pathwayName? : string;
  alterationData?: IAlterationData;
  queryParameter?: any;
  oncoPrintTab?: string;
  changePathwayHandler?: Function;
  addGenomicDataHandler?: (addGenomicData: (alterationData:
ICBioData[]) => void) => void;
  tableComponent?: any;
  isValidGene?: (gene: string) => boolean;
  toast: any;
  view?: string
}
```

A new parameter is added to the PathwayMapper interface called “view” which is optional. This parameter is sent from cBioPortal and it is used as a flag for PatientView functions. Other parameters specific to Read-Only (cBioPortal) Mode are used unchanged. Mandatory parameter `isCbioPortal` refers to modes; `readOnly` or `Full PathwayMapper`. Property called `genes` is used to identify the genes specified from cBioPortal. `alterationData` property is the data specified in the URL and used for the data that is going to be overlaid to the pathways.

`calculatePatientData(cBioAlterationData: ICBioData[])`

This is a new function added to `react-pathway-mapper.tsx` to get alteration data from the PatientView Summary tab. This function is called from the constructor if the `view` property equals “patient”. Normally cBioAlteration data is calculated using `calculateAlterationData()` function. In `calculatePatientData` method a new array is created that contains the gene, the alteration type and alteration percentage which is calculated as 100% for every gene. In order to get the alteration type, “`percentAltered: string`” variable from the `ICBioData` is used since it is not used in other methods in PathwayMapper.

Changes in GenomicDataOverlayManager

`showPatientData(data)`

This new function is added instead of `showGenomicData()` method. In the read-only and Full PathwayMapper, `showGenomicData()` method is used to get every node in the pathway and generate rectangles for the node if there are valid genes that match this pathway. In `showGenomicData()` method every study corresponds to a rectangle in a node and the color of the node is calculated according to the alteration percentage. However in the `showPatientData()` method, some major changes are made to comply with the design choices. Firstly, like in the `showGenomicData()` method, nodes of the pathway are taken one by one and controlled if the genes are present in the data. If the gene in the pathway has a match in the patient data from the cBioPortal then a rectangle is generated and added to this particular node as a background image.

`generateSVGForPatientNode(ele, patientData)`

This method is created to generate rectangles with respect to the PatientView design choices. The method is called for every node in the pathway if it exists in the patient’s data. Firstly the `alterationBoxCount` is calculated. This variable corresponds to the total number of all the mutation types and copy number alterations of the gene and the number of rectangles that is going to be created is decided by this variable. Then the `boundingBox` parameters are set and rectangles for each type are generated by calling `genomicDataRectangleGeneratorPatient()` method. `Alteration type(string)`, `color of the alteration type(string)` and `alteration percentage(number)` are the variables that contain the rectangle information. Finally,

`genomicDataRectangleGeneratorPatient()` method sets the color, innerHTML and size of the rectangles for each alteration.

Changes in these classes and methods have no effect on the existing functionalities and the features of PathwayMapper Read-only or Full PathwayMapper modes.

Changes in cBioPortal-frontend

After the modifications made in PathwayMapper, cBioPortal codebase required changes. A new wrapper React component was created and it was added to the PatientViewPage as a new tab. According to the naming conventions, the component is named as PatientViewPathwayMapper and it is added to the enum classes with the same name.

PatientViewPathwayMapper is responsible for the main operations. `isCBioPortal` property is set to true and `isCollaborative` is set to false to indicate that this is the read-only mode of PathwayMapper. New optional property `view` is set to "patient" to be used as a flag for patient operations in the PathwayMapper. Queried genes in this case the patient's genes are sent to PathwayMapper with `genes` property. Mutation types and copy number alterations are sent to the PathwayMapper through `cBioAlterationData` property. The table that displays the pathways on the right side of the PathwayMapper view is rendered through the `PatientViewPathwayMapperTable` component which is sent using `tableComponent` property. The other properties `changePathwayHandler` and `addGenomicDataHandler` are used to overcome the asynronanizaiton errors when the pathway is changed or the alteration data is completed hence they function as a link between PatientViewPathwayMapper and PathwayMapper. These two components interact with each other through callbacks.

Changes in PathwayMapper Read-only Mode

Toolbar

Disabled features of PathwayMapper in PatientView cBioPortal:

- Add Genes
- Edit Pathway
- Context menu
- Node resize
- Edge handling
- Edge editing
- Qtip

In addition to the disabled features in ResultsView Page "Edit Pathway" and "Add Genes" extensions are decided to be disabled for this view. Since the data types are displayed and construction of the rectangles are different from the PathwayMapper, editing this pathway from the PathwayMapper's Full mode is not suitable.



Figure 1: Toolbar Menu

The buttons left refers to Save as PNG, Save as SVG, Perform Layout and Help respectively. Color schemes for the mutation types and copy number alterations can be found in the Help window.

Important Methods for PathwayMapper

There are 2 methods written specific to PatientViewPathwayMapper. `getCNATypes (number)` is used to get the actual string of the copy number alteration(CNA) types taken from the patient's alteration data. This method returns the string equivalents of the CNA types.

`getQueryGenes(ICBioData [])` method is used to get all of the unique genes of the patient. A gene can have more than one alteration type or CNA hence this method is used to construct an array of genes and it is given to the `genes` property of PathwayMapper component which is used for the matching genes in a pathway.

PathwayTable

A table is used to show the pathways for the genes. The table is created using the altered genes from the patient's clinical information and column information. After the information is provided, a LazyMobXTable component renders the Pathway Table. The aim of the table is to show the best pathways that match the patient's alteration genes.

Pathway name	Score ▼	Genes matched
☒ LUSC-2012-RTK-RAS-PL...	4.00	EGFR MTOR PTEN ...
☐ ESAD-2017-RTK-RAS-PL...	3.00	EGFR PTEN FGFR2
☐ KIRC-2013-RTK-RAS-PL...	3.00	EGFR MTOR PTEN
☐ SKCM-2015-TP53-pathw...	3.00	TP53 CDKN2A CDKN2B
☐ STAD-2014-RTK-RAS-PL...	3.00	EGFR PTEN FGFR2
☐ BLCA-2014-RTK-RAS-PL...	3.00	EGFR MTOR PTEN
☐ GBM-2013-Cell-cycle-...	3.00	CDKN2A CDKN2B ...
☐ HIPPO	3.00	EGFR MTOR PTEN
☐ GBM-2008-Cell-cycle-...	3.00	CDKN2A CDKN2B ...
☐ LUAD-2014-RTK-RAS-PL...	3.00	EGFR MTOR PTEN

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Figure 2: PathwayTable

As it can be observed PathwayName, Score and Genes matched columns are displayed. Pathway name refers to the pathway shown in the view, Score refers to the number of genes matched to the pathway and Genes Matched shows the patient's genes that match to the pathway.

Only the match count ranking option is used to sort the pathways. Every gene altered counts as 100% altered, using other ranking options are identical to match count, hence ranking option is eliminated for PatientViewPathwayMapper whereas different ranking options can be used for ResultsViewPathwayMapper.

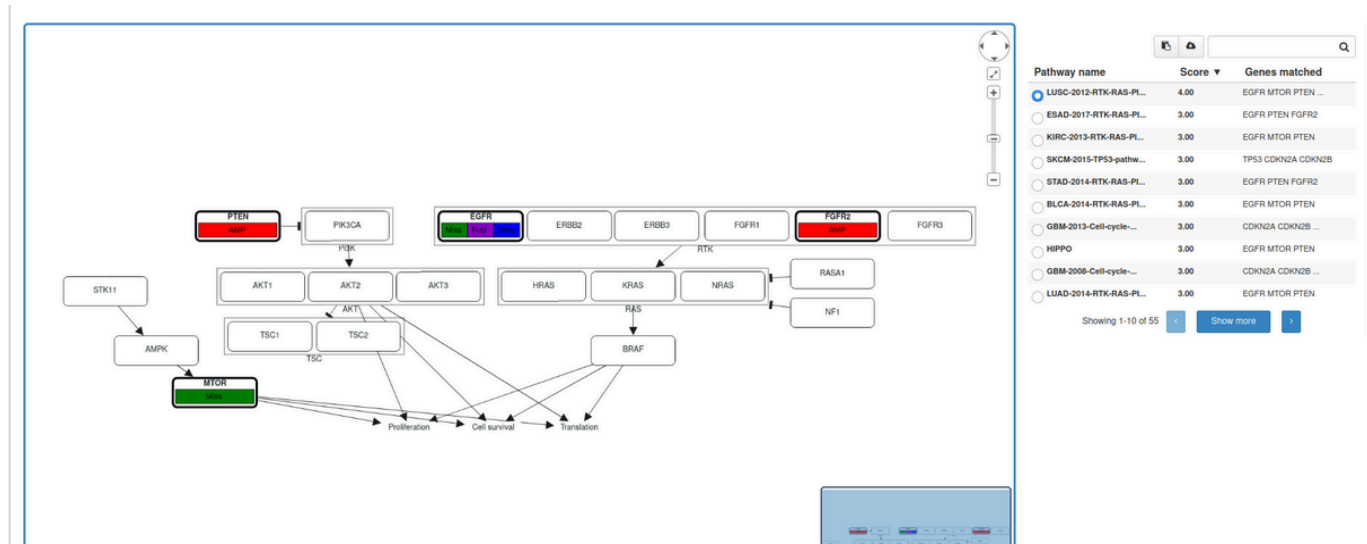


Figure 3: PathwayMapper for PatientView

This figure shows the final result of the implementations. There are 3 different alteration types for the EGFR gene for this particular patient. Two mutation types, Missense and Fusion and one copy number alteration called AMP. In the pathway these three types are observed and colored differently corresponding to the OncoPrint color scheme. On the other hand MTOR, PTEN and FGFR2 have one alteration type. On the PathwayTable matched genes are displayed according to the match count.

Repositories

cBioPortal

I have created a fork to work on cBioPortal.

My commits to cBioPortal fork:

<https://github.com/mervekilcarslan5/cbioportal-frontend/commits/master?author=mervekilcarslan5>

The pull request from the fork to original cBioPortal repository:

<https://github.com/cBioPortal/cbioportal-frontend/pull/3381>

PathwayMapper

I worked on PathwayMapper unstable branch

My commits to PathwayMapper unstable branch:

<https://github.com/iVis-at-Bilkent/pathway-mapper/commits/unstable?author=mervekilcarslan5>

Tasks Left

PathwayMapper for cBioPortal StudyView Page implementation is left for implementation.