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Modeling the conversion between specific IgE test platforms for nut allergens in children and adolescents

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Abstract

Background

Multiplex tests allow for measurement of allergen-specific IgE responses to multiple extracts and molecular allergens and have several advantages for large cohort studies. Due to significant methodological differences, test systems are difficult to integrate in meta-analyses/systematic reviews since there is a lack of datasets with direct comparison. We aimed to create models for statistical integration of allergen-specific IgE to peanut/tree nut allergens from three IgE test platforms.

Methods

Plasma from Canadian and Austrian children/adolescents with peanut/tree nut sensitization and a cohort of sensitized, high-risk, pre-school asthmatics (total n = 166) were measured with three R&D multiplex IgE test platforms: Allergy Explorer version 1 (ALEX) (Macro Array Dx), MeDALL-chip (Mechanisms of Development of Allergy) (Thermo Fisher), and EUROLINE (EUROIMMUN). Skin prick test (n = 51) and ImmunoCAP (Thermo Fisher) (n = 62) results for extracts were available in a subset. Regression models (Multivariate Adaptive Regression Splines, local polynomial regression) were applied if >30% of samples were positive to the allergen. Intra-test correlations between PR-10 and nsLTP allergens were assessed.

Results

Using two regression methods, we demonstrated the ability to model allergen-specific relationships with acceptable measures of fit (r^2 = 94%-56%) for peanut and tree nut sIgE testing at the extract and molecular-level, in order from highest to lowest: Ara h 2, Ara h 6, Jug r 1, Ana o 3, Ara h 1, Jug r 2, and Cor a 9.

Conclusion

Our models support the notion that quantitative conversion is possible between sIgE multiplex platforms for extracts and molecular allergens and may provide options to aggregate data for future meta-analysis.

Abbreviations

ALEX
: Allergy Explorer

Ana o
: cashew allergen

Ara h
: peanut allergen

Cor a
: hazelnut allergen

CRD
: component-resolved diagnosis

ISU
: ISAC standardized units

Jug r
: walnut allergen

loess
: locally estimated scatterplot smoothing

MARS
: multivariate adaptive regression spline

MeDALL-chip
: Mechanisms of development of allergy chip

nsLTP
: non-specific lipid transfer protein

PR-10
: pathogenesis-related subfamily 10

Pru du
: almond allergen

sIgE
: allergen-specific IgE

SPT
: skin prick test

1 INTRODUCTION

Allergen-specific IgE sensitization is routinely assessed during the clinical workup of allergic diseases, including food allergy, allergic rhinitis, and allergic asthma.[1] To overcome the significant degree of cross-reactivity observed due to homology of allergens from the same protein family, component-resolved diagnostic (CRD) testing or molecular allergology was developed, which focuses on individual allergens.[2] Molecular allergology is useful for assessing and predicting food allergies, such as peanut allergy, with a high sensitivity and specificity.[3] To date, ~880 allergens have been acknowledged by the Allergen Nomenclature database of the World Health Organization/International Union of Immunological Societies.[4] As our knowledge of allergens expands, so does the number of platforms used to measure sensitization to these allergens. Consequently, there is a growing demand for strategies that can take advantage of molecular diagnostics by integrating data from different platforms used in cohort studies. However, previously undertaken systematic reviews examining the evidence on CRD testing have been largely limited from performing meta-analyses due to heterogeneity in methods and a shortage of studies comparing different platforms head-to-head.[5]

While single-plex testing methods such as the ImmunoCAP® remain the most widely used for sIgE quantification,[6] they limit the breadth of testing that can be performed because of high costs and serum demands. These are important considerations for birth cohort studies measuring early-life sensitization patterns, where it is important to assess both food and inhalant allergen-specific antibody responses but limited serum volumes available. Multiplex methods tend to have smaller sample requirements and are more cost-effective for large-scale studies relative to single-plex methods.[6] Thus, multiplex IgE assays are often advantageous for both clinical and research purposes, and different versions including some assessing viral responses have been developed.[7, 8]

Multiplex test systems that are currently available include the Immuno Solid-phase Allergen Chip (ISAC) (Thermo Fisher Scientific, Phadia AB), also present in the R&D version as the Mechanisms of development of allergy (MeDALL)-chip.[9] The MeDALL-chip contains up to 176 molecular allergens analyzed using a fluorescence-based detection system.[10] Other tests using alternative approaches have also been launched, including blot-based systems used by EUROLINE (EUROIMMUN), which can be assembled into groups of allergens and extracts customized for the country of measurement, and colorimetric systems like the Allergy Explorer (ALEX) (Macro Array Diagnostics), measuring 156 extracts and 126 molecular allergens.

Despite the advantages of multiplex methods, they are reported to have higher coefficients of variation and lower test sensitivity than single-plex methods.[11] Furthermore, multiplex systems differ from one another in methodologies and units of measurement. For example, the amount of allergen applied on the chip/surface can vary up to 10 000-fold, making inhibition by IgG antibodies more likely to influence IgE measurement.[6] Therefore, it has been argued that results are not directly interchangeable between platforms such as ImmunoCAP and ISAC.[12] Meanwhile, studies have observed strong correlations between

different sIgE platforms for inhalant allergens between ImmunoCAP and ISAC,[12] ALEX and ISAC,[13] and for peanut allergens between ImmunoCAP and ISAC,[14] and EUROLINE and ISAC,[15] which supports the possibility of developing conversion models between platforms despite differences in units of measurement. Given the importance of longitudinal sensitization data, models or data that allow for conversion between test platforms could facilitate data synthesis between studies utilizing different platforms and directly impact knowledge generation.

Therefore, the objective of this study was to develop models that enable the quantitative conversion of sIgE results between different platforms, with a focus on nut allergens. Clinical performance of the platforms was not assessed, as this was beyond the scope of the study. Conversion was performed using two statistical regression methods to harmonize sIgE results obtained by MeDALL-chip, EUROLINE, and ALEX platforms from sensitized and/or nut allergic patients.

2 METHODS

2.1 Study population and clinical assessment

A total of 166 subjects were included in this analysis who met the criteria for one of two studies on pediatric nut allergy or pre-school asthma. Subjects of the Markers of Nut Allergy Study (MONAS) (n = 124) from age 6 months to 17 years were recruited at the allergy clinic at the Hospital for Sick Children (Toronto, Canada; n = 98) or the Department of Pediatrics, Medical University of Vienna (Vienna, Austria; n = 26) based on a peanut or tree nut allergy diagnosis or sensitization that was determined by clinical history, positive SPT, or sIgE tests. Sensitization by SPT (Omega Laboratories LTD) or sIgE (ImmunoCAP, Thermo Fisher) was assessed as part of routine clinical testing. This study was approved by the ethics board of the Hospital for Sick Children (REB #:1000053791) and the Medical University of Vienna (EK Nr 2302/2016). Additionally, 42 children with sensitizations were selected from the Wheezy ER study on pre-school asthma between 3 and 6 years of age (REB #:1000041089), based on inclusion criteria reported previously.[16, 17] These children presented to the Emergency Department at the Hospital for Sick Children with an acute wheezing exacerbation, a history of at least two wheezing episodes during the last 12 months, and displayed sensitization to food and/or inhalant allergens.[18]

2.2 Test systems

The Allergy Explorer version 1 (ALEX, Macro Array Diagnostics) is a nitrocellulose chip-based immunoassay, containing 156 extracts and 126 molecular allergens. Patient plasma (100 µL) was incubated on the chip in a 1:5 dilution with a cross-reactive carbohydrate determinant (CCD) inhibitor-containing diluent. Detection was performed with alkaline phosphatase-labeled anti-human IgE, as previously described.[18] Raptor software (Macro Array Diagnostics) quantified sIgE within a reportable range of 0.3-40 kUA/L. Positive sensitizations

were defined as ≥0.30 kUA/L. Allergens in a different formulation on the new ALEX-2 were not considered for analysis. All kits were purchased by the authors without involvement of the companies.

The Mechanisms of development of allergy (MeDALL)-chip is a fluorochrome-based system measuring sIgE to 176 allergens that are spotted in triplicates onto a glass slide.[19-22] Microarrays were incubated with 35 μL of patient plasma and detected using a fluorochrome-conjugated IgE detection antibody according to published methods within the reportable range of 0.3-100 ISU.[10, 23] Positive sensitizations were defined as ≥0.3 ISU.

The EUROLINE test (EUROIMMUN) is a blot-based test system. Two R&D test panels were performed per patient sample for a total of 12 extracts, 17 allergens and a CCD marker (Appendix S1). Each strip was incubated with 175 μL of patient plasma. Detection was performed with an enzyme-conjugated anti-human IgE antibody, followed by addition of enzyme substrate according to manufacturer's instructions. EuroLineScan software (EUROIMMUN) evaluated sIgE in the reportable range of 0.35-100 kUA/L. Positive sensitizations were defined as ≥0.35 kUA/L.

2.3 Statistical analysis

For each platform (ALEX, MeDALL-chip, and EUROLINE), we determined a dynamic range based on our current data and previous observations (Appendix S1). For ALEX measurements (n = 166), this was defined as between 0.3 and 40 kUA/L, for MeDALL-chip (n = 166) between 0.3 and 100 ISU,[10] and for EUROLINE (n = 121) between 0.35 and 100 kUA/L. Any values greater or less than these values were set to the maximum value or 0, respectively. Since our aim was to directly compare values presented by each platform, we did not perform any additional scaling or centering.

Each extract or allergen was assessed within each platform in a pairwise fashion if at least one other platform contained the corresponding allergen (Table S1, Figure S1). Among these allergens, only those with at least 30% of the samples within the dynamic ranges in one of the tests stated above were used for modeling (Table S2). All other extracts and allergens were excluded from regression analysis. A visual inspection of the pairwise values of some pairwise scatter plots revealed that while there are visible trends, these were not strictly linear and were specific to each comparison. To accurately and consistently model this behavior, we opted to employ local polynomial regression (loess)[24] and multivariate adaptive regression splines (MARS).[25]

Local polynomial regression was conducted as follows: Before beginning model training, each data matrix was first row-wise randomized to minimize any potential data collection effects. For local regression, the only parameter we needed to optimize per model was the span parameter to control the local environment of the polynomial regression. To find the best span parameter, after randomization, the data matrix was split into 5 sections for 5-fold cross-validation. Four of these 5 sections are then used to fit loess regressions for any given

span value, and the remaining section is used for calculation of the residual sum of squares (rss). This procedure is repeated five times using each section as a test set for each model and span value. The mean of the rss is calculated for these models and was used as the minimization target for numerical optimization using base R's optimize function, which utilizes a combination of golden section search and successive parabolic interpolation.[26] Whenever a span value failed to converge for the loess algorithm, an arbitrarily large number was used instead of rss as penalty. For each comparison, this winning span parameter is then used to fit the entire dataset for the final model. For each model trained, we manually inspected model parameters, scatterplots overlaid with model fits and residual vs fitted plots for any aberrant behavior.

For MARS regression, we employed 5-fold cross-validation (nfold) with 30 iterations (ncross) in order to avoid overfitting. Due to our small dataset, our variance method (varmod.method) was constructed using linear regression for standard deviation estimation. To avoid excessive model complexity, we finalized the resulting regression model using "exhaustive" pruning. All analysis was conducted using R statistical software[27] version 3.6.0. For MARS regression, earth package version 5.1.1,[28] and for loess regression, stats package within the base R distribution was used.

3 RESULTS

3.1 Patient characteristics

The median age of the 166 patients was 6.5 years (IQR: 4.6-12.1 years), with a male predominance observed (62%) (Table S3). The majority of the patients had a clinical history of atopy, including atopic dermatitis (66%), food allergy (76%), asthma (67%), or allergic rhinitis (47%). Food allergy was more prevalent in the MONAS group (90%), enrolling children with peanut and/or tree nut allergy or sensitization, whereas asthma was more prevalent in the Wheezy ER group, focusing on moderate-to-severe pre-school asthmatics (100%). Since only IgE results were compared, these two groups were combined to allow for investigation of allergens in children with significant sensitizations to food and inhalants.

3.2 Qualitative agreement of sensitization status across different test methods

Different test systems operate with different amounts of protein, extracts or allergens, and dynamic ranges. The alignment and sensitivity of detection were first evaluated across test systems measuring the same outcome (Figure 1). Among the twelve extracts common to ALEX and EUROLINE, the blot-based approach (EUROLINE) reported more sensitizations at the extract level than the colorimetric, chip-based approach (ALEX), with over twice as many positive signals to macadamia, sesame and Brazil nut, and substantial differences for milk, egg, and almond. Almost perfect alignment in detection of peanut extract sIgE was achieved (Figure 1A).

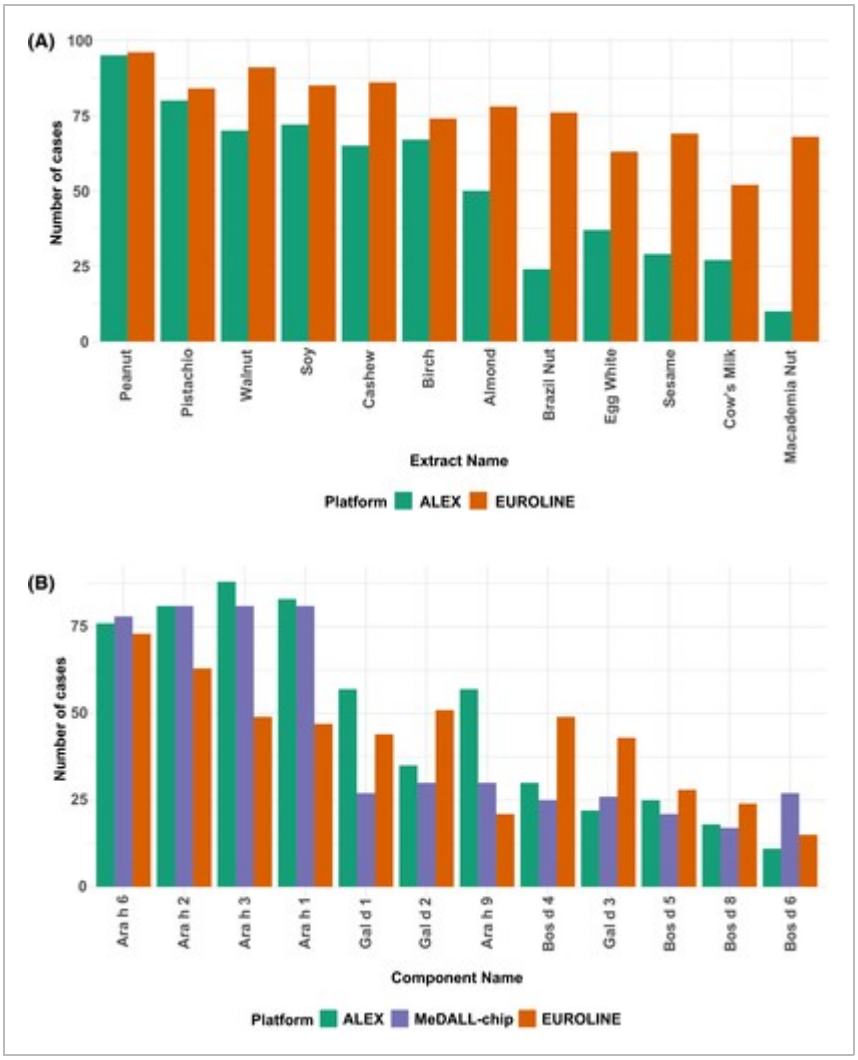


FIGURE 1

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Number of positive sensitizations reported by sIgE test platforms illustrates test agreement between (A) allergen extracts on ALEX and EUROLINE and (B) molecular allergens on ALEX, MeDALL-chip, and EUROLINE. Only the subjects with corresponding measurements in all 3 platforms are shown (n = 121)

Detection of twelve molecular allergens from peanut, milk, and egg was also compared between the three platforms (Figure 1B). The peanut allergens Ara h 1, 2, and 3 were more frequently positive on the ALEX and MeDALL-chip compared to EUROLINE, whereas sensitization to the cow's milk and egg allergens, Bos d 4, Gal d 2, and Gal d 3, were more frequently positive on EUROLINE than ALEX and MeDALL-chip (Figures S2 and S3). CCD markers were positive in 20% of MeDALL-chip and 18% of EUROLINE measurements, compared to 14% of ALEX measurements in the presence of a CCD-inhibitor (Table S4).

In general, the ALEX and MeDALL-chip platforms reported comparable numbers of sensitization (Figure S4). Among the 85 shared allergens, ALEX was more frequently positive than MeDALL-chip for the food allergens Gal d 1, Gal d 5, Ara h 8, Ara h 9, Cor a 9, and Fag e 2. Conversely, MeDALL-chip was more frequently positive than ALEX for inhalant allergens

such as Bet v 2, Fel d 2, and Der f 2, among others. Overall, strong positive correlations were observed between ALEX and MeDALL-chip for the majority of allergens (Figure S5).

3.3 Quantitative conversion models for nut extract allergens

To assess the conversion between different sIgE test platforms, the loess and MARS modeling approaches were applied to each pairwise comparison of platforms. In the MARS method, the model fit can be assessed by the coefficient of determination (r^2), with 1 indicating a perfect model fit where 100% of the variability in the data is explained by the model. MARS modeling was used to explain the relationship then compared to the more flexible loess method; regions where the two modeling approaches aligned were considered as an indicator of the robustness of the models.

Peanut extract sIgE results were compared between the following platforms: ALEX, EUROLINE, ImmunoCAP testing performed in a clinical laboratory (n = 59), and skin prick test (SPT) (n = 62). As ImmunoCAP is the most widely used sIgE test, we assessed conversions between ALEX vs ImmunoCAP and EUROLINE vs ImmunoCAP (Figure 2A and B). In both comparisons, the values predicted by both loess and MARS models exhibited good alignment within the range of 0.35-25 kUA/L of ImmunoCAP units. Overall, the MARS modeling was able to account for 89% of the variability in the conversion between peanut ALEX vs ImmunoCAP, and 71% of the variability in the conversion between peanut EUROLINE vs ImmunoCAP comparison (Table S5). Parameter estimates for all model equations are available in the online supplement (Appendix S2). Acceptable convertibility was also observed between ALEX vs EUROLINE platforms for peanut extract (r^2 = 84%) (Figure 2C).

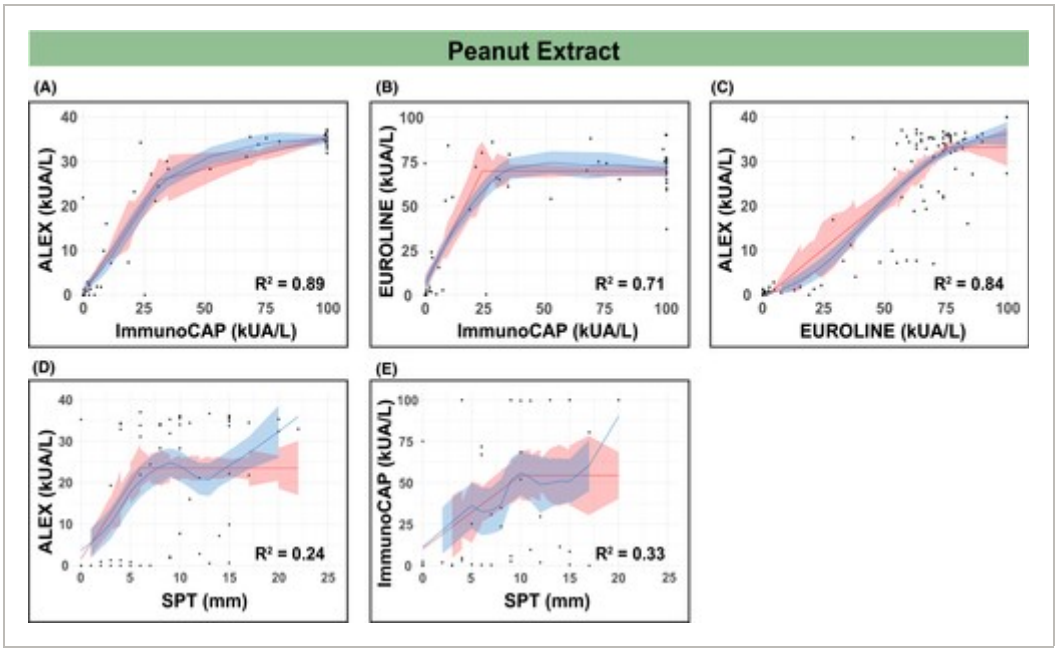


FIGURE 2

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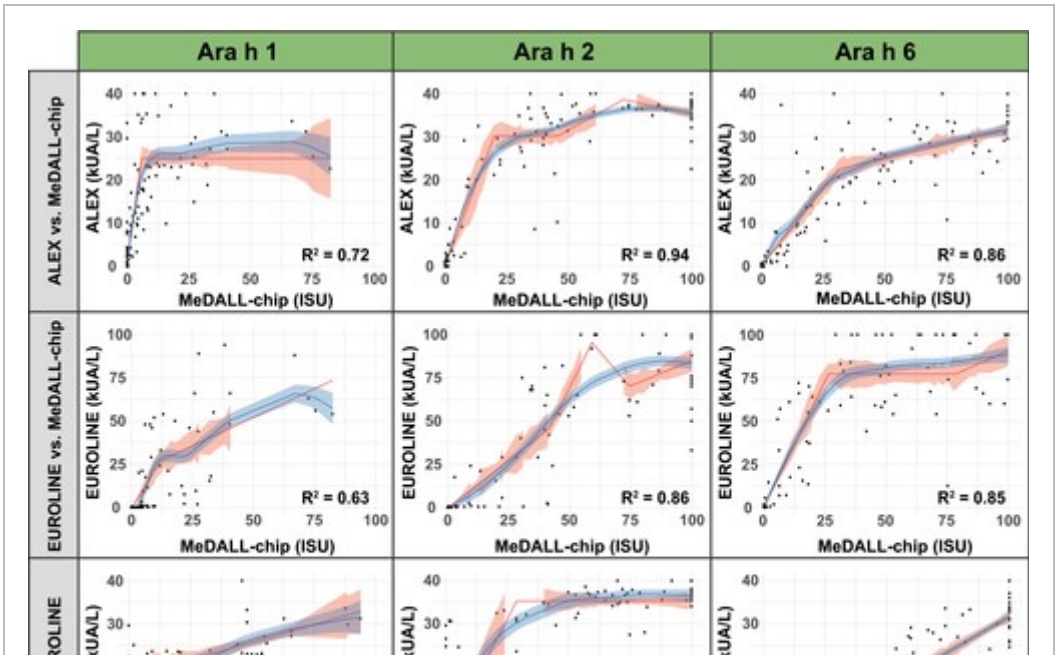
Modeling of peanut extract sIgE pairwise comparisons demonstrates convertibility between pairwise comparisons of ImmunoCAP, ALEX, and EUROLINE (A-C), but poor model fit for conversions with skin prick test (D, E). Blue = loess modeling, red = MARS modeling, and ribbon = 95% confidence interval

Tree nut extract sIgE conversion for almond, walnut, and hazelnut was assessed between the ALEX, EUROLINE, and ImmunoCAP platforms (Figure S6). The MARS modeling for ALEX vs ImmunoCAP values accounted for the majority of variability in walnut sIgE measurements (92%) and a moderate degree of variability in almond (70%) and hazelnut (66%) (Table S5). Similarly, EUROLINE vs ImmunoCAP and ALEX vs EUROLINE comparisons reported higher r^2 values for walnut extract at 82% and 92%, compared to almond extract at 69% and 70%, respectively.

In contrast, interconversion of sIgE and SPT using this modeling approach was less useful, as evidenced by low r^2 values. The MARS conversion models for peanut extract accounted for only 24% of the variability between ALEX vs SPT and 32% of variability between ImmunoCAP vs SPT (Figure 2D and E).

3.4 Quantitative conversion models for molecular nut allergens

Modeling was applied to molecular peanut allergens Ara h 1, 2, and 6 for the following platforms: ALEX, MeDALL-chip, and EUROLINE (Figure 3). The MARS model fit varied between allergens and platforms. Ara h 2 exhibited the highest overall r^2 values (84%-94%), which was greatest between ALEX vs MeDALL-chip, and was followed by Ara h 6 (85%-88%) and Ara h 1 (63%-72%). Tree nut allergen sIgE was also compared between ALEX vs MeDALL-chip, listed in order of model fit: Jug r 1 (78%), Ana o 3 (76%), Jug r 2 (62%), and Cor a 9 (56%) (Figure 4). When comparing ALEX vs MeDALL-chip, ALEX exhibited a reduced dynamic range above the amount of 25-35 kUA/L (based on internal ImmunoCAP calibration standard on ALEX).



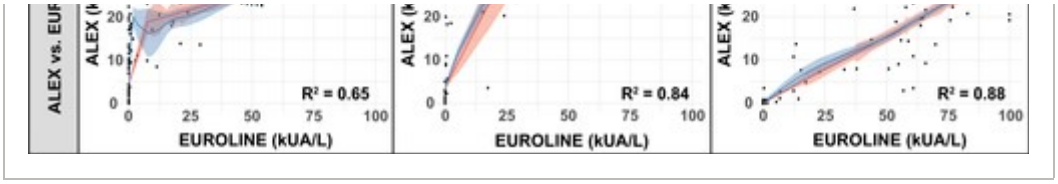


FIGURE 3

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Modeling of Ara h 1, Ara h 2, and Ara h 6 sIgE demonstrates convertibility between pairwise comparisons of ALEX, MeDALL-chip, and EUROLINE sIgE test platforms. Blue = loess modeling, red = MARS modeling, and ribbon = 95% confidence interval

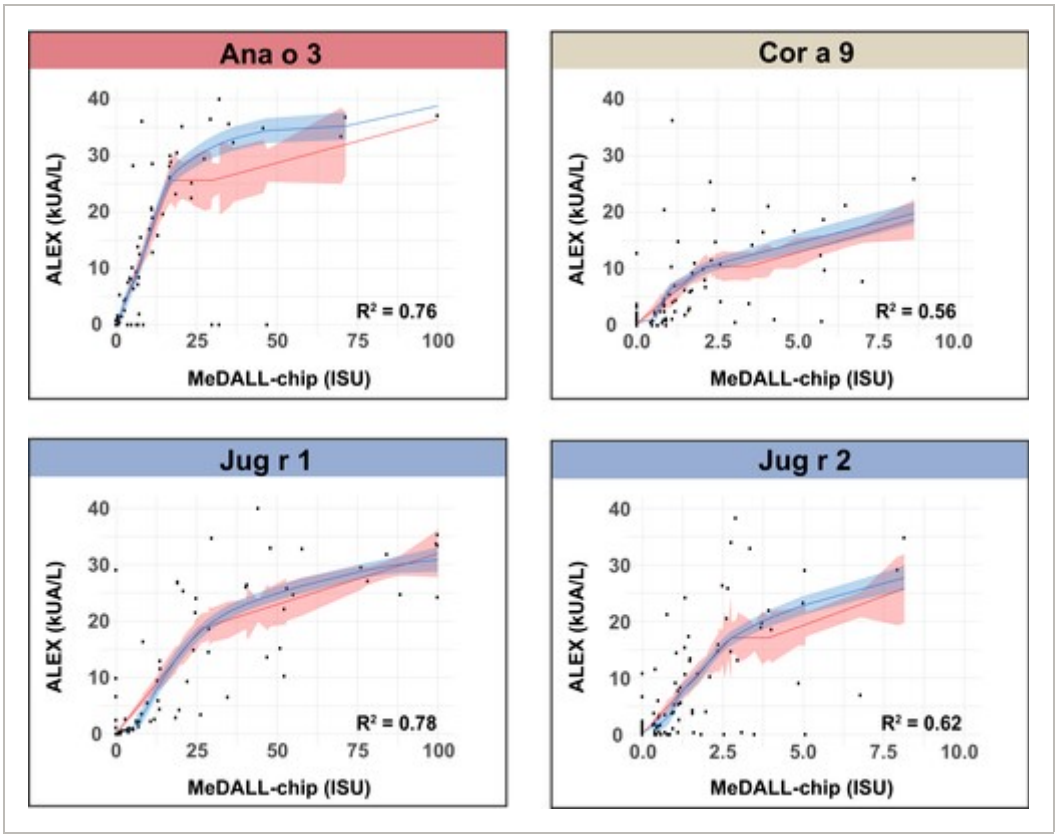


FIGURE 4

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Modeling of Ana o 3, Cor a 9, Jug r 1, and Jug r 2 sIgE demonstrates convertibility between pairwise comparisons of ALEX and MeDALL-chip sIgE test platforms. Blue = loess modeling, red = MARS modeling, and ribbon = 95% confidence interval

3.5 Correlations between PR-10 and nsLTP molecular allergens

Cross-reactivity within protein families due to sequence and structural homology is of significant importance. The PR-10 and nsLTP families play a central role in this context. We sought to quantitatively compare sIgE levels detected by ALEX and MeDALL-chip using the Pearson correlation coefficient (*r*) as a surrogate for the degree of cross-reactivity. Among

the PR-10 family proteins (Aln g 1, Ara h 8, Bet v 1, Cor a 1.0401, Gly m 4, and Mal d 1), the observed intra-test correlations tended to be lower on ALEX (Figure 5A) than on MeDALL-chip (Figure 5B). MeDALL-chip also reported a larger proportion of positive PR-10 co-sensitizations compared to ALEX when sIgE was evaluated at the positive test cutoff (Figure S7).

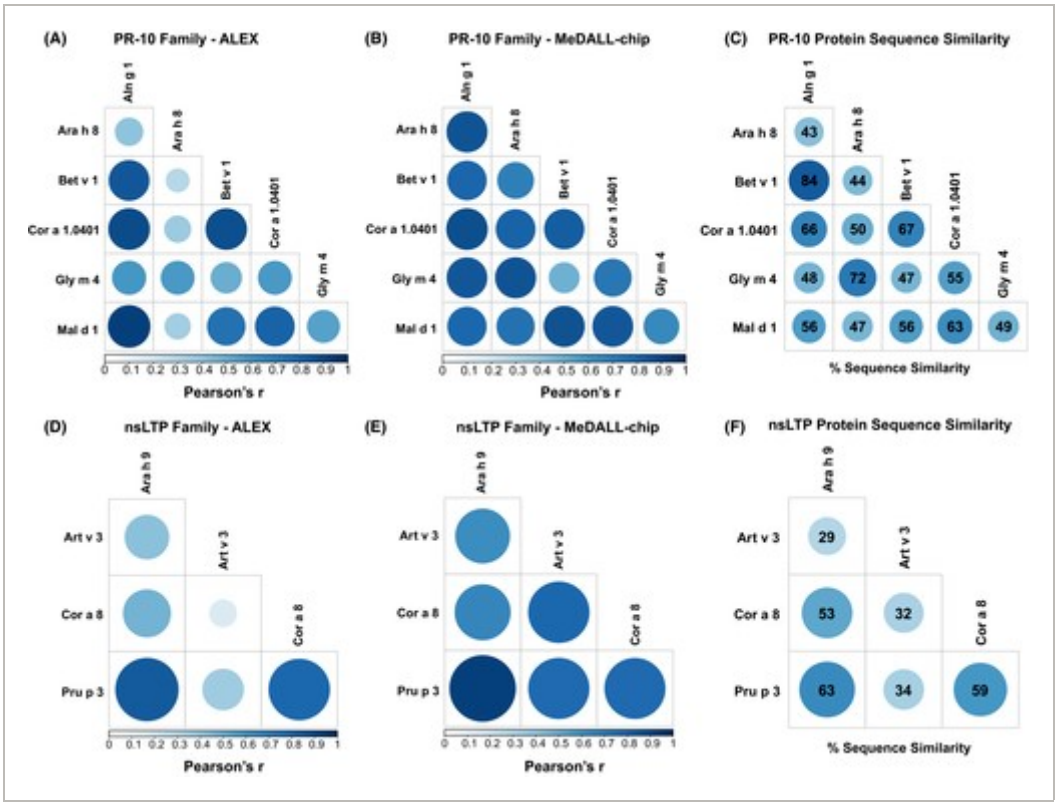


FIGURE 5

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Correlations of sIgE levels to PR-10 and nsLTP allergens are reflective of cross-reactivity resulting from protein sequence similarities and differ between multiplex platforms. A, Correlation of PR-10 allergens on ALEX, (B) correlation of PR-10 allergens on MeDALL-chip, (C) percentage of PR-10 protein sequence similarity, (D) correlation of nsLTP allergens on ALEX, (E) correlation of nsLTP allergens on MeDALL-chip (F) percentage of nsLTP protein sequence similarity. Pearson correlation coefficient (*r*) is depicted by both color intensity and circle size

In the context of protein sequence homology, the prototypical Bet v 1 allergen shares higher sequence similarity with other tree pollen allergens such as Aln g 1 (84%) and Cor a 1 (67%) as compared to homologous food allergens such as Ara h 8 (44%) (Figure 5C, Table S6). Accordingly, there was a strong correlation between the pollen allergens Bet v 1-Cor a 1 on both the ALEX (*r* = .88) and MeDALL-chip (*r* = .82). In comparison, a weaker correlation was observed on the ALEX for the correlations between the pollen-food pairs Bet v 1-Ara h 8 (ALEX: *r* = .28, MeDALL-chip: *r* = .68) and Cor a 1-Ara h 8 (ALEX: *r* = .37, MeDALL-chip: *r* = .80). Among nsLTP allergens (Ara h 9, Art v 3, Cor a 8, Pru p 3), weaker correlations also tended to be reported by ALEX (Figure 5C) than MeDALL-chip (Figure 5D). However, a strong correlation between Ara h 9-Pru p 3 was present on both platforms (ALEX: *r* = .83, MeDALL-

chip: r = .92), mirroring the high sequence similarity (Figure 5F).

4 DISCUSSION

This study outlines statistical models for interconversion between three multiplex sIgE tests: the ALEX, MeDALL-chip, and EUROLINE platforms. Using two regression methods, we demonstrated the ability to model allergen-specific relationships with acceptably high fit for peanut and tree nut sIgE testing at the extract and allergen level, including Ara h 1, Ara h 2, Ara h 6, Ana o 3, Cor a 9, Jug r 1, and Jug r 2. Our findings support the notion that quantitative conversion is reasonably possible between sIgE multiplex platforms for extracts and allergens.

For peanut allergens, the MARS regression models explained 63%-94% of the variability in the data from different platforms. Importantly, these models reported high coefficients of determination for Ara h 2 (r^2 = 84%-94%) and Ara h 6 (r^2 = 85%-88%), which are the most discriminative marker proteins for peanut allergy.[29] For tree nut allergens, our models explained 56%-92% of variability in the data of extracts and allergens from almond, walnut, hazelnut, and cashew. Conversion between SPT and sIgE performed poorly (r^2 = 24%-32%), consistent with previously reported lack of agreement between these tests.[30]

Previous studies comparing multiplex sIgE platforms have primarily reported only the level of semi-quantitative/quantitative agreement or correlation. Buzzulini et al[31] compared food allergens on the ALEX and ImmunoCAP and observed an overestimation of ALEX at lower sIgE levels and an underestimation at higher sIgE levels compared to ImmunoCAP. Our models reflected the tendency for the linear range of the ALEX to end at approximately 30 kUA/L in ImmunoCAP units. Although the linear ranges of the ImmunoCAP and MeDALL-chip exceed that of the ALEX, their ranges encompass the frequently used 95% cutoff of 15 kUA/L for peanut sIgE, which could allow for interconversion in the most important range for extrapolation of clinical relevance.[32] Correlations beyond 30 kUA/L between ALEX and ImmunoCAP require individual assessment of each allergen. For inhalant allergens, additional comparison studies have found significant correlations between ALEX and ISAC within three cohorts,[13, 33, 34] supporting the potential utility of these conversion methods for other allergens.

Cross-reactivity patterns on the multiplex test platforms were also compared. We observed that the MeDALL-chip tended to report higher intra-family correlations between PR-10 and nsLTP allergens, suggesting that cross-reactive antibodies may have a broader impact on test results in this context. Similarly, Heffler et al observed that PR-10 and nsLTP allergens were more frequently positive and had greater mean values on the ISAC chip compared to ALEX.[13] Discrepancies may result from different concentrations of allergen spotted on the respective platforms. Differences in natural and recombinant allergen production may also contribute to variation, as seen for Ara h 1 and Jug r 1 in the comparison of ALEX vs MeDALL-chip (Table S2). The CCD blocking protocols also differed between platforms. The use of a

CCD-inhibitor in the ALEX but not the EUROLINE and MeDALL-chip may account for the lower number of positive sensitizations identified, in particular for glycosylated allergens.

Strengths of this study include the large cohort of individuals with food allergen sensitizations, allowing for the generation of models for several major food allergens. Our analysis utilized two independent modeling methods consistently applied to each comparison, but which were capable of capturing trends specific to different allergens and platforms. Moreover, two independent cohorts and two sites (Toronto and Vienna) were included. Although model cross-validation was performed, limitations of this study include the lack of an independent validation in a third cohort large enough to assess the generalizability of these proposed models. With additional cohorts using these different test systems, further validation of these models is possible. Lastly, all measurements were performed using research chips in a research laboratory and without provocation tests; therefore, conclusions for clinical decision-making are limited. Applications of this methodology are targeted toward addressing the challenges of performing global collaborations, such as the pooling of data and harmonization of phenotypic definitions between studies that are required for genetic research on food allergy.[32] This methodology could also be useful in combination with alternative IgE quantification strategies to expand allergy research in countries where established test platforms are cost-prohibitive.[35, 36]

In summary, this study illustrates the ability to integrate sIgE results from different test systems using statistical modeling. Further validation of these conversion models for peanut and tree nut allergens could establish a method for the harmonization of sIgE data produced by different test systems.

CONFLICTS OF INTEREST

Dr Lupinek reports personal fees from Thermo Fisher, outside the submitted work. Dr Valenta has received research grants from Viravaxx, Vienna, Austria and serves as a consultant for this company, and received grants from HVD Life-Sciences, Vienna, Austria, outside the submitted work. Dr Upton reports personal fees from Kaleo, personal fees from ALK, personal fees from Bausch Health, is a member of the advisory board of Emerade, and is a sub-investigator on clinical trials of DBV Therapeutics, Aimmune, Regeneron, and CIHR, outside the submitted work; and is Section Chair of Food Allergy and Anaphylaxis, Canadian Society of Allergy and Clinical Immunology and is a member of the Healthcare Advisory Board, Food Allergy Canada. Dr Eiwegger is a site PI of a DBV sponsored global study, reports grants from Innovation Fund Denmark, CIHR, is a site CO-I of a Regeneron sponsored study, outside the submitted work. He is the Co-I or scientific lead in three investigator-initiated oral immunotherapy trials supported by the Allergy and Anaphylaxis Program at SickKids, outside of the submitted work. He reports personal fees from ALK and is on a local and international advisory board of ALK. Outside of this project, Dr Eiwegger collaborates with MADX in a government-funded project. Dr Eiwegger serves as associate editor for Allergy and is in the editorial board of the IAA and the review board of JACI. The

other authors have nothing to disclose.

AUTHOR CONTRIBUTIONS

JAH performed sample measurements, contributed to data analysis, and wrote the manuscript. AC performed the statistical modeling and wrote the manuscript. CL contributed to sample measurement. RV critically reviewed the manuscript. LD, RD, MGB, AD, CL, SW, MAF, AM, and KS collected data. PS, JEMU, ZS, and TE designed the studies. AR contributed to statistical analysis. TE designed the study, contributed to generation of the manuscript, and supervised the project. All authors discussed the results and commented on the manuscript.

Supporting Information

Filename	Description
all14529-sup-0001-AppendixS1.docx Word document, 37.7 KB	Appendix S1
all14529-sup-0002-AppendixS2.pdf PDF document, 13.2 MB	Appendix S2
all14529-sup-0003-FigS1-S7.pdf PDF document, 613.1 KB	Fig S1-S7

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Supplementary Information: Modelling the conversion between specific IgE test platforms for nut allergens in children and adolescents

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Supplementary Methods

EUROLINE Measurement

The two EUROLINE R&D test panels used were DPA-Dx Pediatrics 2 and Food 4. DPA-Dx Pediatrics 2 measured the following molecular allergens: rAra h 1 rAra h 2, rAra h 3, rAra h 5, rAra h 6, rAra h 7, rAra h 9, rBet v 1, nBos d 4, nBos d 5, nBos d 6, nBos d 8, nBos d lactoferrin, nGal d 1, nGal d 2, nGal d 3, nGal d 4, and CCD marker. Food 4 measured the following allergen extracts: egg white, cow's milk, sesame, soy bean, brazil nut, almond, pistachio, walnut, macadamia nut, peanut, cashew, birch, and CCD marker. The EUROLINE testing protocol was performed with 175 µl of patient plasma diluted in 250 µl of universal buffer for 2 hours at room temperature.

Sample Measurement

Plasma samples from the MONAS Vienna cohort were pre-diluted 1:2 in phosphate-buffered saline. To account for this dilution, all software quantified sIgE values from each platform were subsequently multiplied by a factor of two for these samples.

There were no missing sIgE values from samples that were measured. Subjects without measurement for a platform due to insufficient sample were excluded from regression analysis related to that platform only.

Determination of Dynamic Range

For the ALEX, the dynamic range of the test was defined to be between 0.3-40 kUA/L based on the manufacturer's protocol and further manual inspection of scatterplots. The manufacturer's stated measurement range was 0.3-50 kUA/L, however upon further manual inspection of scatterplots, we observed that observations rarely exceeded 40 kUA/L and plateaued prior to this value. Therefore, we set the dynamic range to be within 0.3-40 kUA/L.

For the MeDALL-chip, the dynamic range of 0.3-100 ISU was defined using previously published observations[1].

For the EUROLINE, the dynamic range of the test was defined as the concentrations of 0.35-100 kUA/L as stated by the manufacturer's protocol, and in accordance with our manual inspection of scatterplots.

Software and Computational Environment

ALEX measurements were quantified with Raptor version 1.1.3.2 (Macro Array Diagnostics). EUROLINE measurements were quantified with EuroLineScan software version 3.4.14 (EUROIMMUN).

Plotting was done using ggplot2 version 3.11[2] and corrplot version 0.84[3]. Protein sequence similarities were generated with protr package version 1.6-2[4] using UniProt IDs in Table S6.

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Table S1: All allergens considered for comparison between platforms

ALEX-1 and MeDALL-chip		ALEX-1 and EUROLINE		MeDALL-chip and EUROLINE
Molecular Allergens		Extracts	Molecular Allergens	Molecular Allergens
Act d 1	Der f 2	Ana o	**Ara h 1**	**Ara h 1**
Act d 2	Der p 1	**Ara h**	**Ara h 2**	**Ara h 2**
Act d 5	Der p 2	Ber e	Ara h 3	Ara h 3
Aln g 1	Der p 5	Bet v	**Ara h 6**	**Ara h 6**
Alt a 1	Der p 7	Bos d	Ara h 9	Ara h 9
Amb a 1	Der p 10	Gal d	Bos d 4	Bos d 4
Amb a 4	Der p 11	Gly m	Bos d 5	Bos d 5
Ana o 3	Der p 23	**Jug r**	Bos d 6	Bos d 6
Ani s 1	Equ c 1	Mac inte	Bos d 8	Bos d 8
Ani s 3	Fag e 2	Pis v	Gal d 1	Bos d LF
Api m 1	Fel d 1	**Pru du**	Gal d 2	Gal d 1
Api g 1	Fel d 2	Ses i	Gal d 3	Gal d 2
Ara h 1	Fel d 4		Gal d 4	Gal d 3
Ara h 2	Gal d 1			
Ara h 3	Gal d 2			
Ara h 6	Gal d 3			
Ara h 8	Gal d 5			
Ara h 9	Gly m 4			
Art v 1	Gly m 5			
Art v 3	Gly m 6			
Asp f 6	Hev b 1			
Ber e 1	Hev b 3			
Bet v 1	Hev b 5			
Bet v 2	**Jug r 1**			
Bla g 1	**Jug r 2**			
Bla g 2	Mal d 1			
Bla g 5	Mus m 1			
Bos d 4	Ole e 1			
Bos d 5	Par j 2			
Bos d 6	Pen m 1			
Bos d 8	Phl p 1			
Can f 1	Phl p 2			
Can f 2	Phl p 5.0101			
Can f 3	Phl p 6			
Che a 1	Phl p 7			
Cla h 8	Phl p 12			
Cor a 9	Pla l 1			
Cor a 1.0401	Pla a 1			
Cor a 8	Pol d 5			
Cor a 14	Pru p 3			
Cup a 1	Ses i 1			
Der f 1	Ves v 5			

* Bolded allergens were included in modelling analysis

Table S2: List of allergen comparisons meeting the criteria for modelling on each platform

	Allergen Test System				
Allergen	**SPT**	**ImmunoCAP**	**ALEX-1**	**MeDALL-chip**	**EUROLINE**
Extract					
Ara h	x	x	x		x
Cor a		x	x		
Jug r		x	x		x
Pru du		x	x		x
Molecular Allergens*					
Ana o 3			rAna o 3	rAna o 3	
Ara h 1			nAra h 1	rAra h 1	rAra h 1
Ara h 2			rAra h 2	rAra h 2	rAra h 2
Ara h 6			nAra h 6	nAra h 6	rAra h 6
Cor a 9			nCor a 9	nCor a 9	
Jug r 1			nJug r 1	rJug r 1	
Jug r 2			nJug r 2	nJug r 2	

*n: natural allergen, r: recombinant allergen.

Table S3: Demographics and Patient Sample Characteristics

	All Subjects (n = 166)		MONAS (n = 124)		Wheezy ER Study (n = 42)	
	Summary	**n/N**	**Summary**	**n/N**	**Summary**	**n/N**
Age (Median [IQR])	6.5 [4.6-12.1]	163	10.0 [5.5-13.5]	122	4.7 [3.9-5.4]	41
Sex (Male %)	62%	103/165	63%	75/119	68%	28/41
Atopic Dermatitis (%)	66%	108/163	60%	74/123	85%	34/40
Food Allergies (%)	76%	125/165	90%	112/124	32%	13/41
Asthma (%)	67%	111/165	56%	70/124	100%	41/41
Allergic Rhinitis (%)	47%	57/122	47%	57/122	N/A	N/A

Table S4: CCD Marker by Allergen Platform

CCD Marker	**n/N (%)**
ALEX	
CCD Marker (Hom s Lactoferrin)	23/166 (14)
MeDALL-Chip	
CCD Marker	30/166 (18)
EUROLINE	
CCD Marker	24/121 (20)

Table S5: MARS and Loess Model Fit Statistics

Allergen	Comparison	MARS R^2	Loess Residual Standard Error (RSE)
Ara h	ALEX vs. ImmunoCAP	0.89	5.24
Ara h	EUROLINE vs. ImmunoCAP	0.71	18.59
Ara h	ALEX vs. SPT	0.24	13.89
Ara h	ImmunoCAP vs. SPT	0.33	4.76
Ara h	ALEX vs. EUROLINE	0.84	6.43
Ara h 1	ALEX vs. MeDALL-chip	0.72	6.67
Ara h 1	EUROLINE vs. MeDALL-chip	0.63	13.15
Ara h 1	ALEX vs. EUROLINE	0.65	5.93
Ara h 2	ALEX vs. MeDALL-chip	0.94	4.06
Ara h 2	EUROLINE vs. MeDALL-chip	0.86	15.53
Ara h 2	ALEX vs. EUROLINE	0.84	6.54
Ara h 6	ALEX vs. MeDALL-chip	0.86	4.90
Ara h 6	EUROLINE vs. MeDALL-chip	0.85	15.72
Ara h 6	ALEX vs. EUROLINE	0.88	4.75
Pru du	ALEX vs. ImmunoCAP	0.70	2.48
Pru du	EUROLINE vs. ImmunoCAP	0.69	11.65
Pru du	ALEX vs. EUROLINE	0.57	3.16
Jug r	ALEX vs. ImmunoCAP	0.92	3.56
Jug r	EUROLINE vs. ImmunoCAP	0.82	14.79
Jug r	ALEX vs. EUROLINE	0.71	6.19
Cor a	ALEX vs. ImmunoCAP	0.66	7.49
Ana o 3	ALEX vs. MeDALL-chip	0.76	5.80
Cor a 9	ALEX vs. MeDALL-chip	0.56	4.31
Jug r 1	ALEX vs. MeDALL-chip	0.78	4.80
Jug r 2	ALEX vs. MeDALL-chip	0.62	5.53

Table S6: Allergen UniProt IDs for Determination of Sequence Similarities

Allergen	**UniPROT ID**
PR-10	
Aln g 1	P38948
Ara h 8	Q6VT83
Bet v 1	P15494
Cor a 1.0401	Q9SWR4
Gly m 4	P26987
Mal d 1	P43211
nsLTP	
Ara h 9	B6CEX8
Art v 3	P0C088
Cor a 8	Q9ATH2
Pru p 3	P81402

Figure Legends

Figure S1: Schematic of IgE measurement and modelling method between ALEX, EUROLINE, and MeDALL-chip.

Figure S2: Total number of positive sensitizations reported by ALEX or EUROLINE (n = 121) for a) common allergen extracts and b) common molecular allergens.

Figure S3: Total number of positive sensitizations reported by EUROLINE or MeDALL-chip (n = 121) for common molecular allergens.

Figure S4: Total number of positive sensitizations reported by ALEX or MeDALL-chip (n = 166) for common molecular allergens.

Figure S5: Pearson correlation matrix of molecular allergens common to ALEX and MeDALL-chip (n = 166).

Figure S6: Modelling of almond, walnut, and hazelnut extract sIgE values demonstrates convertibility between pairwise comparisons of ALEX, MeDALL-chip, and EUROLINE sIgE test platforms. Blue = loess modelling, red = MARS modelling, ribbon = 95% confidence interval.

Figure S7: Positive co-sensitizations between PR-10 family and nsLTP family allergens reported by ALEX and MeDALL-chip platforms highlights the sensitivity of MeDALL-chip for detection of cross-reactivity. Sensitizations were dichotomized at the respective test cut-offs for ALEX (0.3 kUA/L) and MeDALL-chip (0.3 ISU) and the Jaccard similarity coefficient was reported for A) PR-10 allergens on ALEX (B) PR-10 allergens on MeDALL-chip, C) nsLTP allergens on ALEX, D) nsLTP allergens on MeDALL-chip. The Jaccard similarity coefficient for each pair of allergens was calculated as the proportion of individuals sensitized to both allergens out of the total number of individuals sensitized to either allergen.

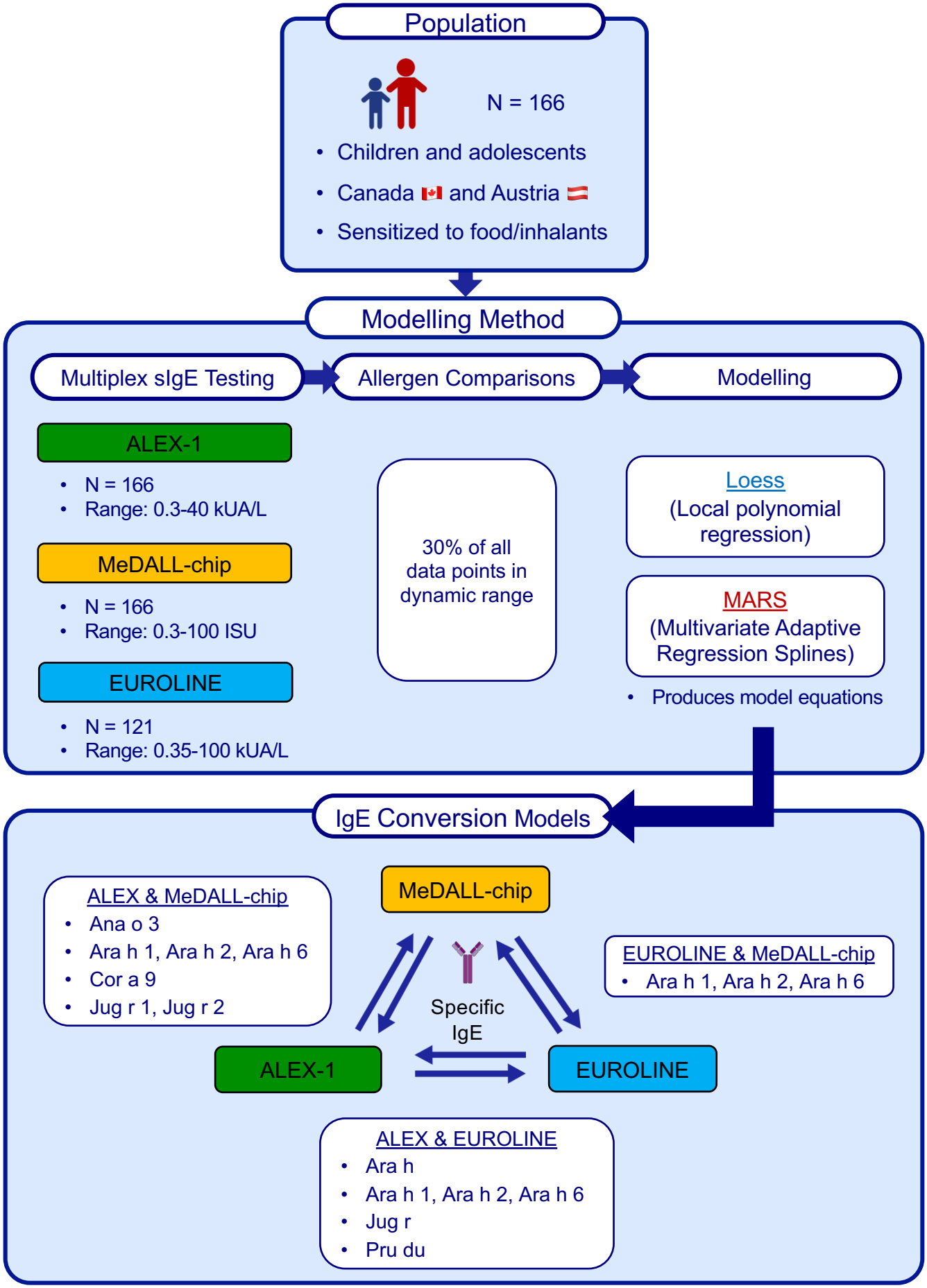
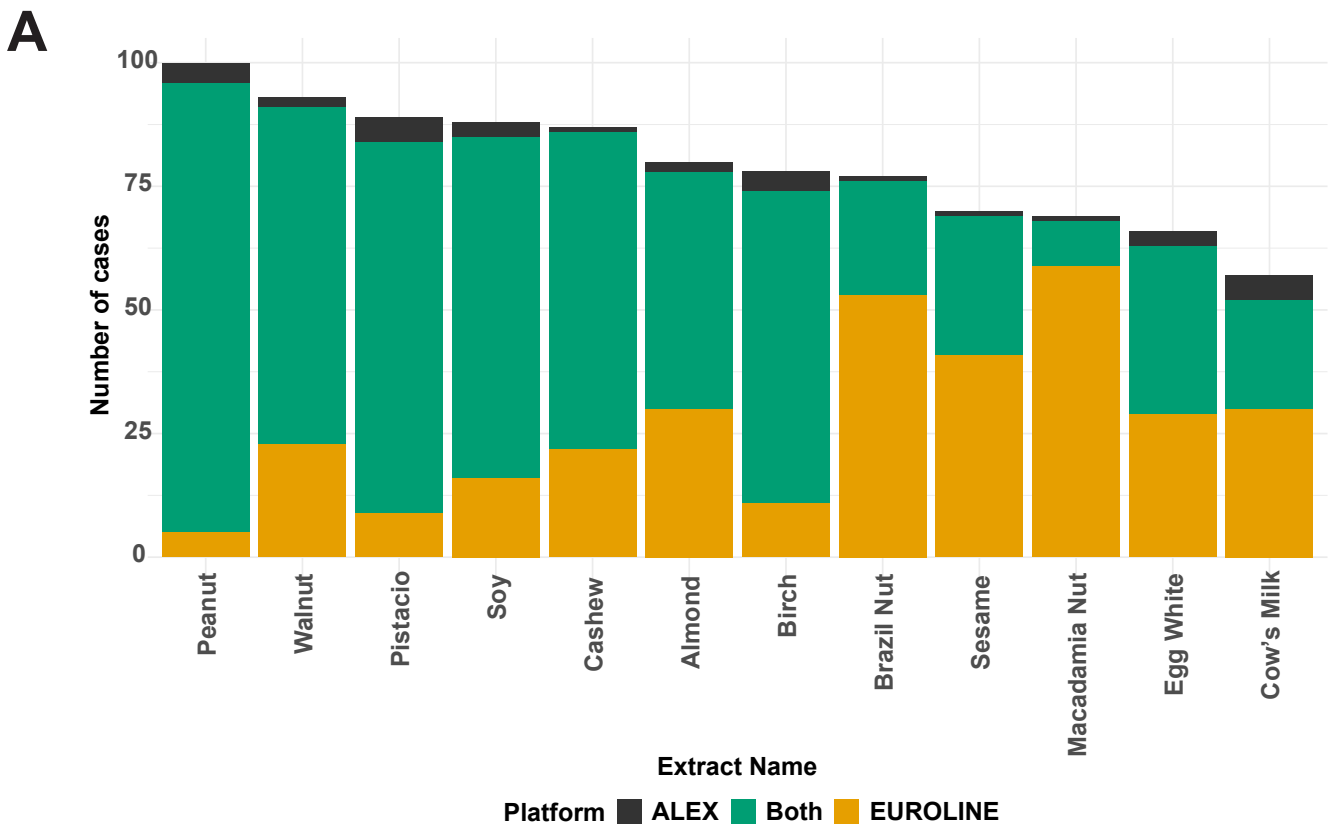

Population
N = 166
Children and adolescents
Canada and Austria
Sensitized to food/inhalants
Modelling Method
Multiplex sIgE Testing
Allergen Comparisons
Modelling
ALEX-1
N = 166
Range: 0.3-40 kUA/L
MeDALL-chip
N = 166
Range: 0.3-100 ISU
EUROLINE
N = 121
Range: 0.35-100 kUA/L
30% of all data points in dynamic range
Loess
(Local polynomial regression)
MARS
(Multivariate Adaptive Regression Splines)
Produces model equations
IgE Conversion Models
ALEX & MeDALL-chip
Ana o 3
Ara h 1, Ara h 2, Ara h 6
Cor a 9
Jug r 1, Jug r 2
MeDALL-chip
Specific IgE
EUROLINE & MeDALL-chip
Ara h 1, Ara h 2, Ara h 6
ALEX-1
EUROLINE
ALEX & EUROLINE
Ara h
Ara h 1, Ara h 2, Ara h 6
Jug r
Pru du

Figure S1


A
100
75
50
25
0
Number of cases
Peanut
Walnut
Pistacio
Soy
Cashew
Almond
Birch
Brazil Nut
Sesame
Macadamia Nut
Egg White
Cow's Milk
Extract Name
Platform ALEX Both EUROLINE

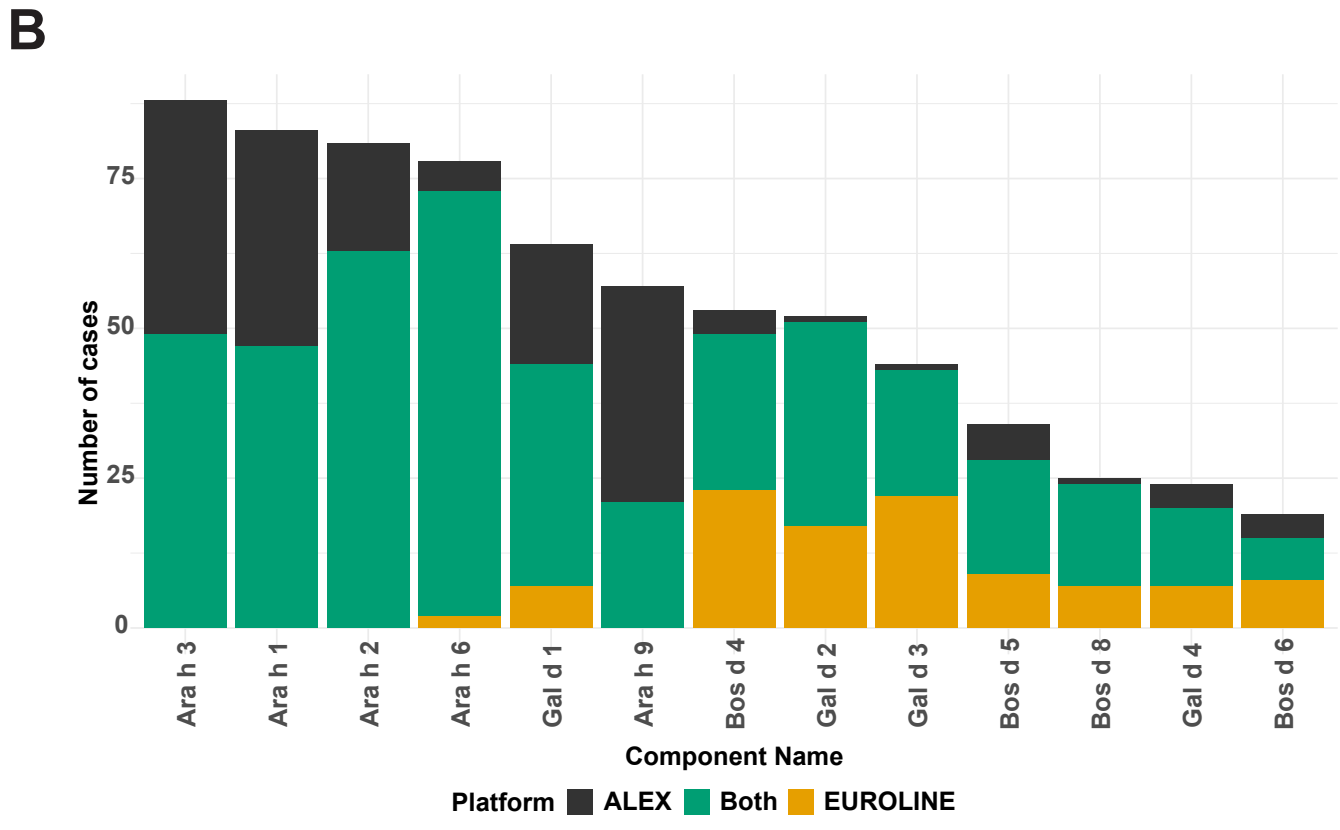

B
75
50
25
0
Number of cases
Ara h 3
Ara h 1
Ara h 2
Ara h 6
Gal d 1
Ara h 9
Bos d 4
Gal d 2
Gal d 3
Bos d 5
Bos d 8
Gal d 4
Bos d 6
Component Name
Platform ALEX Both EUROLINE

Figure S2

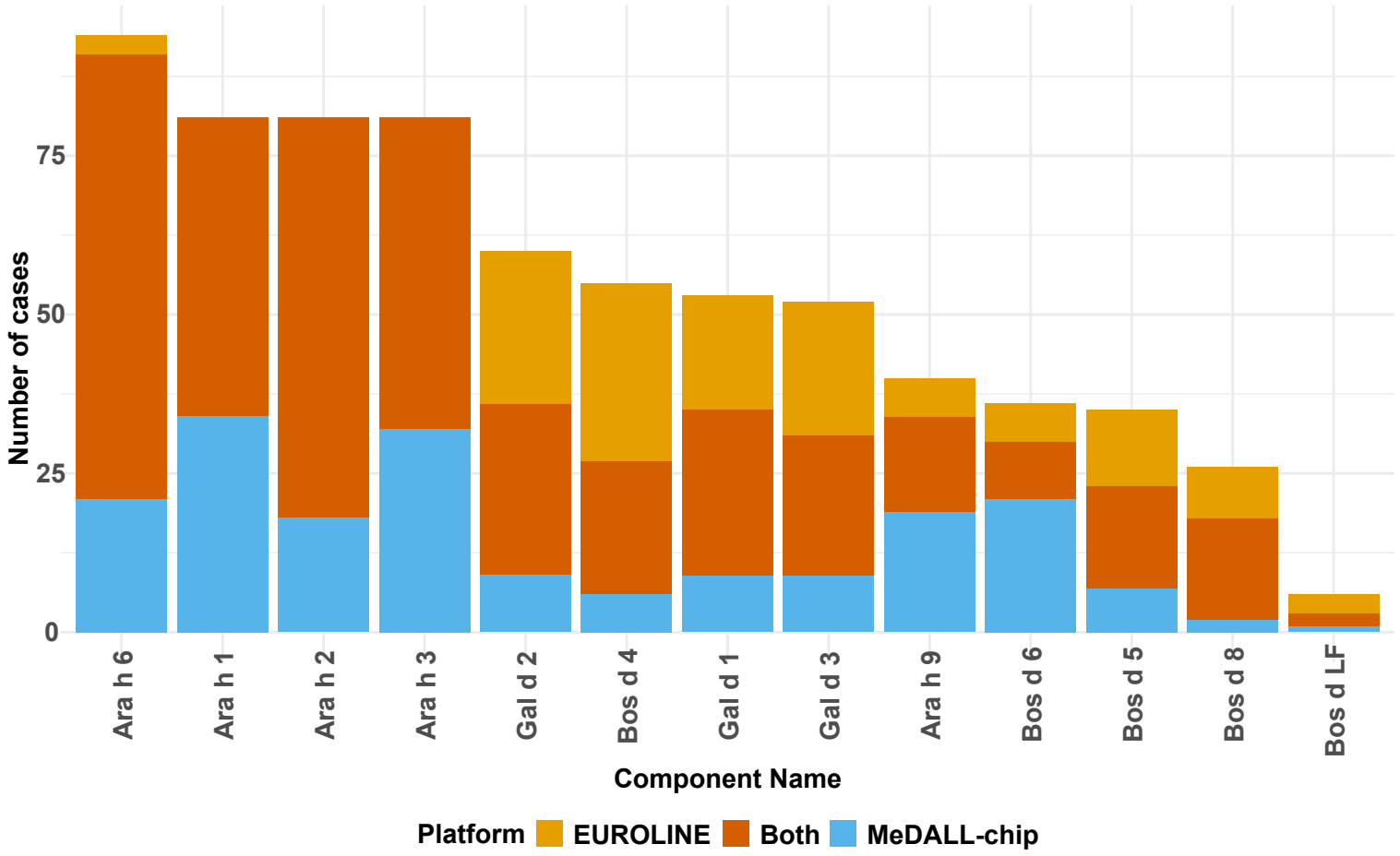

Number of cases
75
50
25
0
Ara h 6
Ara h 1
Ara h 2
Ara h 3
Gal d 2
Bos d 4
Gal d 1
Gal d 3
Ara h 9
Bos d 6
Bos d 5
Bos d 8
Bos d LF
Component Name
Platform
EUROLINE
Both
MeDALL-chip

Figure S3

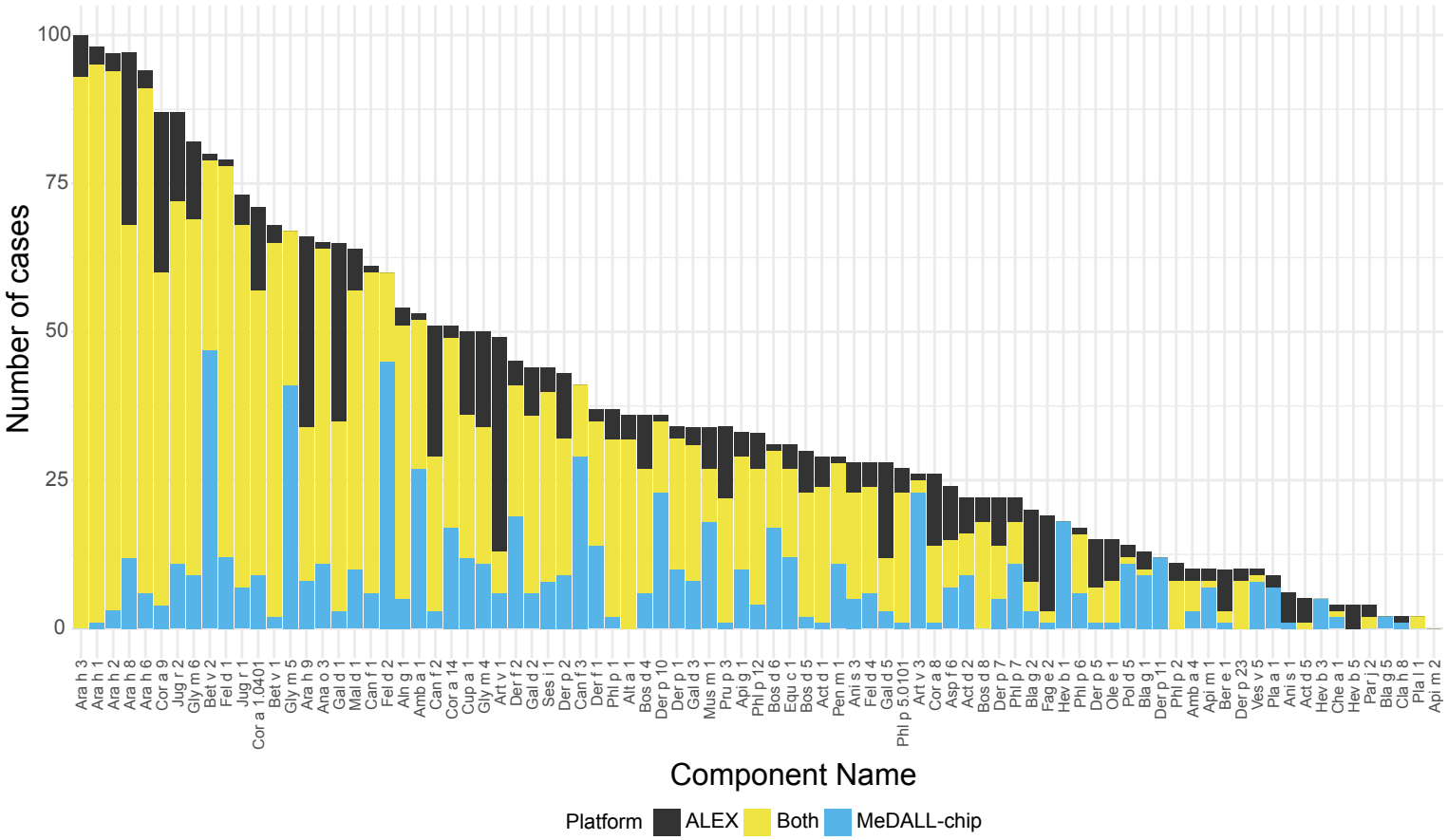

Number of cases
100
75
50
25
0
Component Name
Platform
ALEX
Both
MeDALL-chip

Figure S4

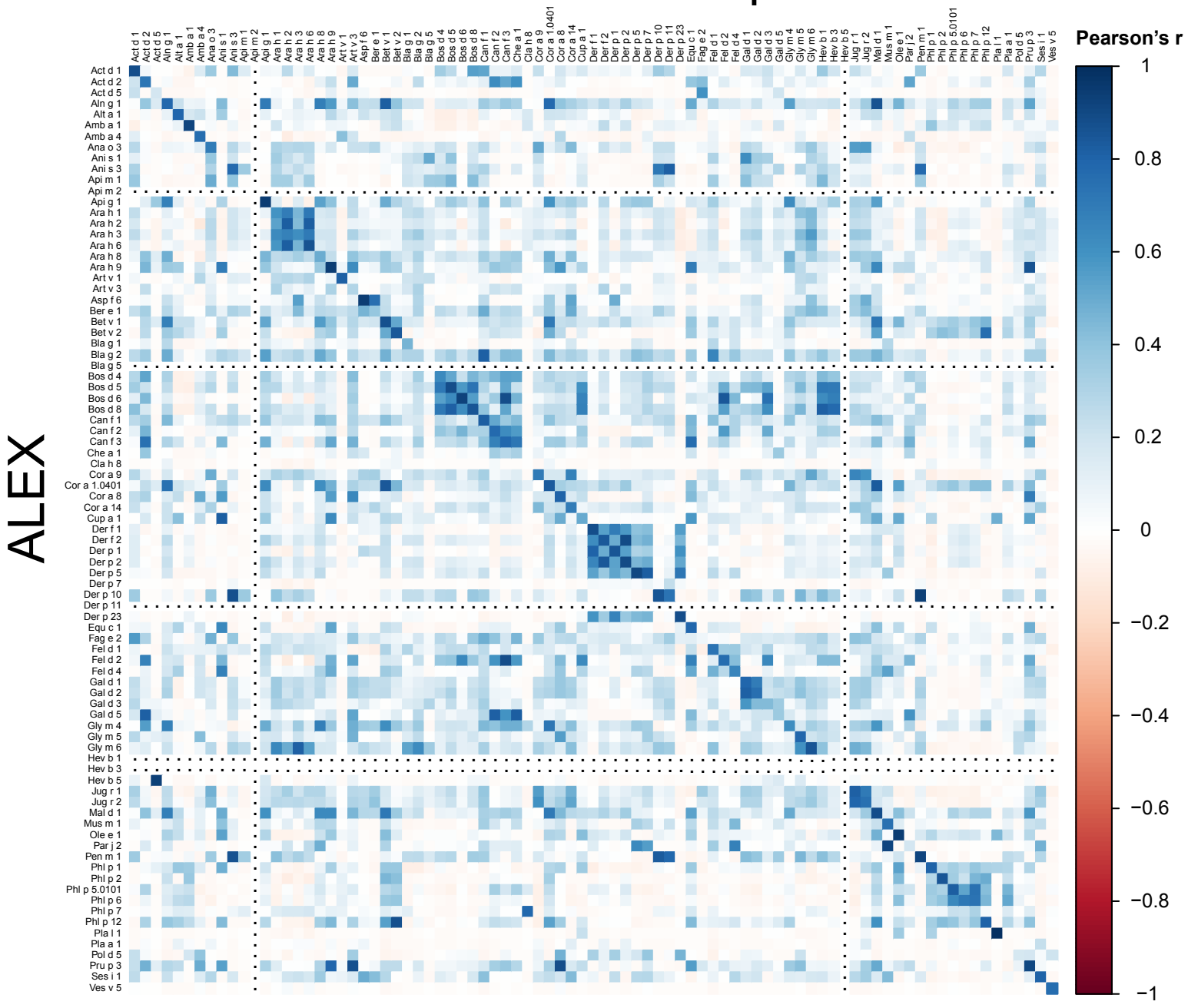


Figure S5

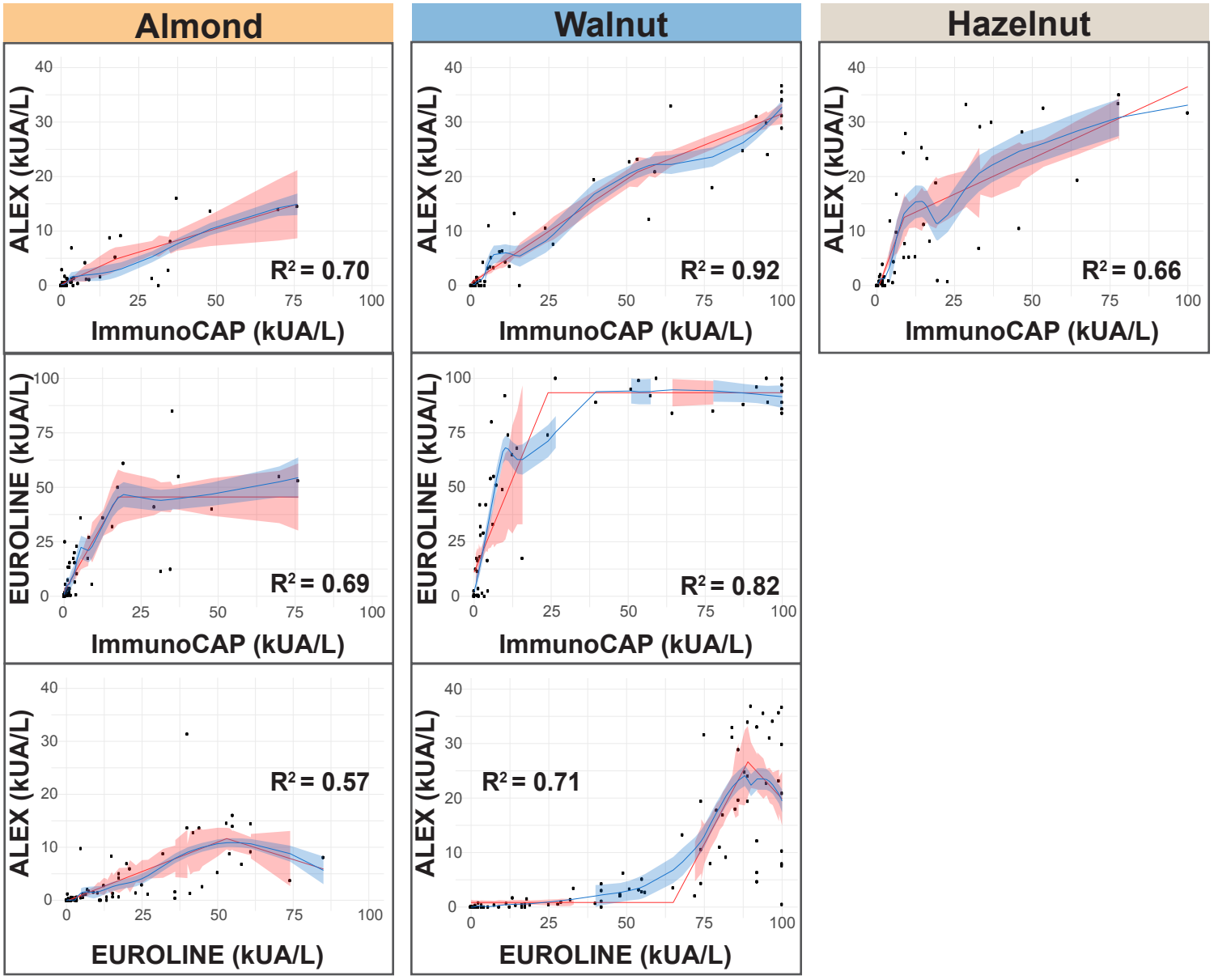

Almond
Walnut
Hazelnut
ALEX (kUA/L)
ImmunoCAP (kUA/L)
R² = 0.70
R² = 0.92
R² = 0.66
EUROLINE (kUA/L)
ImmunoCAP (kUA/L)
R² = 0.69
R² = 0.82
ALEX (kUA/L)
EUROLINE (kUA/L)
R² = 0.57
R² = 0.71

Figure S6

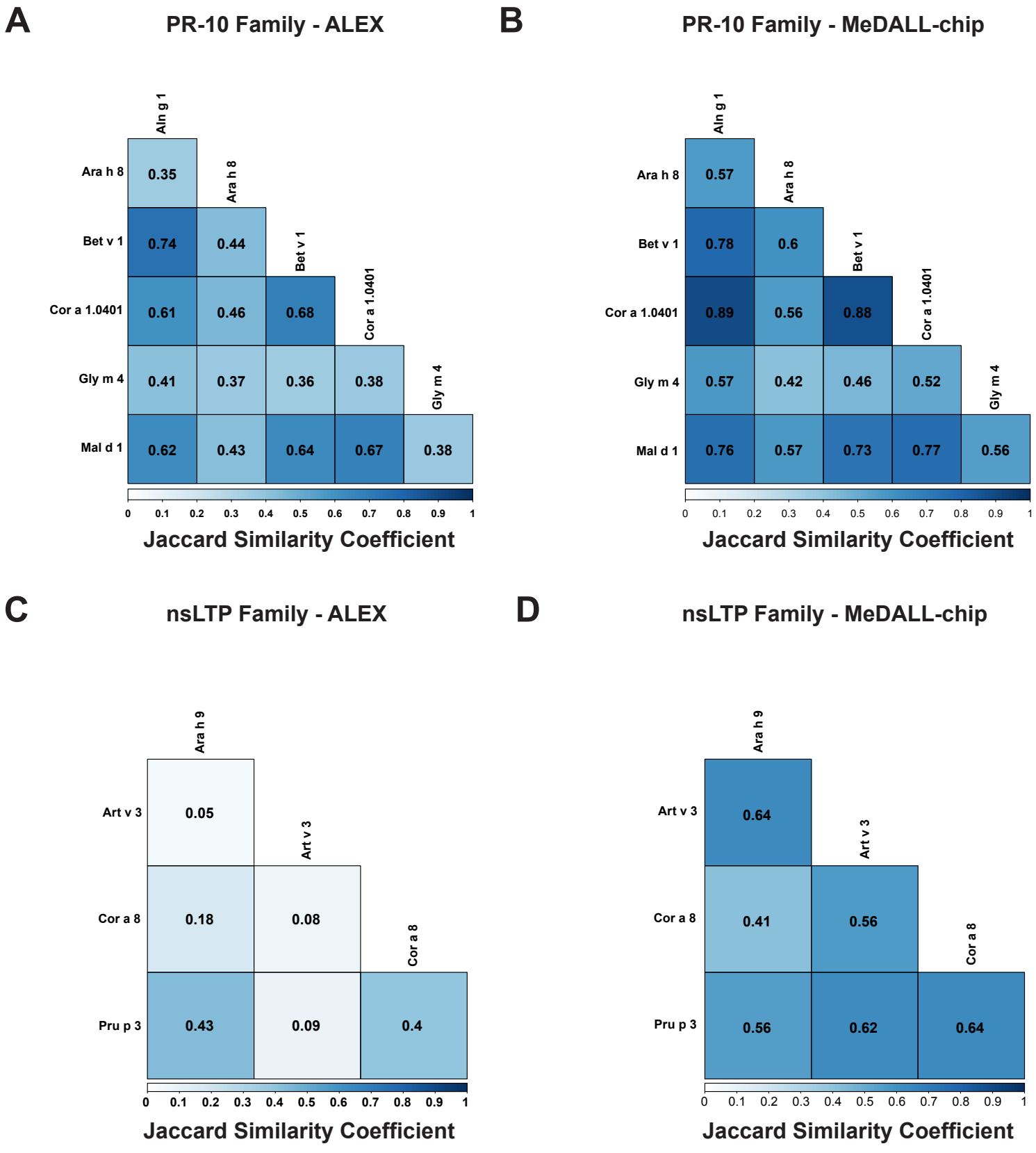

A
PR-10 Family - ALEX
Aln g 1
Ara h 8
Bet v 1
Cor a 1.0401
Gly m 4
Ara h 8 0.35
Bet v 1 0.74 0.44
Cor a 1.0401 0.61 0.46 0.68
Gly m 4 0.41 0.37 0.36 0.38
Mal d 1 0.62 0.43 0.64 0.67 0.38
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1
Jaccard Similarity Coefficient
B
PR-10 Family - MeDALL-chip
Aln g 1
Ara h 8
Bet v 1
Cor a 1.0401
Gly m 4
Ara h 8 0.57
Bet v 1 0.78 0.6
Cor a 1.0401 0.89 0.56 0.88
Gly m 4 0.57 0.42 0.46 0.52
Mal d 1 0.76 0.57 0.73 0.77 0.56
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1
Jaccard Similarity Coefficient
C
nsLTP Family - ALEX
Ara h 9
Art v 3
Cor a 8
Art v 3 0.05
Cor a 8 0.18 0.08
Pru p 3 0.43 0.09 0.4
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1
Jaccard Similarity Coefficient
D
nsLTP Family - MeDALL-chip
Ara h 9
Art v 3
Cor a 8
Art v 3 0.64
Cor a 8 0.41 0.56
Pru p 3 0.56 0.62 0.64
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1
Jaccard Similarity Coefficient

Figure S7

Supplementary Information: Modelling the conversion between specific IgE test platforms for nut allergens in children and adolescents

Model Summaries and Equations

ALEX vs. EUROLINE 3

Ara h 1 3
Ara h 2 6
Ara h 6 9
Ara h 12
Jug r 15
Pru du 18

ALEX vs. ImmunoCAP 21

Ara h 21
Cor a 24
Jug r 27
Pru du 30

ALEX vs. MeDALL-chip 33

Ana o 3 33
Ara h 1 36
Ara h 2 39
Ara h 6 42
Cor a 9 45
Jug r 1 48
Jug r 2 51

EUROLINE vs. ALEX 54

Ara h 1 54
Ara h 2 57
Ara h 6 60
Ara h 63
Jug r 66
Pru du 69

EUROLINE vs. ImmunoCAP 72

Ara h 72
Jug r 75
Pru du 78

EUROLINE vs. MeDALL-chip 81

Ara h 1 81
Ara h 2 84
Ara h 6 87

ImmunoCAP vs. ALEX *90*

Ara h **90**
Cor a **93**
Jug r **96**
Pru du **99**

ImmunoCAP vs. EUROLINE *102*

Ara h **102**
Jug r **105**
Pru du **108**

MeDALL-chip vs. ALEX *111*

Ana o 3 ..... **111**
Ara h 1 ..... **114**
Ara h 2 ..... **117**
Ara h 6 ..... **120**
Cor a 9 ..... **123**
Jug r 1 ..... **126**
Jug r 2 ..... **129**

MeDALL-chip vs. EUROLINE *132*

Ara h 1 ..... **132**
Ara h 2 ..... **135**
Ara h 6 ..... **138**

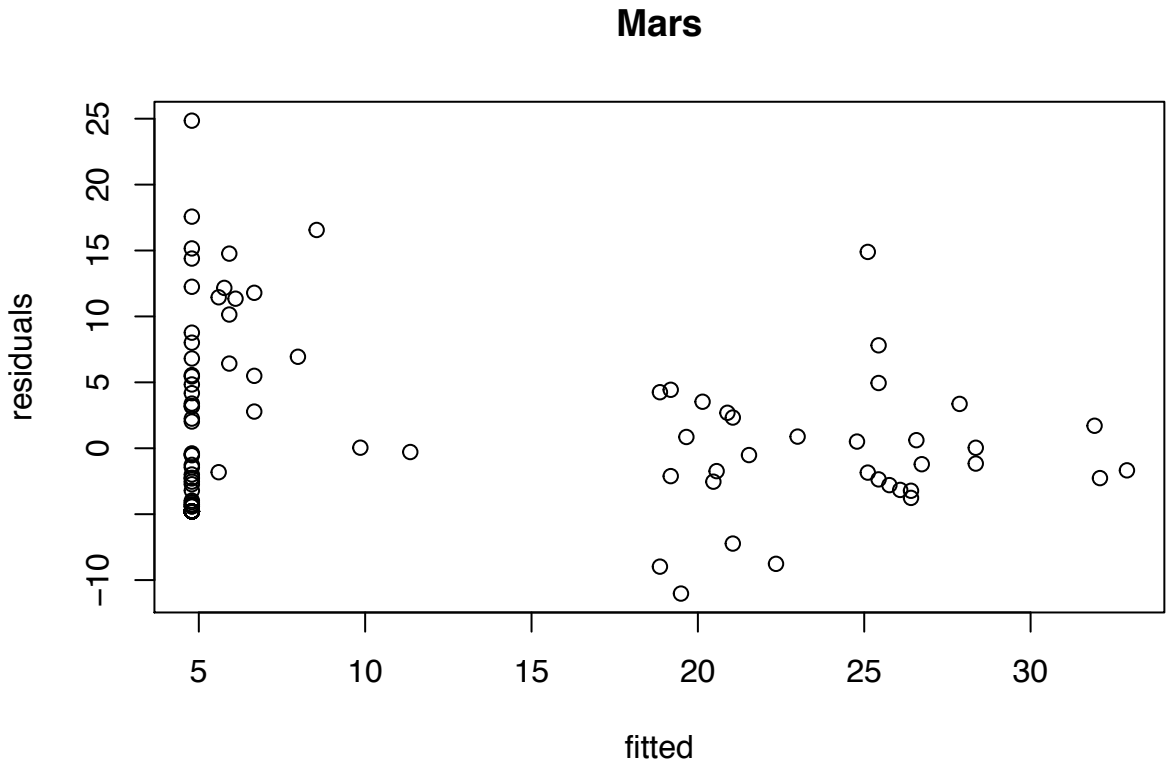
Predicting Ara h 1 in alex using data from euro

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##               coefficients
## (Intercept)     18.8591461
## h(7.5-df[,3])   -1.8758023
## h(df[,3]-7.5)    0.1622775
##
## Selected 3 of 3 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 3 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 44.76682  RSS 4978.366  GRSq 0.6264175  RSq 0.6509079  CVRSq 0.6099298
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.95 sd 0.21    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.661    iter.rsq 0.064
##
## stddev of predictions:
```

Residuals vs Fitted

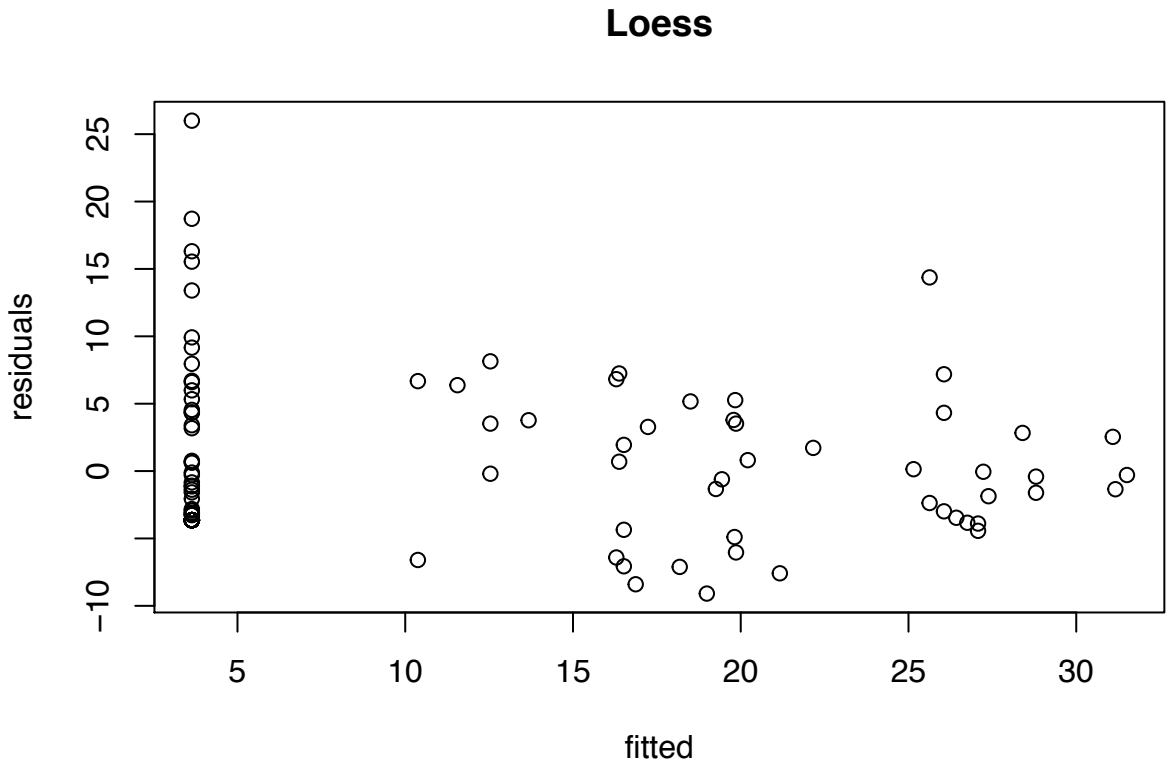


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 5.54
## Residual Standard Error: 5.93
## Trace of smoother matrix: 6.08  (exact)
##
## Control settings:
##   span     :  0.7375388
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



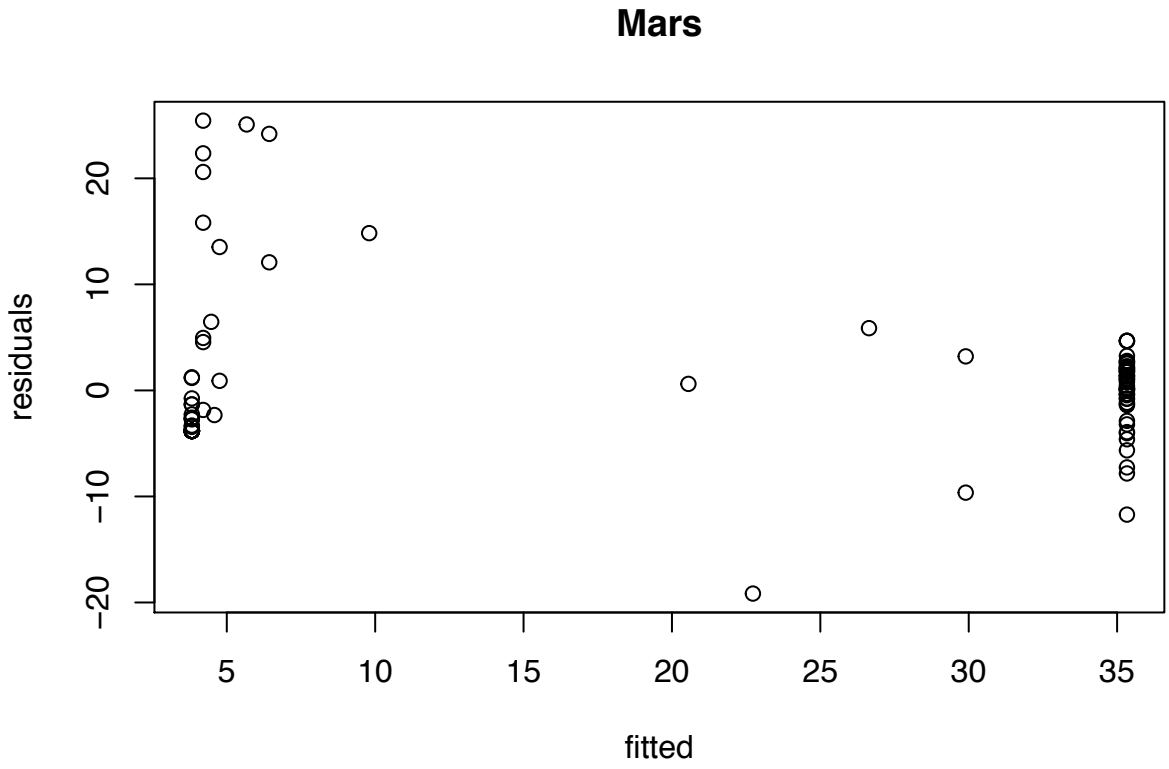
Predicting Ara h 2 in alex using data from euro

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##              coefficients
## (Intercept)     35.331842
## h(29-df[,3])    -1.086539
##
## Selected 2 of 4 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 4 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 1 (additive model)
## GCV 46.5906  RSS 5361.384  GRSq 0.8347427  RSq 0.8402054  CVRSq 0.8182102
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.19 sd 0.39    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.582    iter.rsq 0.103
##
## stddev of predictions:
```

Residuals vs Fitted

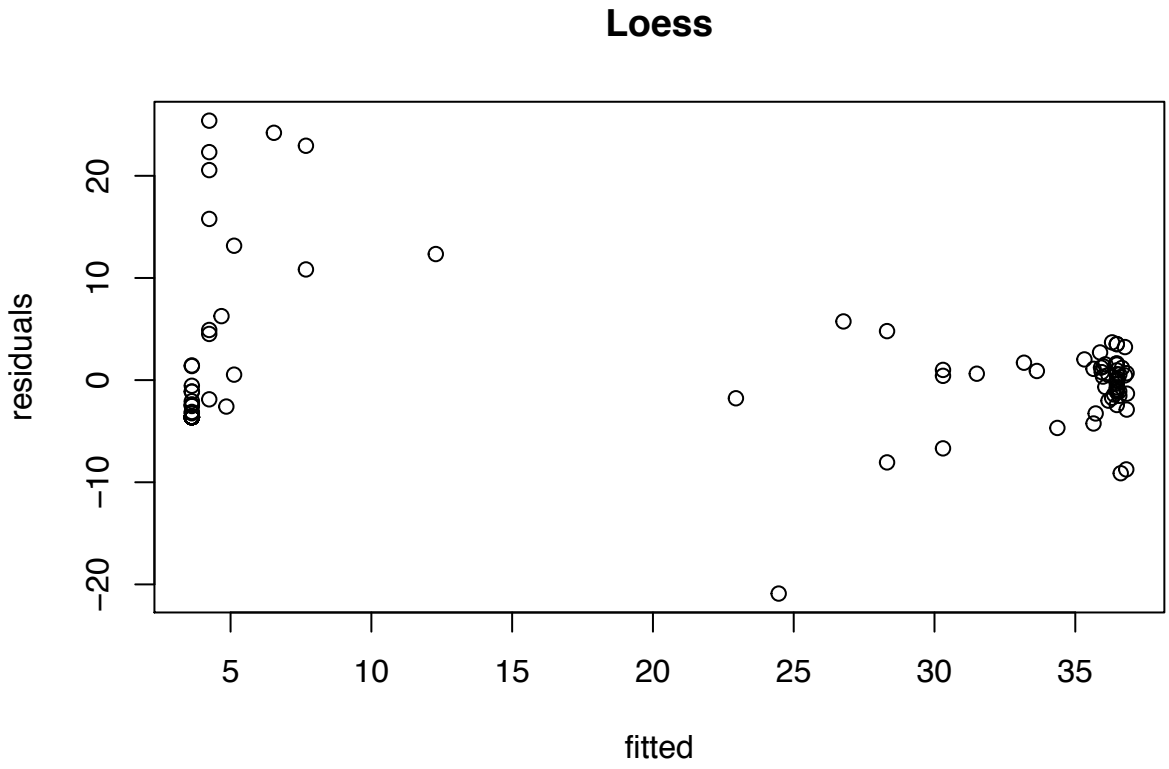


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 4.05
## Residual Standard Error: 6.54
## Trace of smoother matrix: 4.4  (exact)
##
## Control settings:
##   span     :  0.6718861
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



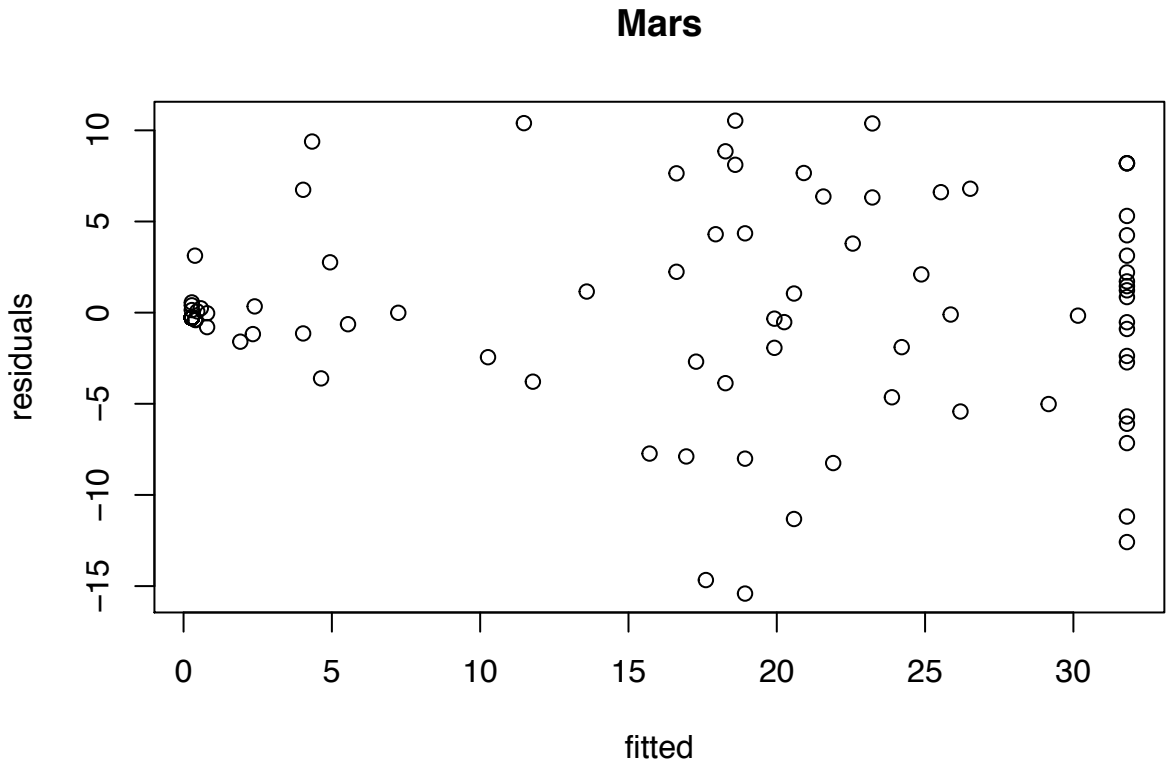
Predicting Ara h 6 in alex using data from euro

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##              coefficients
## (Intercept)    16.6185946
## h(54-df[,3])   -0.3025820
## h(df[,3]-54)    0.3301527
##
## Selected 3 of 4 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 4 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 23.79046  RSS 2645.657  GRSq 0.8695405  RSq 0.8780928  CVRSq 0.8581803
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.01 sd 0.12    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.456    iter.rsq 0.315
##
## stddev of predictions:
```

Residuals vs Fitted

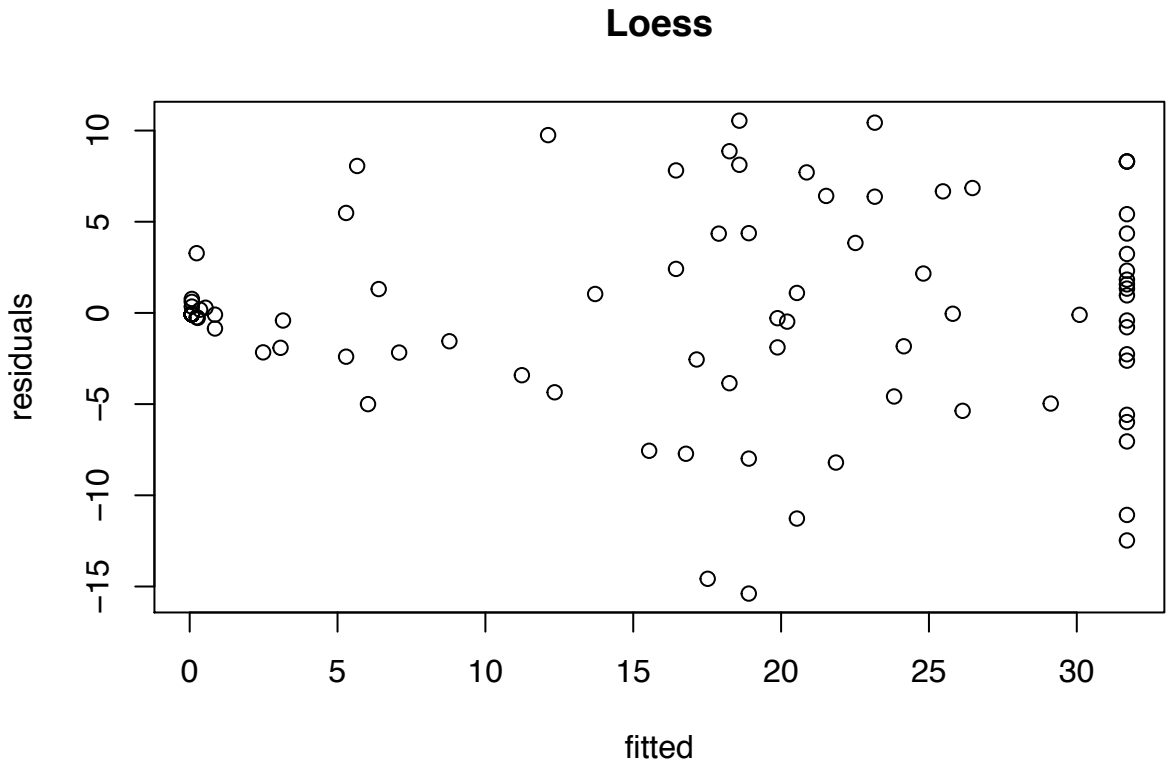


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 3.97
## Residual Standard Error: 4.745
## Trace of smoother matrix: 4.31  (exact)
##
## Control settings:
##   span     :  0.6091542
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



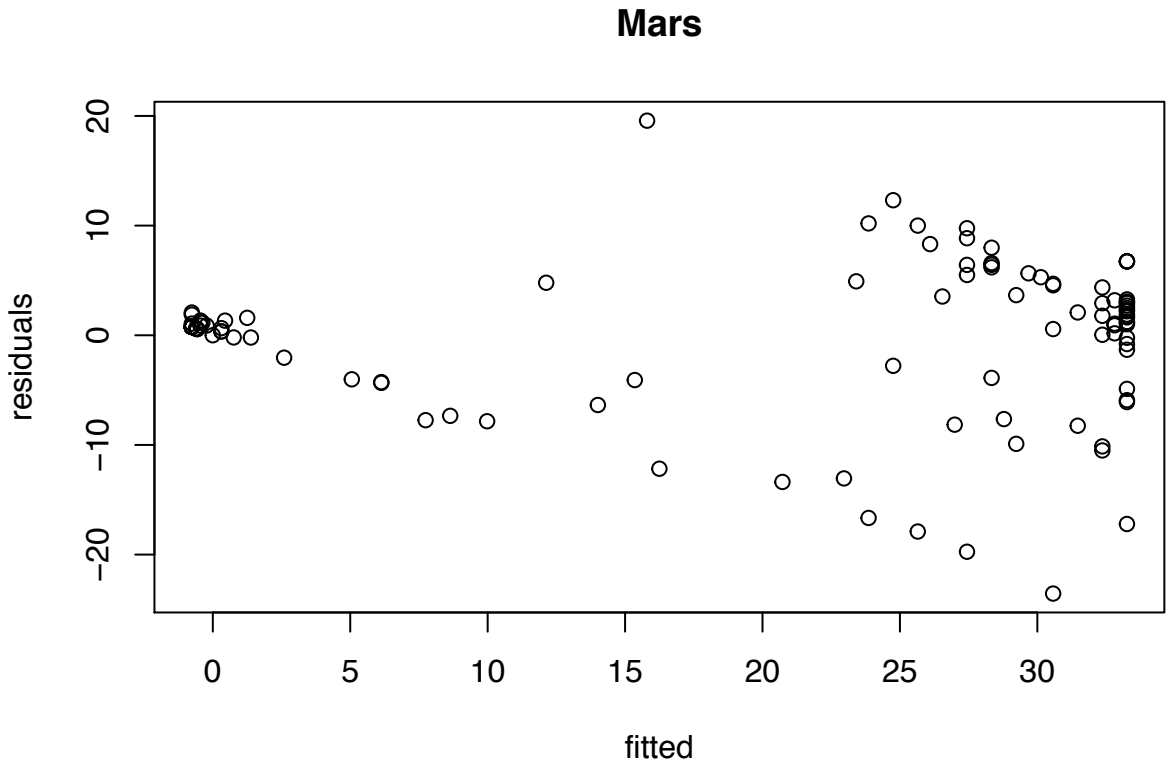
Predicting Ara h in alex using data from euro

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##              coefficients
## (Intercept)    33.2604577
## h(76-df[,3])   -0.4476784
##
## Selected 2 of 5 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 5 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 1 (additive model)
## GCV 43.4813  RSS 5003.584  GRSq 0.8334435  RSq 0.8389491  CVRSq 0.8084319
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.75 sd 0.60    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.63    iter.rsq 0.426
##
## stddev of predictions:
```

Residuals vs Fitted

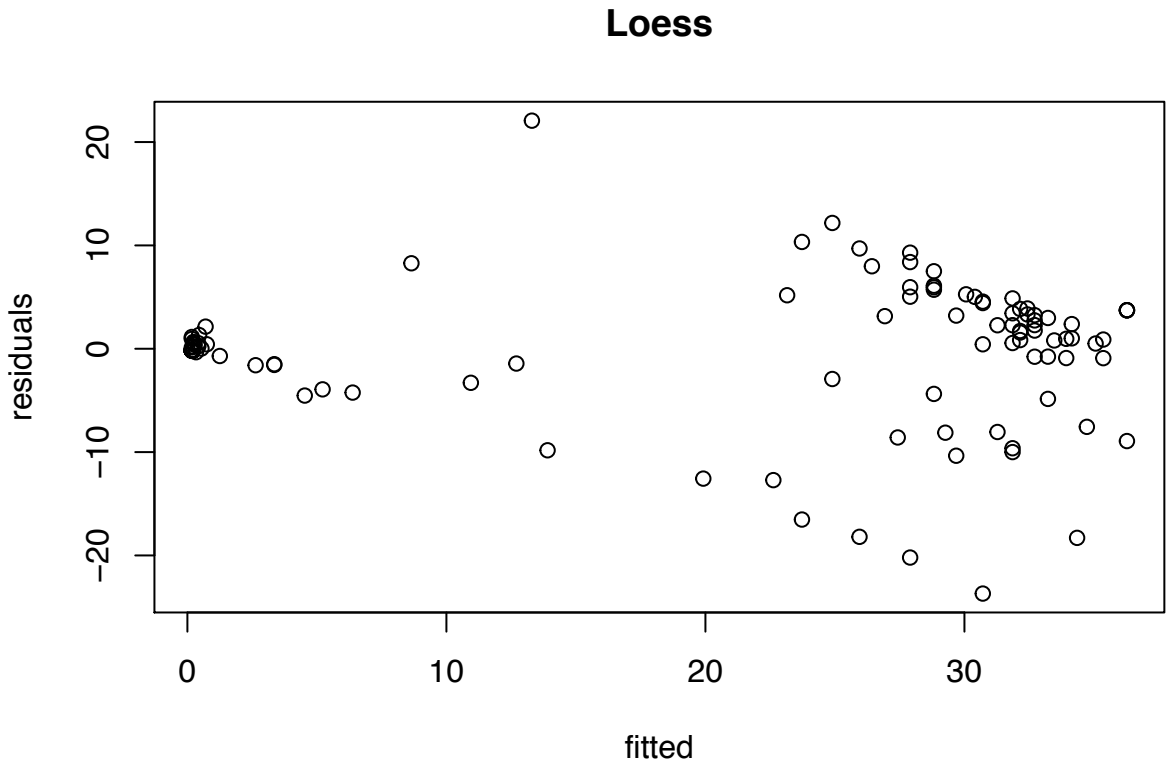


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 4.48
## Residual Standard Error: 6.432
## Trace of smoother matrix: 4.88  (exact)
##
## Control settings:
##   span     :  0.6063523
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



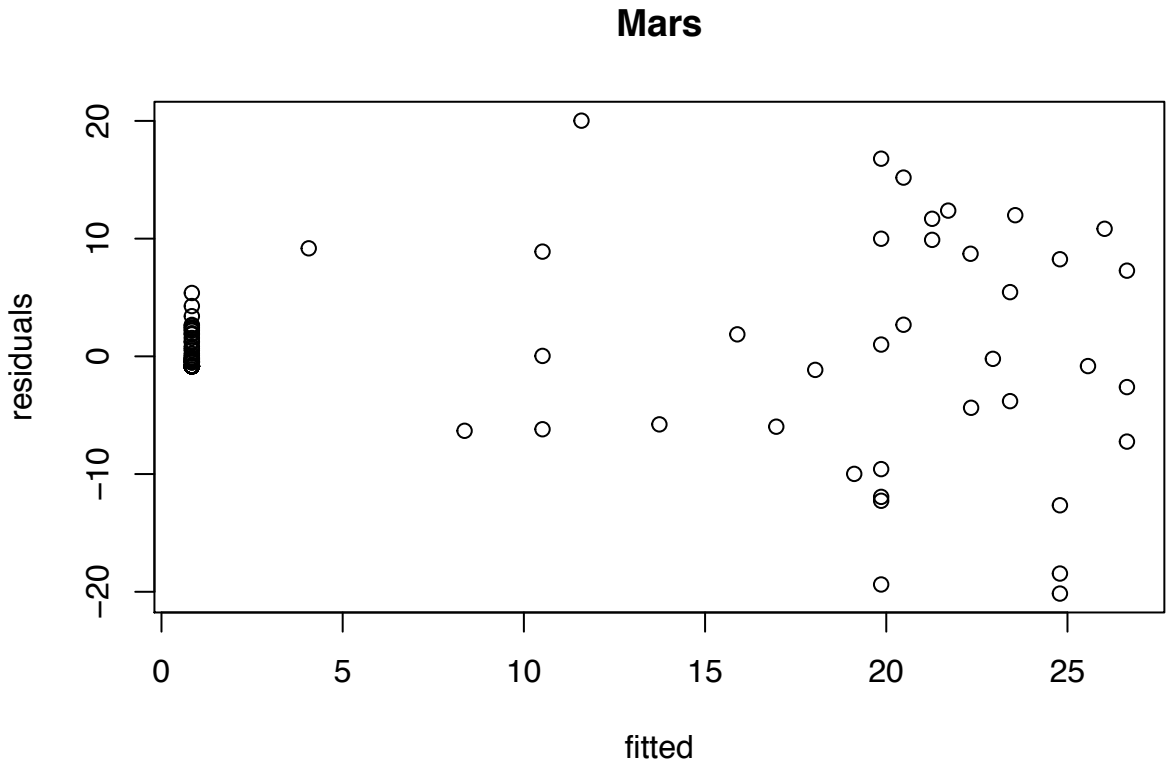
Predicting Jug r_nut in alex using data from euro

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##              coefficients
## (Intercept)     0.8380772
## h(df[,3]-65)    1.0751411
## h(df[,3]-89)   -1.6917062
##
## Selected 3 of 7 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 7 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 37.90256  RSS 4215.016  GRSq 0.6938577  RSq 0.7139271  CVRSq 0.587897
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.35 sd 0.74    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.463    iter.rsq 0.450
##
## stddev of predictions:
```

Residuals vs Fitted

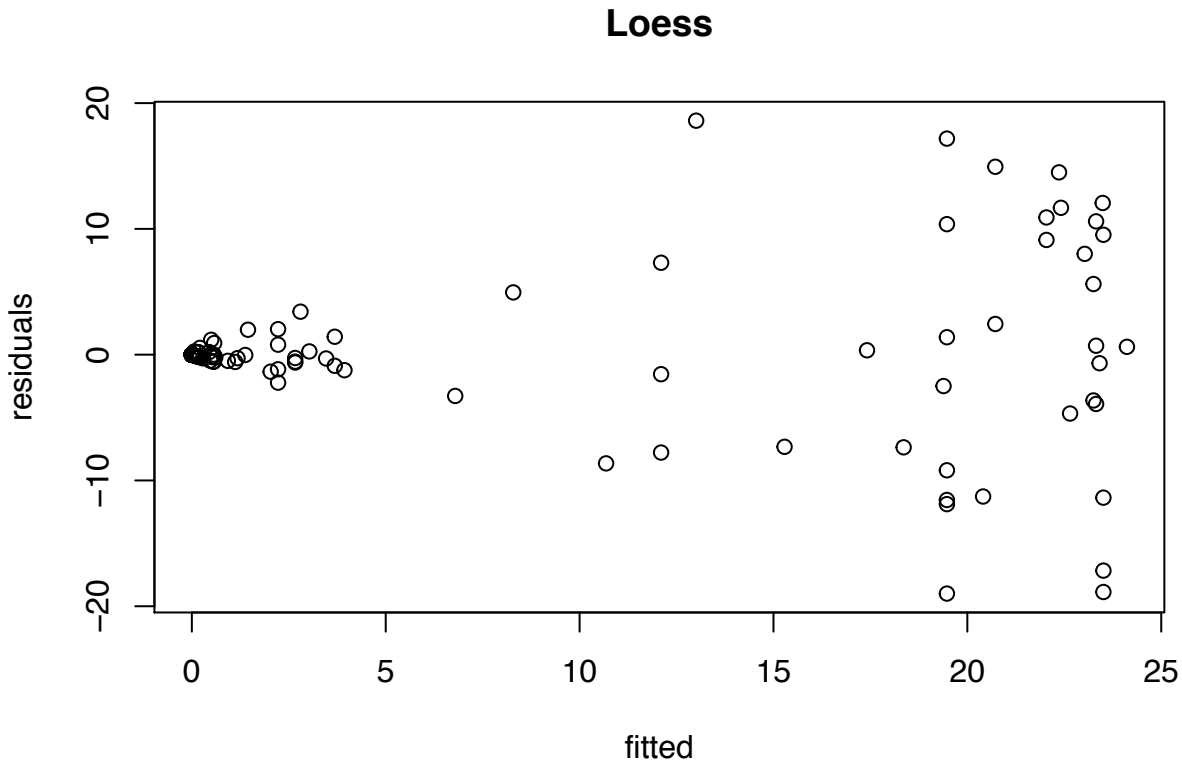


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 13.14
## Residual Standard Error: 6.194
## Trace of smoother matrix: 14.54  (exact)
##
## Control settings:
##   span     :  0.2474202
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



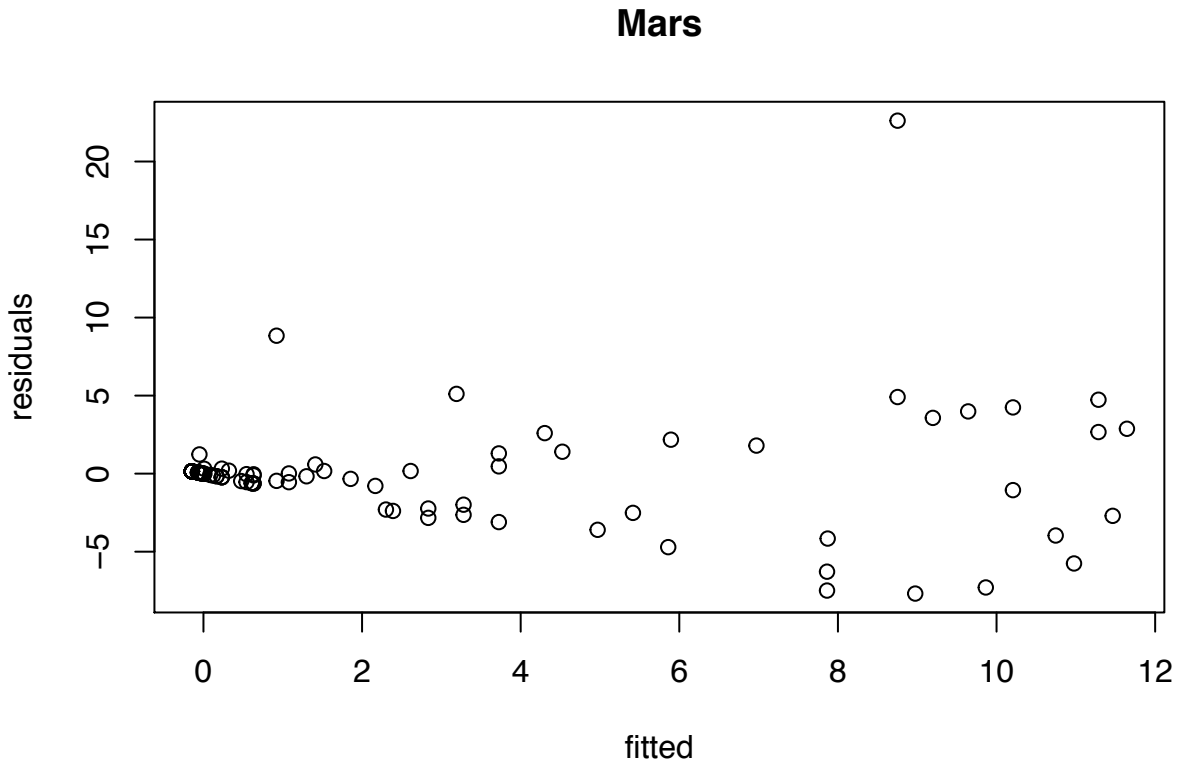
Predicting Pru du in alex using data from euro

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##              coefficients
## (Intercept)    11.6442753
## h(53-df[,3])   -0.2224630
## h(df[,3]-53)   -0.1796852
##
## Selected 3 of 5 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 5 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 10.05737  RSS 1118.446  GRSq 0.5386672  RSq 0.5689101  CVRSq 0.2287923
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.81 sd 0.98    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.189    iter.rsq 0.427
##
## stddev of predictions:
```

Residuals vs Fitted

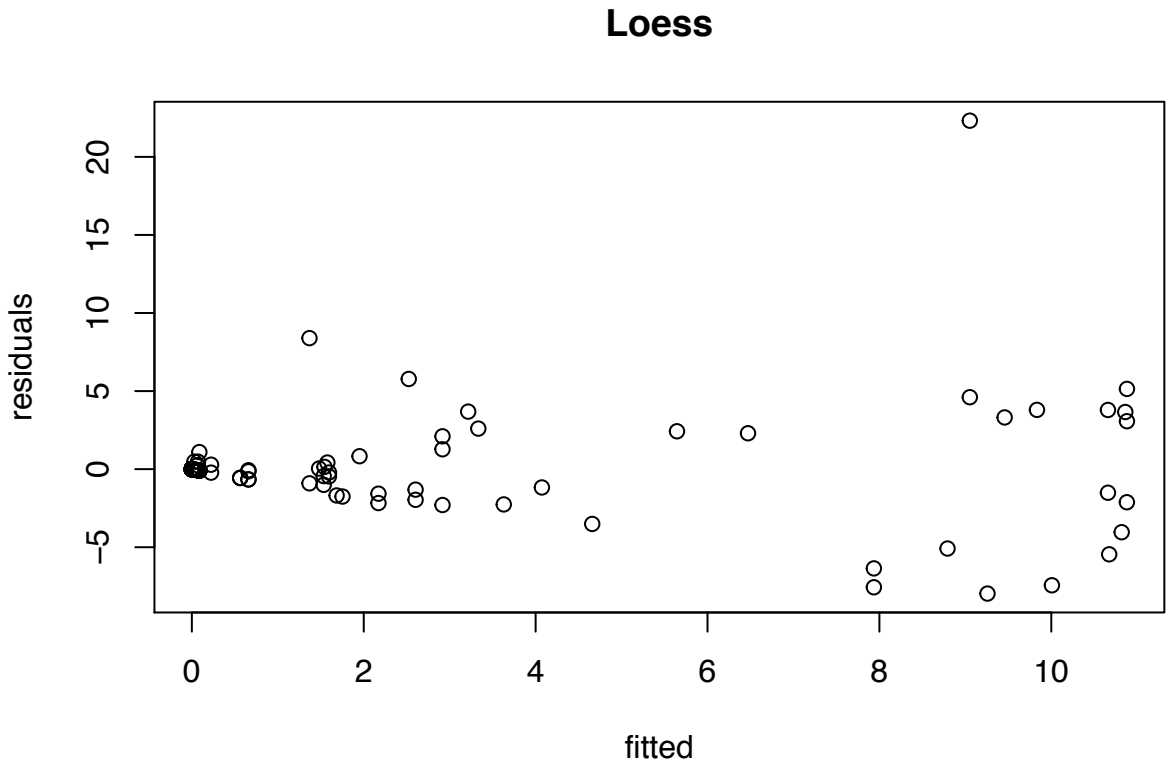


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 9.57
## Residual Standard Error: 3.163
## Trace of smoother matrix: 10.57  (exact)
##
## Control settings:
##   span     :  0.3866283
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



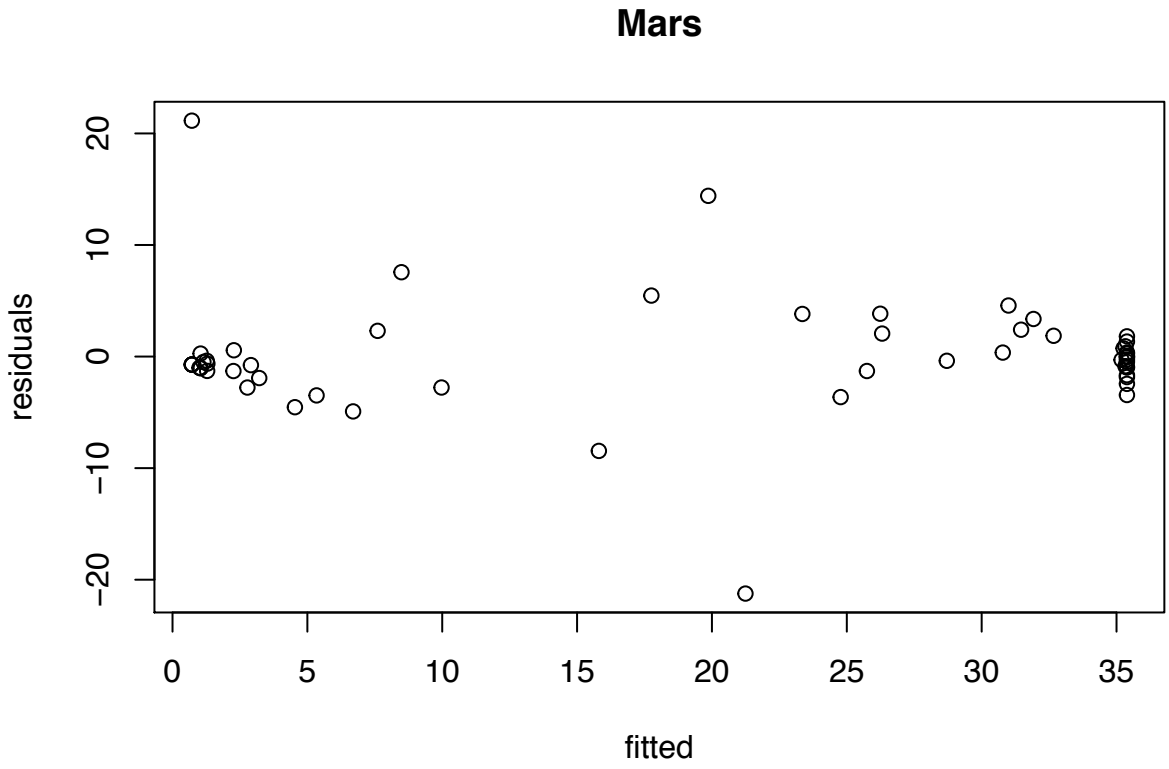
Predicting Ara h in alex using data from immunocap

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)       25.7456141
## h(30.85-df[,3])   -0.8113120
## h(df[,3]-30.85)    0.1394277
##
## Selected 3 of 4 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 4 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 30.55728  RSS 1479.92  GRSq 0.8784896  RSq 0.8949453  CVRSq 0.8463719
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.93 sd 0.25    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.429    iter.rsq 0.123
##
## stddev of predictions:
```

Residuals vs Fitted

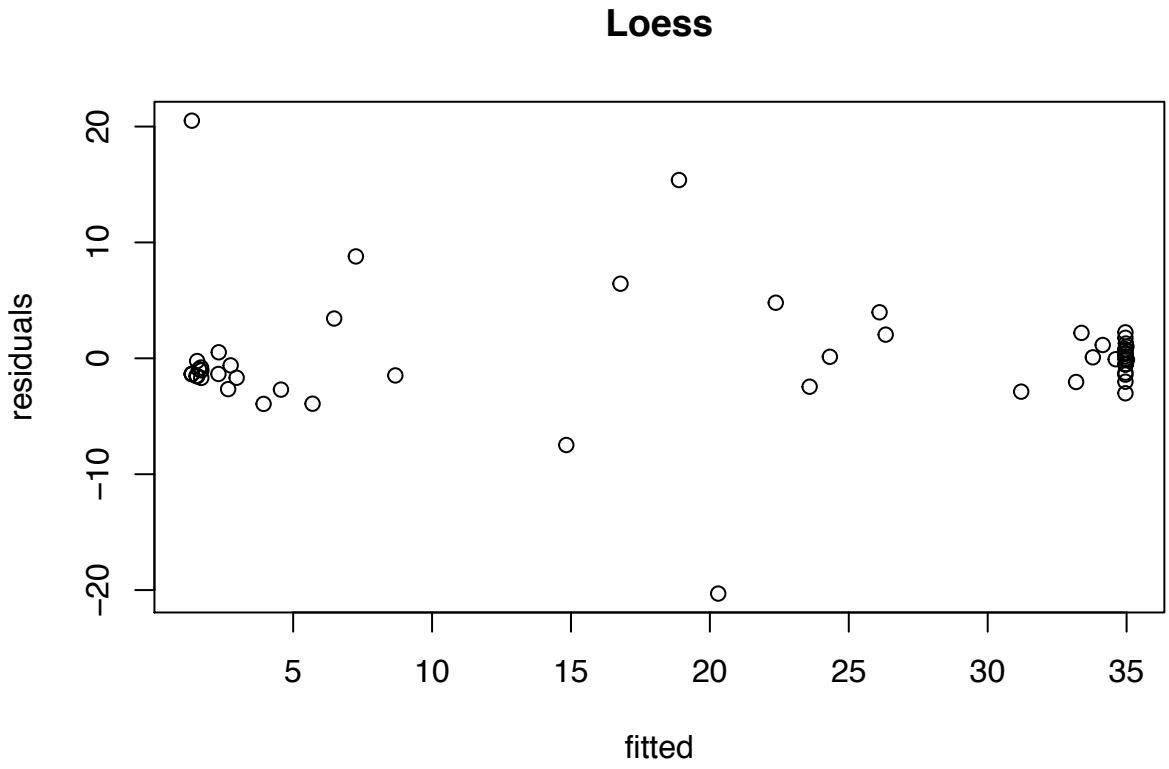


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 58
## Equivalent Number of Parameters: 5.04
## Residual Standard Error: 5.238
## Trace of smoother matrix: 5.53  (exact)
##
## Control settings:
##   span     :  0.5705542
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



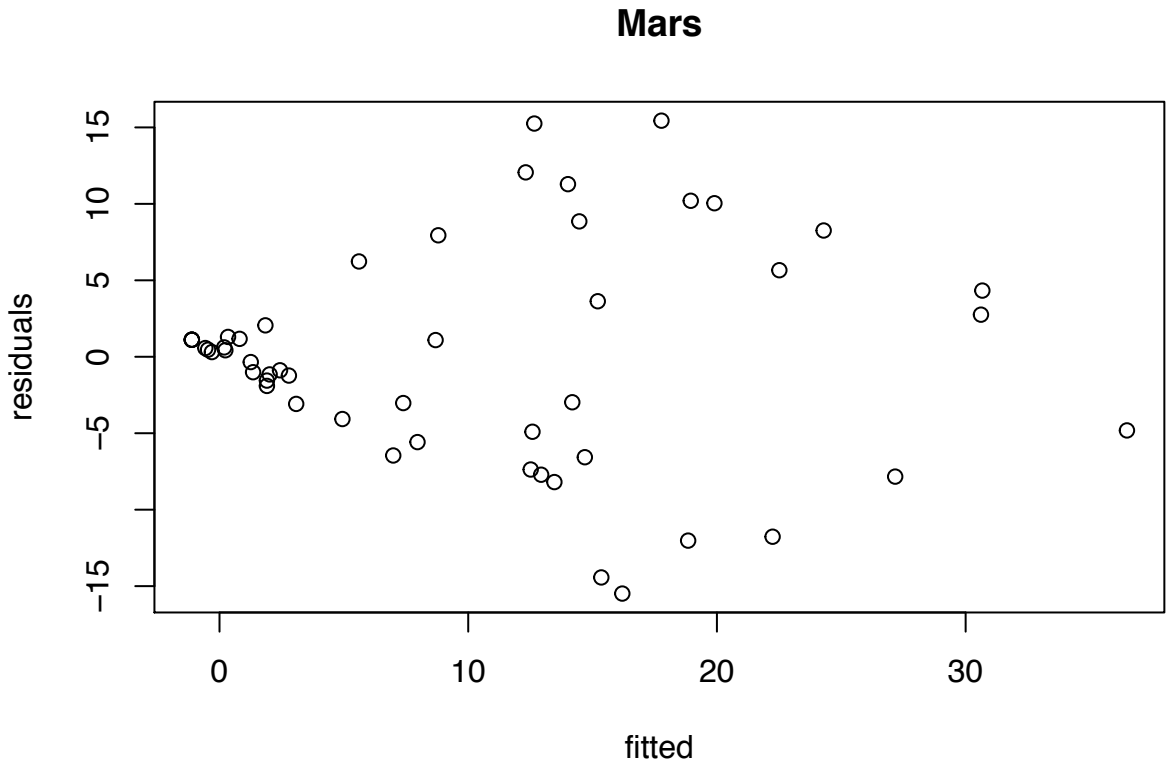
Predicting Cor a_hazel in alex using data from immunocap

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##               coefficients
## (Intercept)     12.5123836
## h(8.8-df[,3])   -1.5482674
## h(df[,3]-8.8)    0.2628684
##
## Selected 3 of 4 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 4 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 59.65639  RSS 2475.155  GRSq 0.5935364  RSq 0.6559692  CVRSq 0.4155711
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.93 sd 0.25    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.742    iter.rsq 0.648
##
## stddev of predictions:
```

Residuals vs Fitted

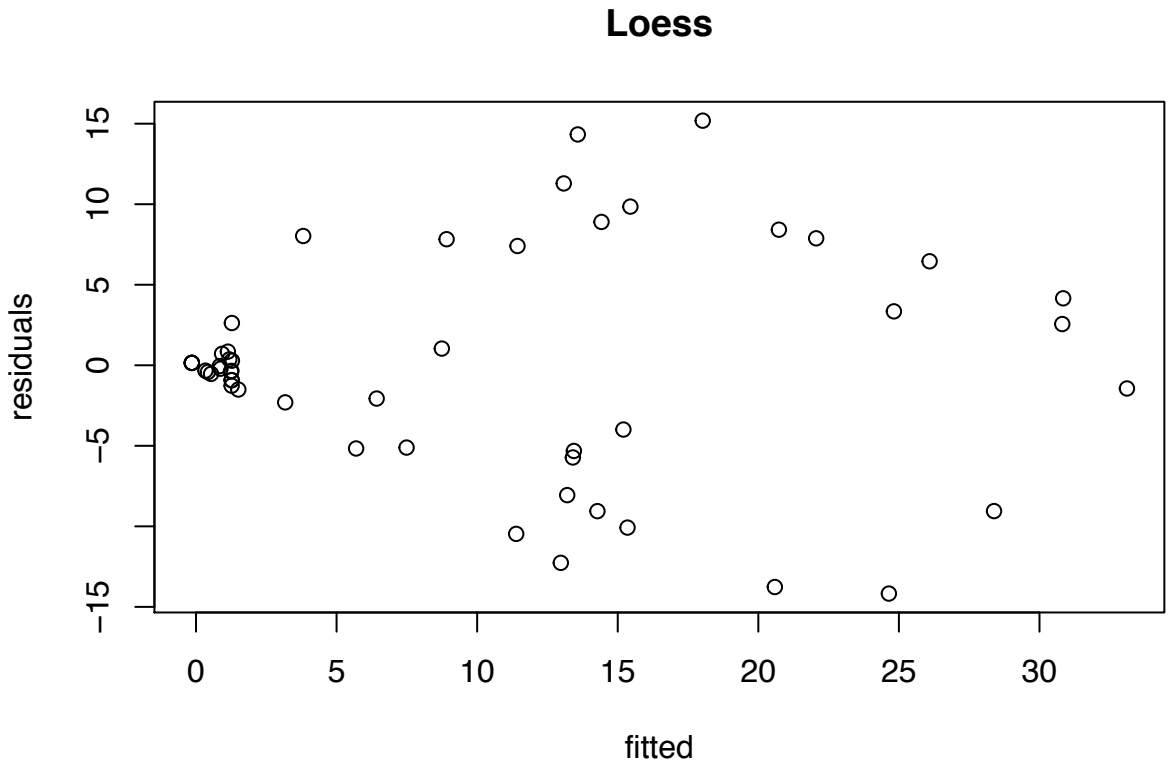


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 51
## Equivalent Number of Parameters: 8.69
## Residual Standard Error: 7.486
## Trace of smoother matrix: 9.6  (exact)
##
## Control settings:
##   span     :  0.4248078
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



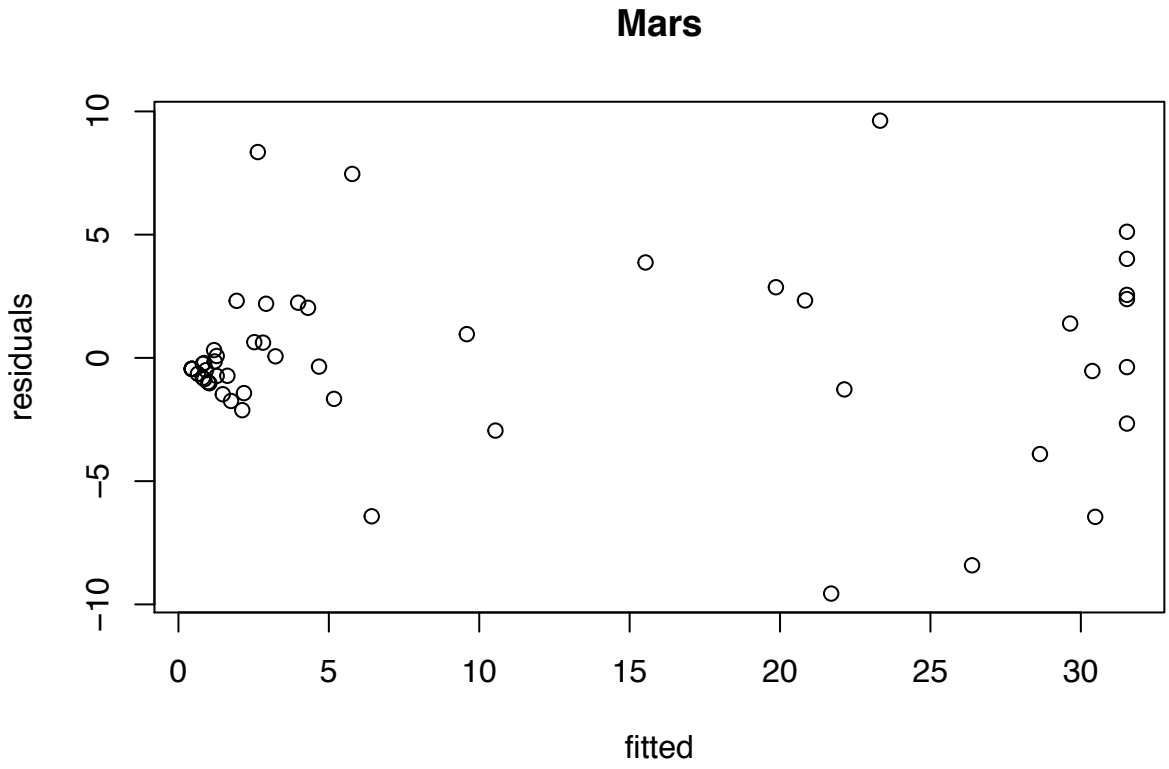
Predicting Jug r_nut in alex using data from immunocap

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)       20.8300136
## h(53.52-df[,3])   -0.3808787
## h(df[,3]-53.52)    0.2302740
##
## Selected 3 of 3 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 3 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 14.04327  RSS 624.4053  GRSq 0.9116636  RSq 0.9244942  CVRSq 0.8870036
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.00 sd 0.00    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.365    iter.rsq 0.196
##
## stddev of predictions:
```

Residuals vs Fitted

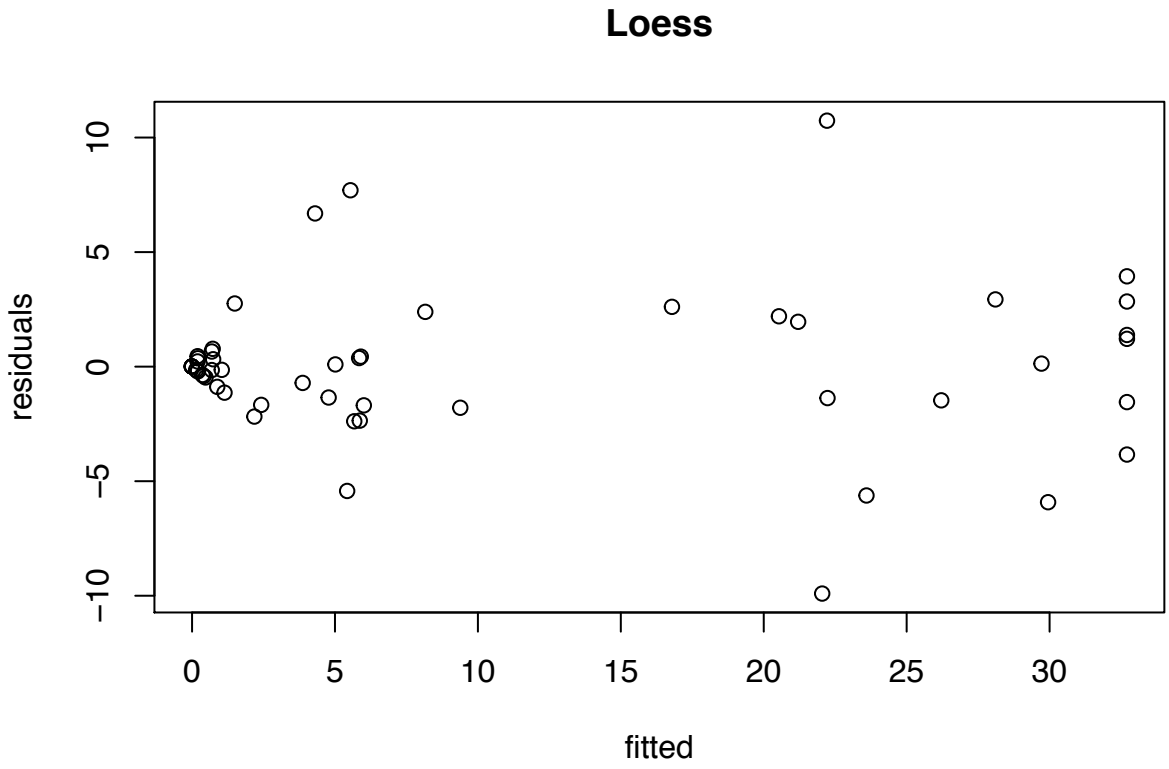


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 54
## Equivalent Number of Parameters: 10.06
## Residual Standard Error: 3.564
## Trace of smoother matrix: 11.13  (exact)
##
## Control settings:
##   span     :  0.3486913
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



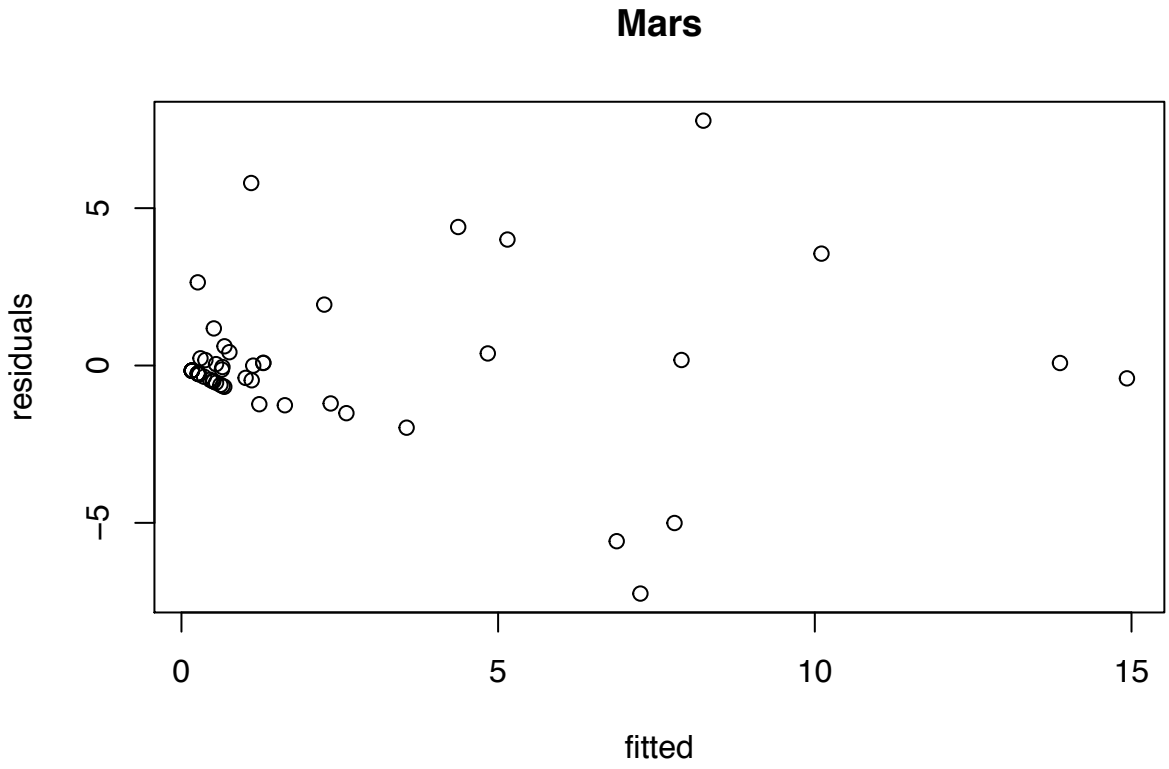
Predicting Pru du in alex using data from immunocap

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                coefficients
## (Intercept)       4.8367290
## h(17.5-df[,3])   -0.2670021
## h(df[,3]-17.5)    0.1725039
##
## Selected 3 of 3 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 3 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 6.255721  RSS 278.1479  GRSq 0.6462082  RSq 0.6975956  CVRSq 0.06247637
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.77 sd 0.42    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.183    iter.rsq 0.218
##
## stddev of predictions:
```

Residuals vs Fitted

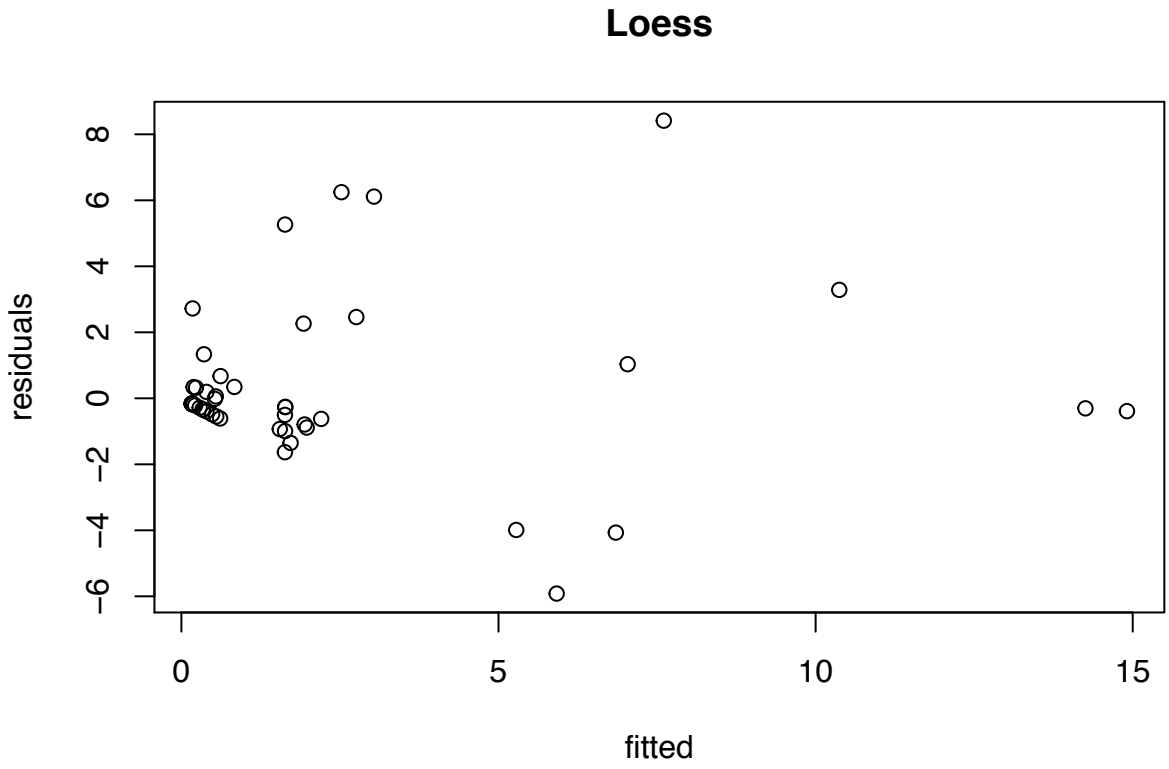


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 54
## Equivalent Number of Parameters: 6.12
## Residual Standard Error: 2.477
## Trace of smoother matrix: 6.74  (exact)
##
## Control settings:
##   span     :  0.7208353
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



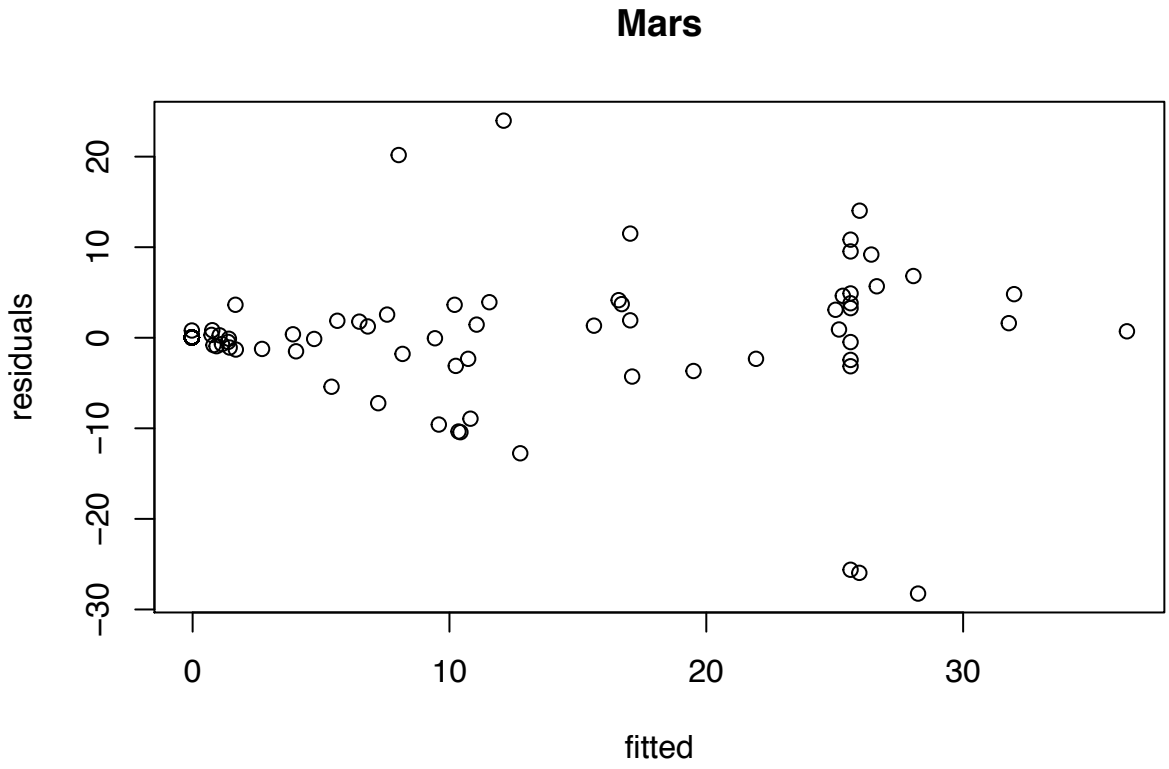
Predicting Ana o 3 in alex using data from medall

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)       25.6173722
## h(17.07-df[,3])   -1.5025113
## h(df[,3]-29.86)    0.1534255
##
## Selected 3 of 4 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 4 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 30.27058  RSS 4726.769  GRSq 0.7460477  RSq 0.7582113  CVRSq 0.6799132
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.89 sd 0.74    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.265    iter.rsq 0.495
##
## stddev of predictions:
```

Residuals vs Fitted

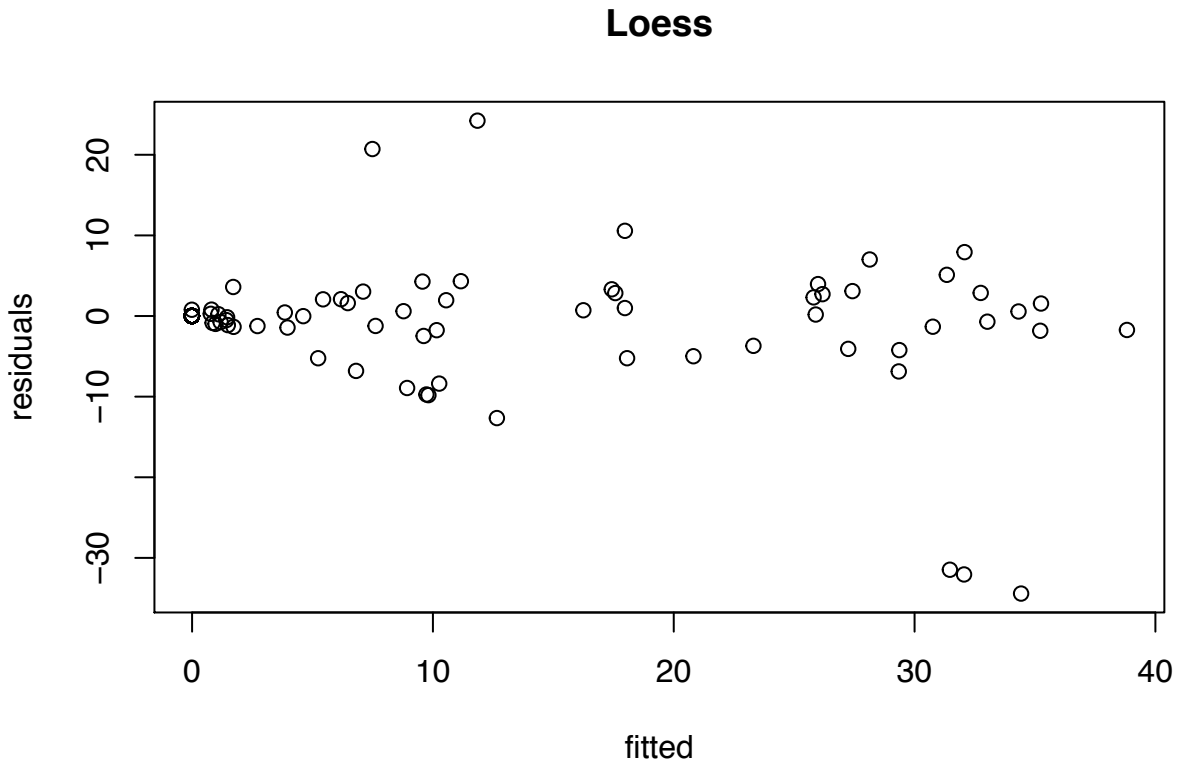


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 166
## Equivalent Number of Parameters: 5.25
## Residual Standard Error: 5.795
## Trace of smoother matrix: 5.75  (exact)
##
## Control settings:
##   span     :  0.849544
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



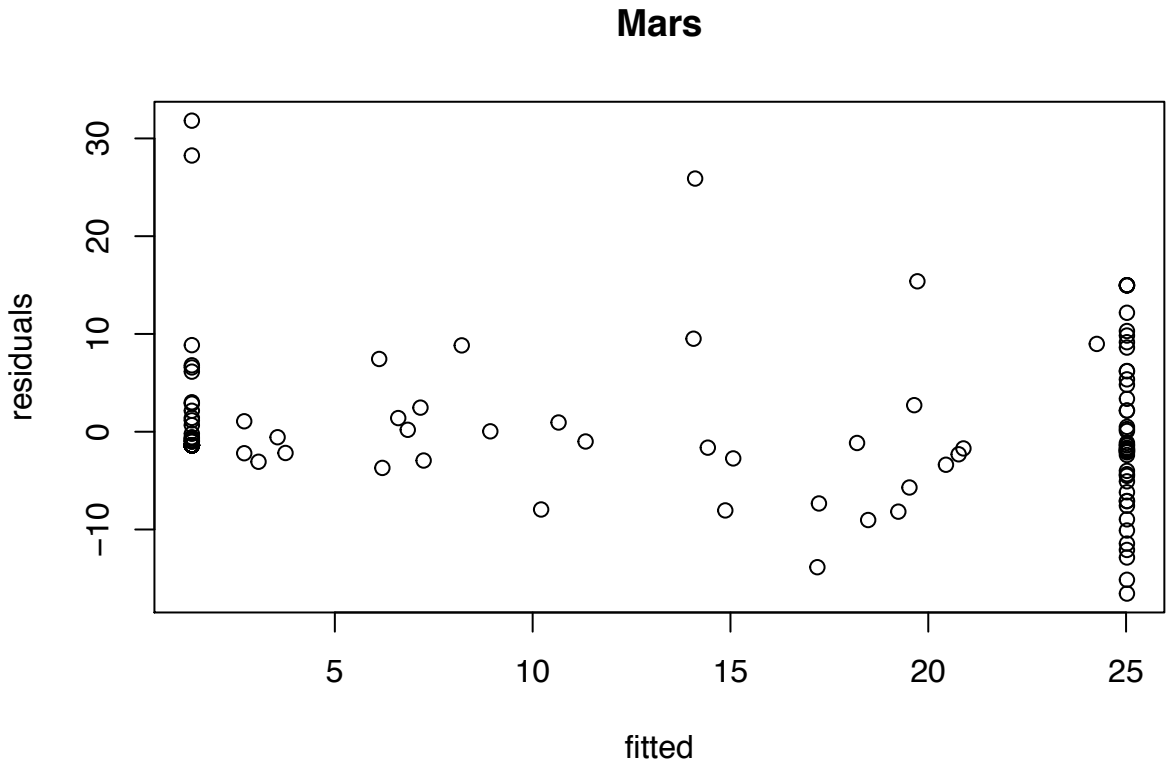
Predicting Ara h 1 in alex using data from medall

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                coefficients
## (Intercept)       25.022154
## h(5.89-df[,3])    -4.013017
##
## Selected 2 of 4 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 4 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 1 (additive model)
## GCV 45.33558  RSS 7256.15  GRSq 0.7101684  RSq 0.717152  CVRSq 0.6914563
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.21 sd 0.44    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.541    iter.rsq 0.069
##
## stddev of predictions:
```

Residuals vs Fitted

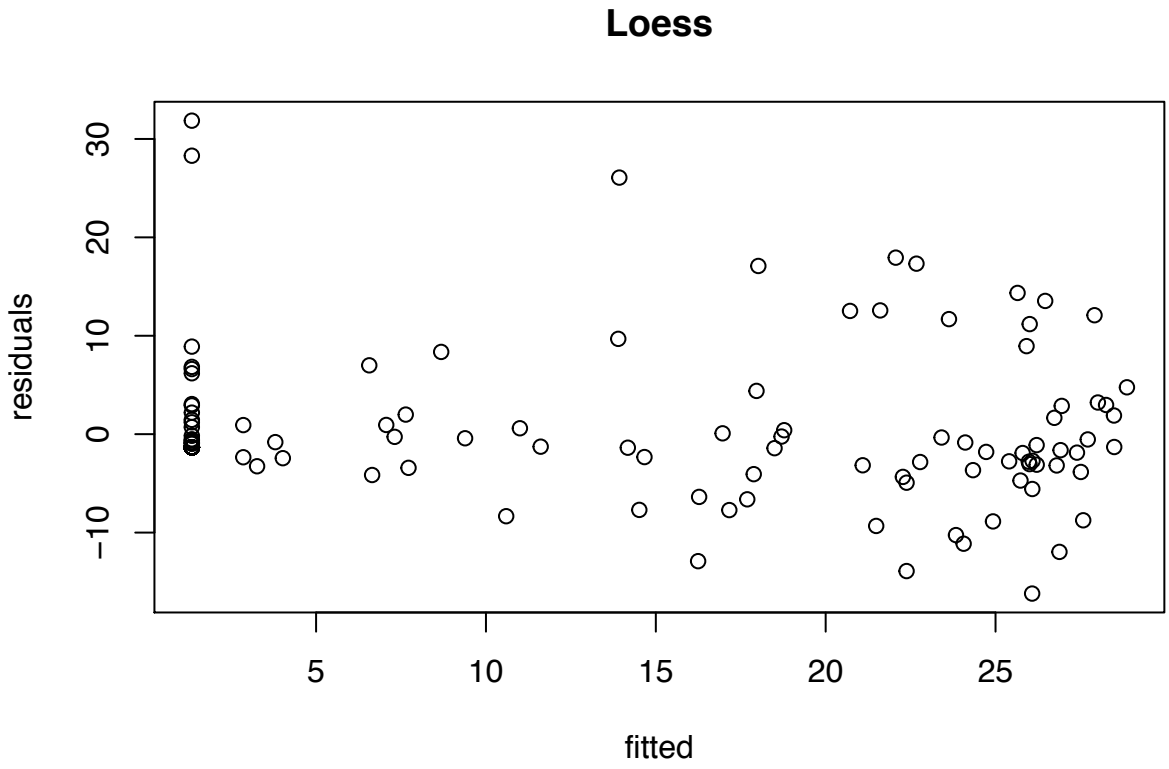


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 166
## Equivalent Number of Parameters: 6.04
## Residual Standard Error: 6.668
## Trace of smoother matrix: 6.64  (exact)
##
## Control settings:
##   span     :  0.655475
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



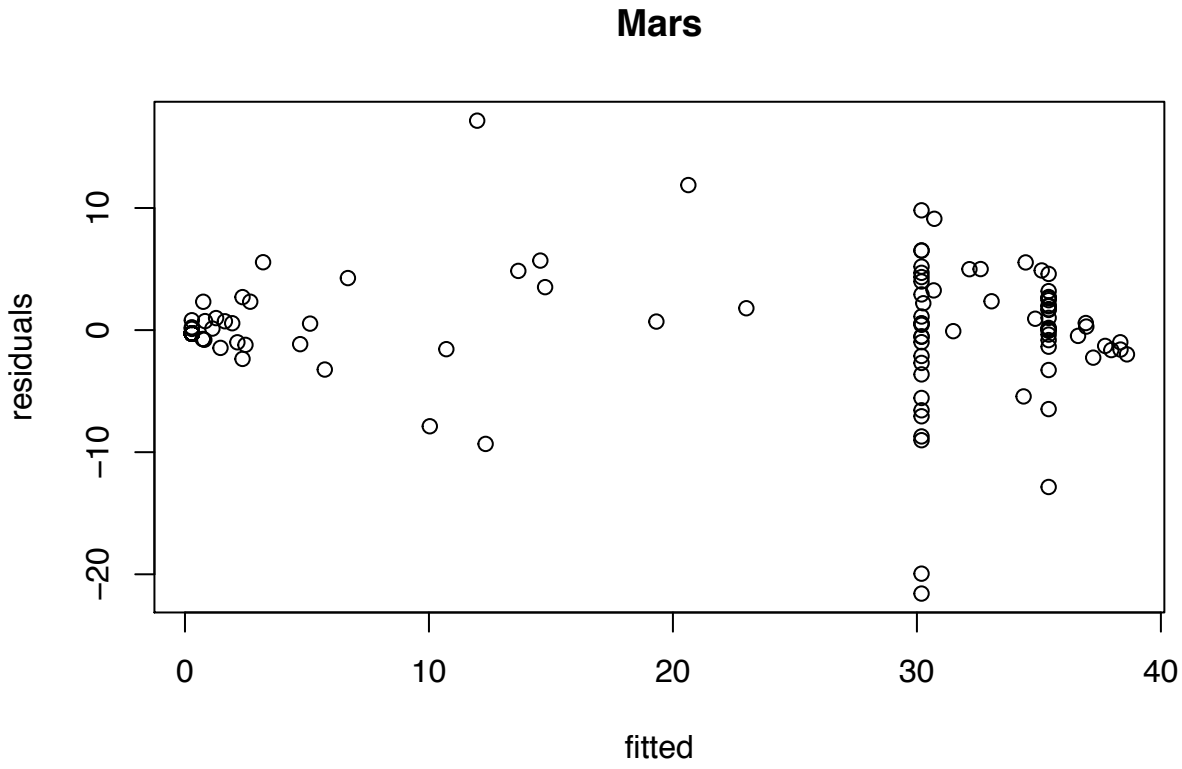
Predicting Ara h 2 in alex using data from medall

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)       30.1888418
## h(19.87-df[,3])   -1.5051215
## h(df[,3]-45.56)    0.3161821
## h(df[,3]-72.19)   -0.4315967
##
## Selected 4 of 5 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 5 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 3 (additive model)
## GCV 18.08781  RSS 2754.686  GRSq 0.9323921  RSq 0.9372197  CVRSq 0.928852
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.75 sd 0.47    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.307    iter.rsq 0.290
##
## stddev of predictions:
```

Residuals vs Fitted

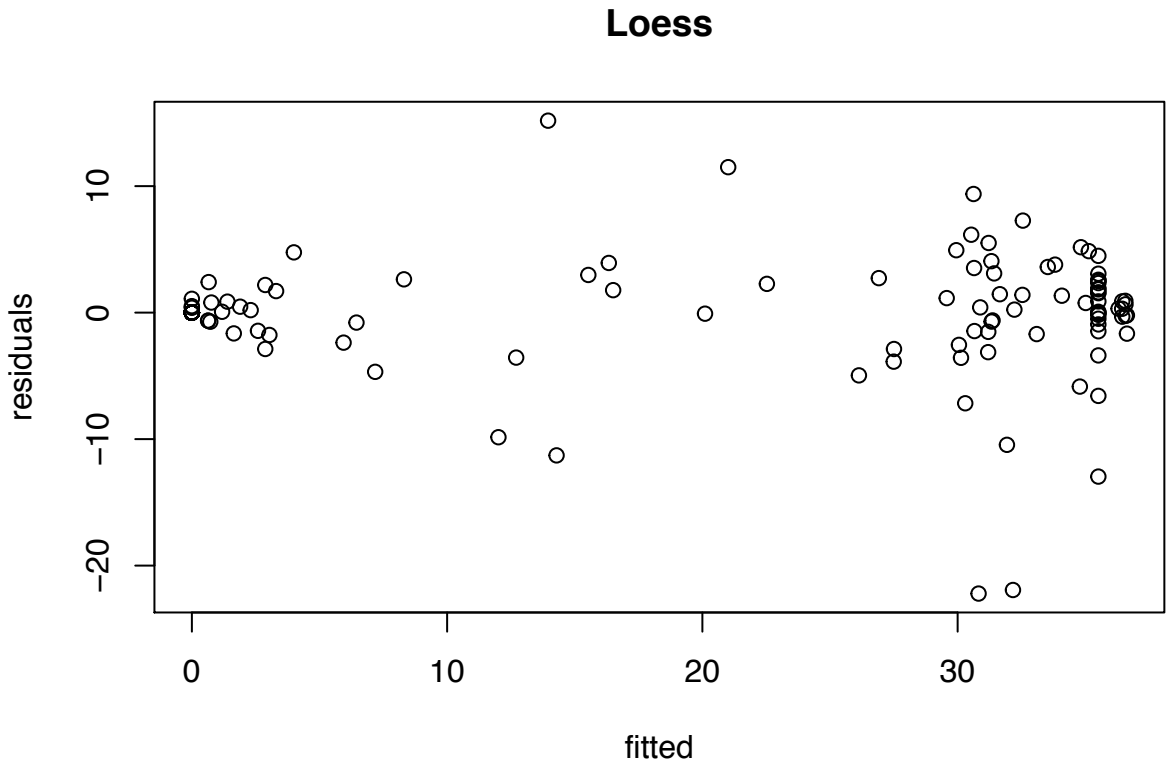


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 166
## Equivalent Number of Parameters: 4.53
## Residual Standard Error: 4.056
## Trace of smoother matrix: 4.94  (exact)
##
## Control settings:
##   span     :  0.7375388
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



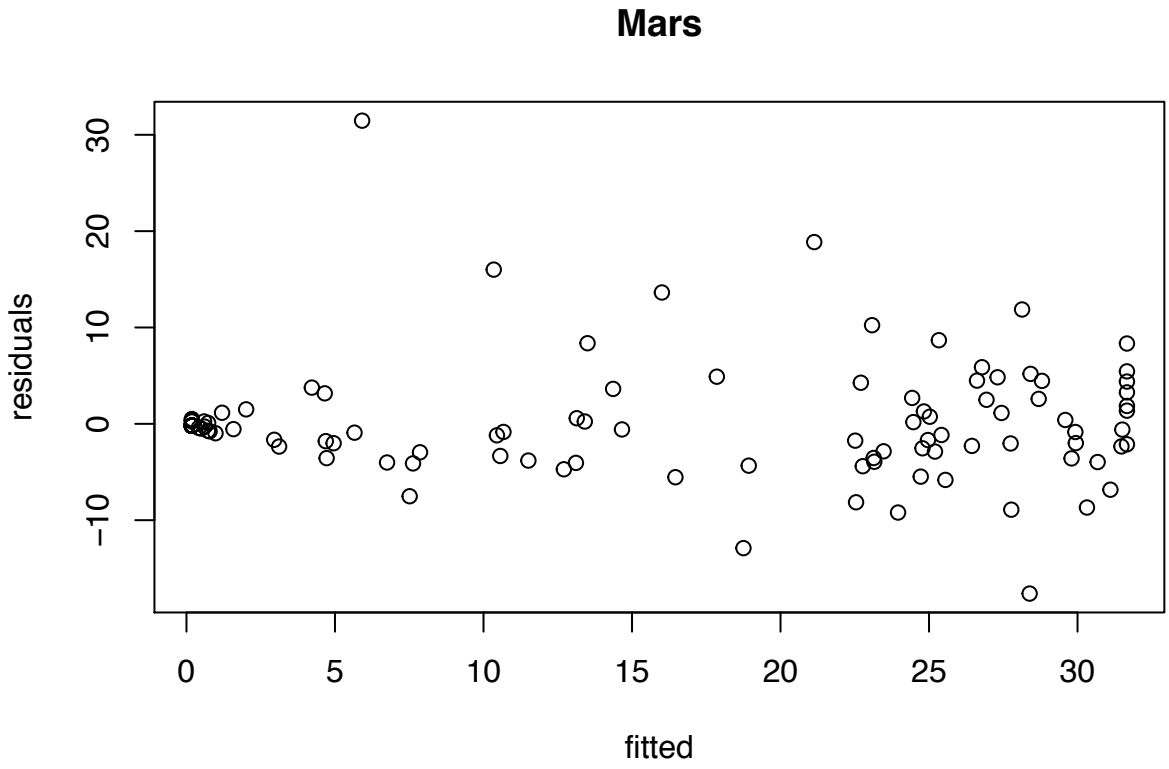
Predicting Ara h 6 in alex using data from medall

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)       22.5434268
## h(31.44-df[,3])   -0.7112749
## h(df[,3]-31.44)    0.1330260
##
## Selected 3 of 3 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 3 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 24.45549  RSS 3818.74  GRSq 0.8562183  RSq 0.863105  CVRSq 0.8477045
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.03 sd 0.24    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.289    iter.rsq 0.305
##
## stddev of predictions:
```

Residuals vs Fitted

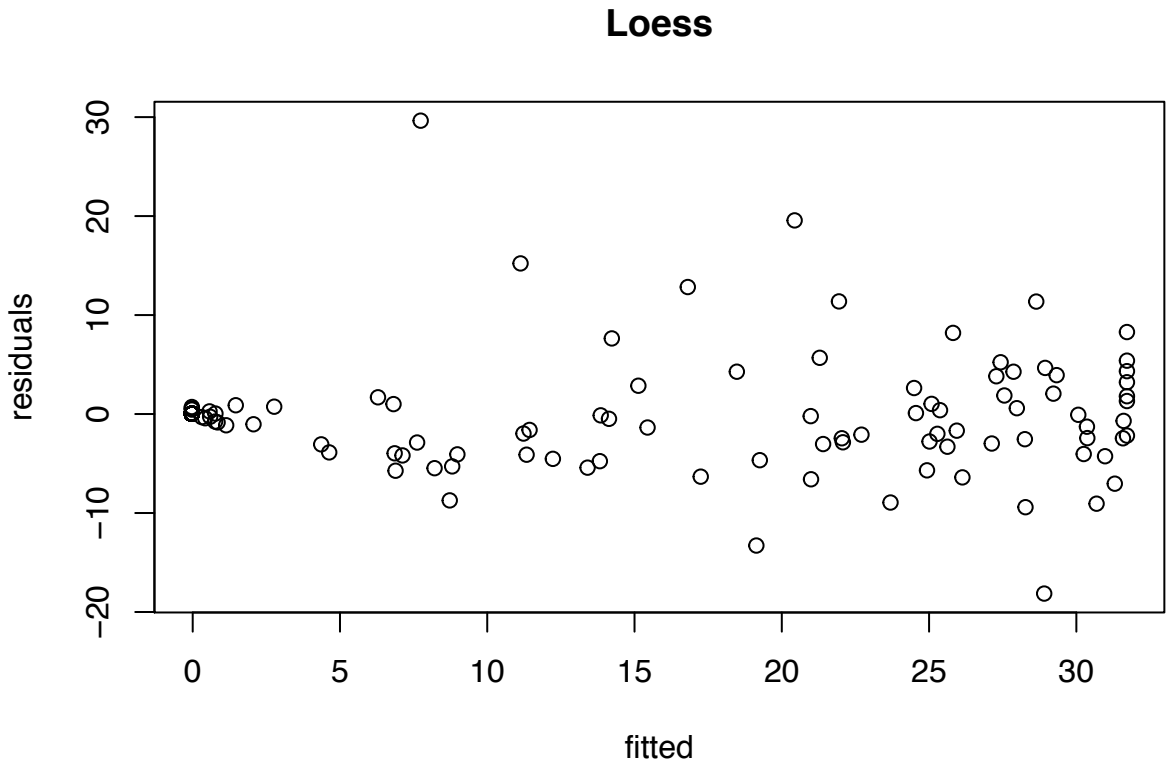


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 166
## Equivalent Number of Parameters: 5.98
## Residual Standard Error: 4.897
## Trace of smoother matrix: 6.57  (exact)
##
## Control settings:
##   span     :  0.6062306
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



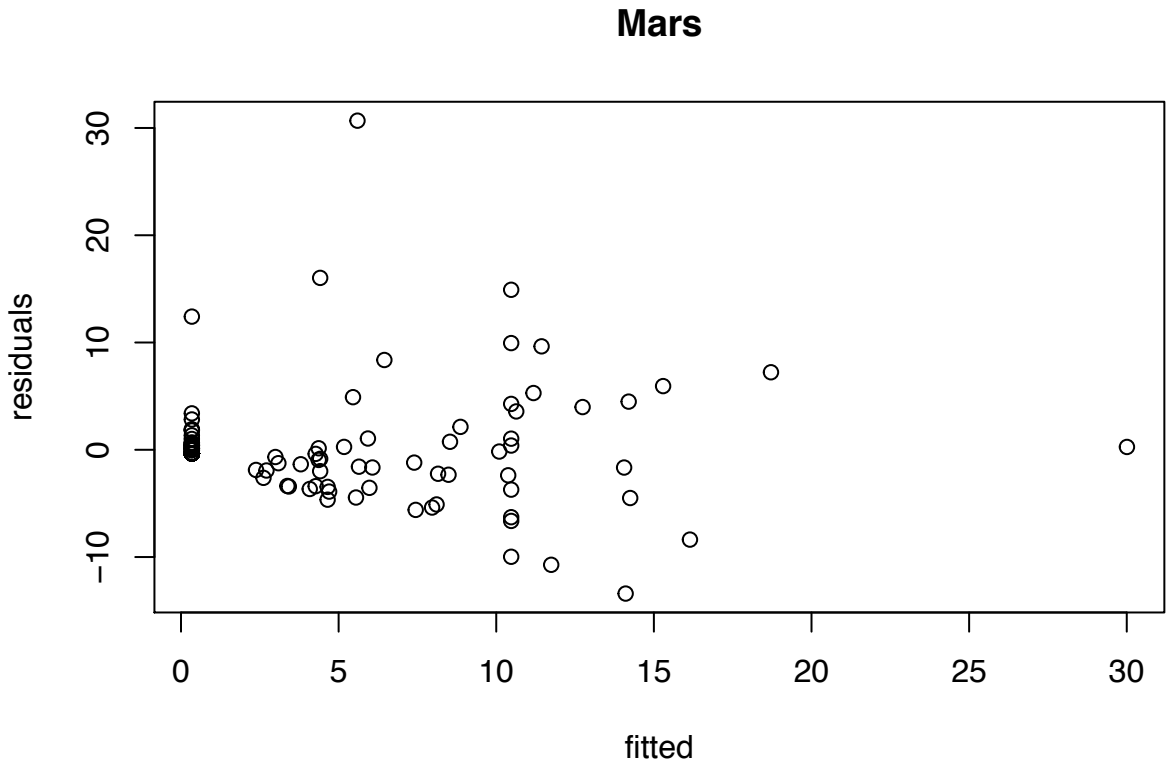
Predicting Cor a 9 in alex using data from medall

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                coefficients
## (Intercept)       10.474149
## h(2.14-df[,3])    -4.733535
## h(df[,3]-3.49)     1.606229
##
## Selected 3 of 4 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 4 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 18.84002  RSS 2941.881  GRSq 0.5428686  RSq 0.5647639  CVRSq 0.4512437
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.96 sd 0.26    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.253    iter.rsq 0.183
##
## stddev of predictions:
```

Residuals vs Fitted

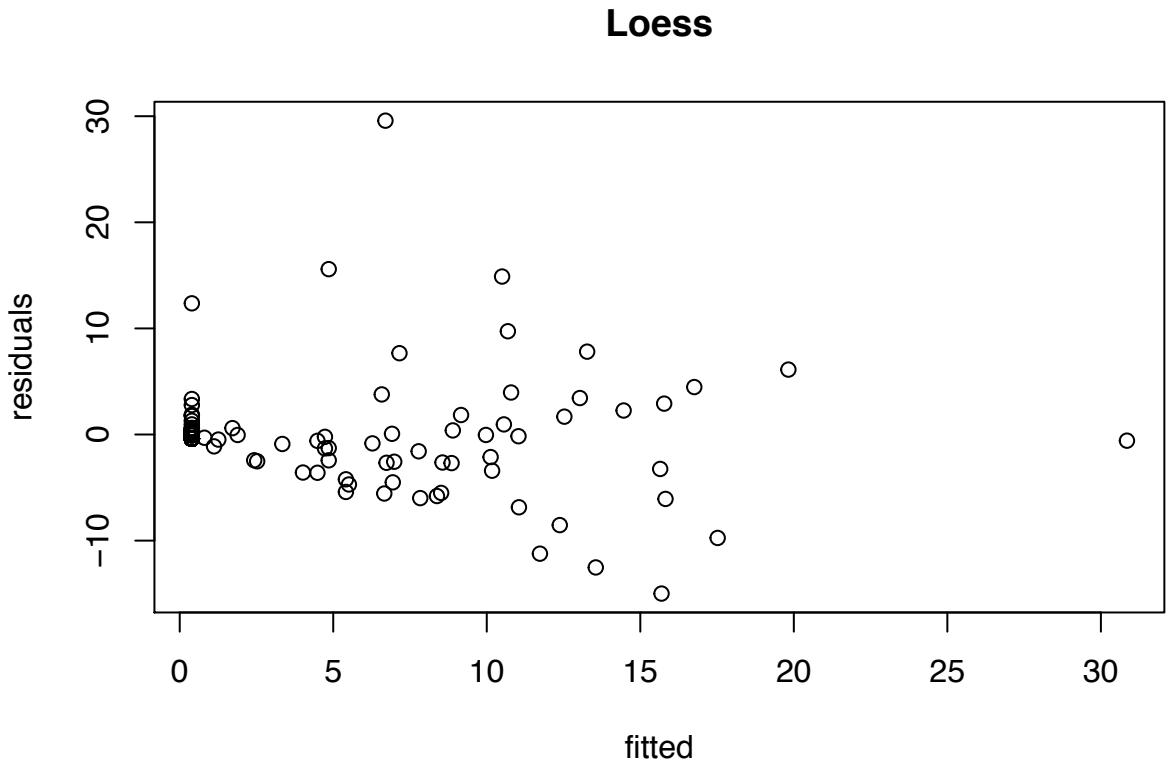


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 166
## Equivalent Number of Parameters: 5.41
## Residual Standard Error: 4.308
## Trace of smoother matrix: 5.93  (exact)
##
## Control settings:
##   span     :  0.7781151
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



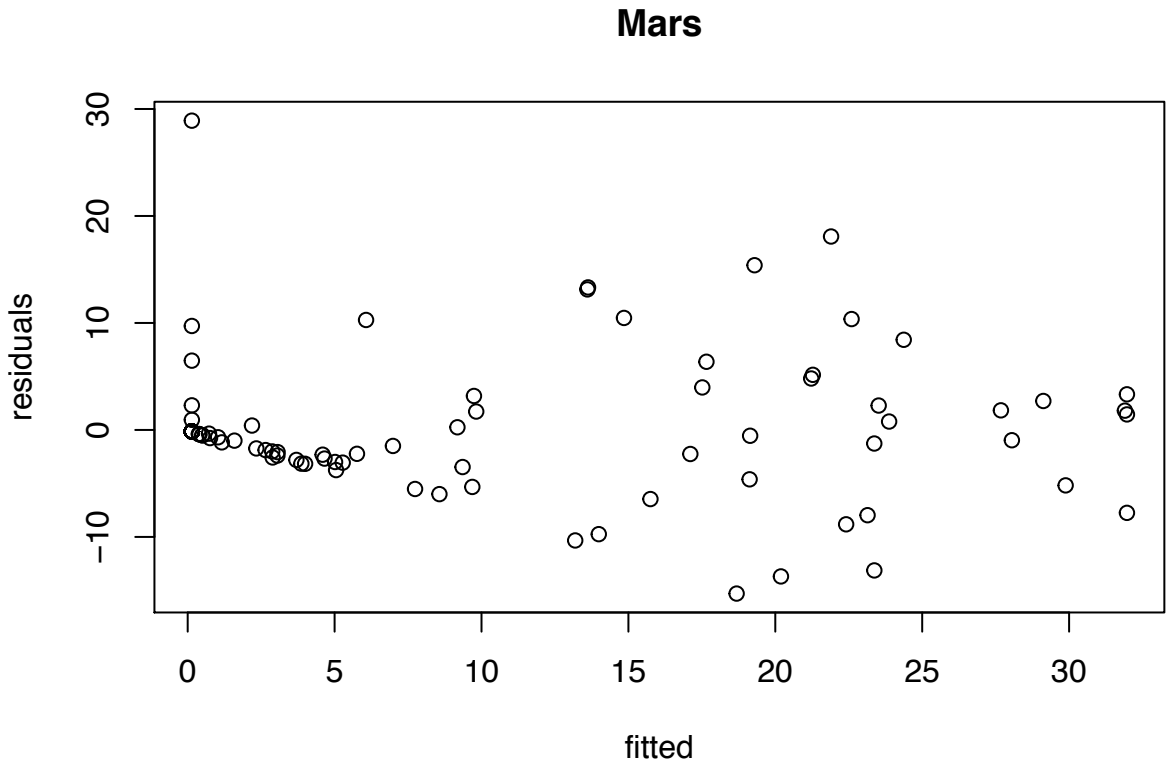
Predicting Jug r 1 in alex using data from medall

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)       18.6834844
## h(26.36-df[,3])   -0.7034141
## h(df[,3]-26.36)    0.1804065
##
## Selected 3 of 4 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 4 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 24.0356  RSS 3753.173  GRSq 0.7688283  RSq 0.7799008  CVRSq 0.7329099
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.95 sd 0.46    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.276    iter.rsq 0.056
##
## stddev of predictions:
```

Residuals vs Fitted

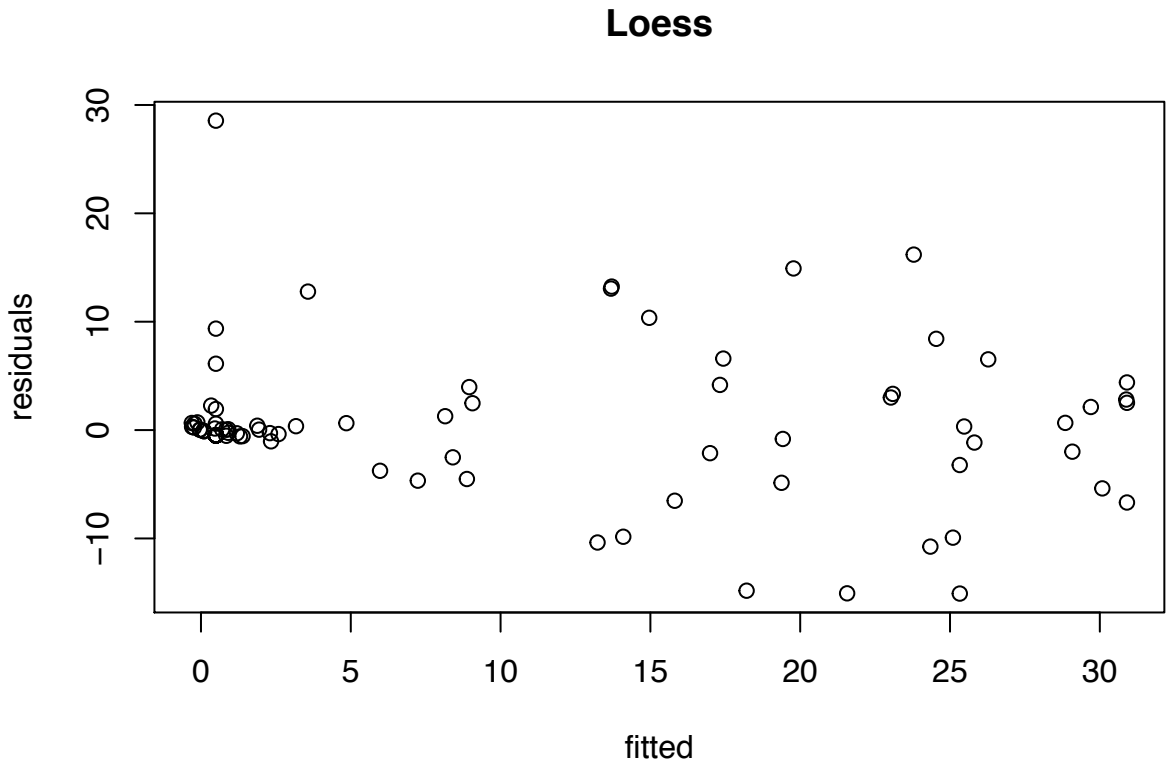


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 166
## Equivalent Number of Parameters: 6.33
## Residual Standard Error: 4.801
## Trace of smoother matrix: 6.97  (exact)
##
## Control settings:
##   span     :  0.6563859
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



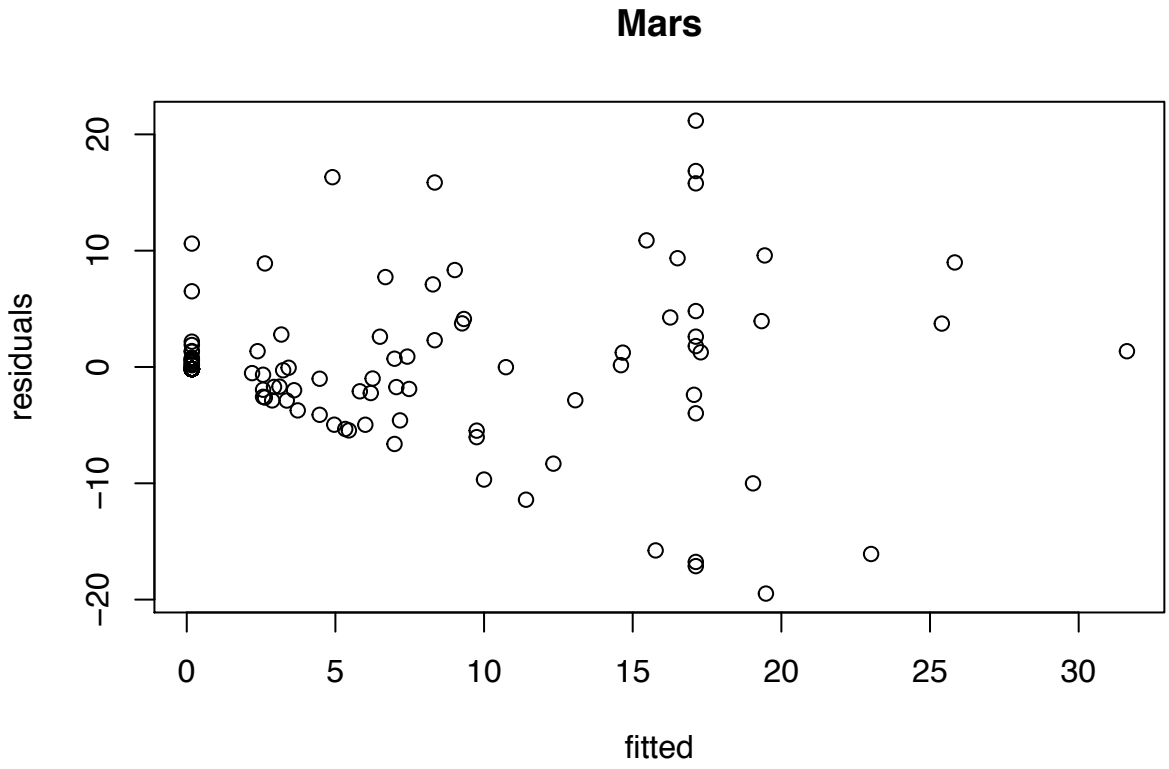
Predicting Jug r 2 in alex using data from medall

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                coefficients
## (Intercept)       17.122569
## h(2.76-df[,3])    -6.141882
## h(df[,3]-3.93)     2.068701
##
## Selected 3 of 5 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 5 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 29.86827  RSS 4663.949  GRSq 0.601299  RSq 0.6203957  CVRSq 0.5014982
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.23 sd 0.81    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.355    iter.rsq 0.348
##
## stddev of predictions:
```

Residuals vs Fitted

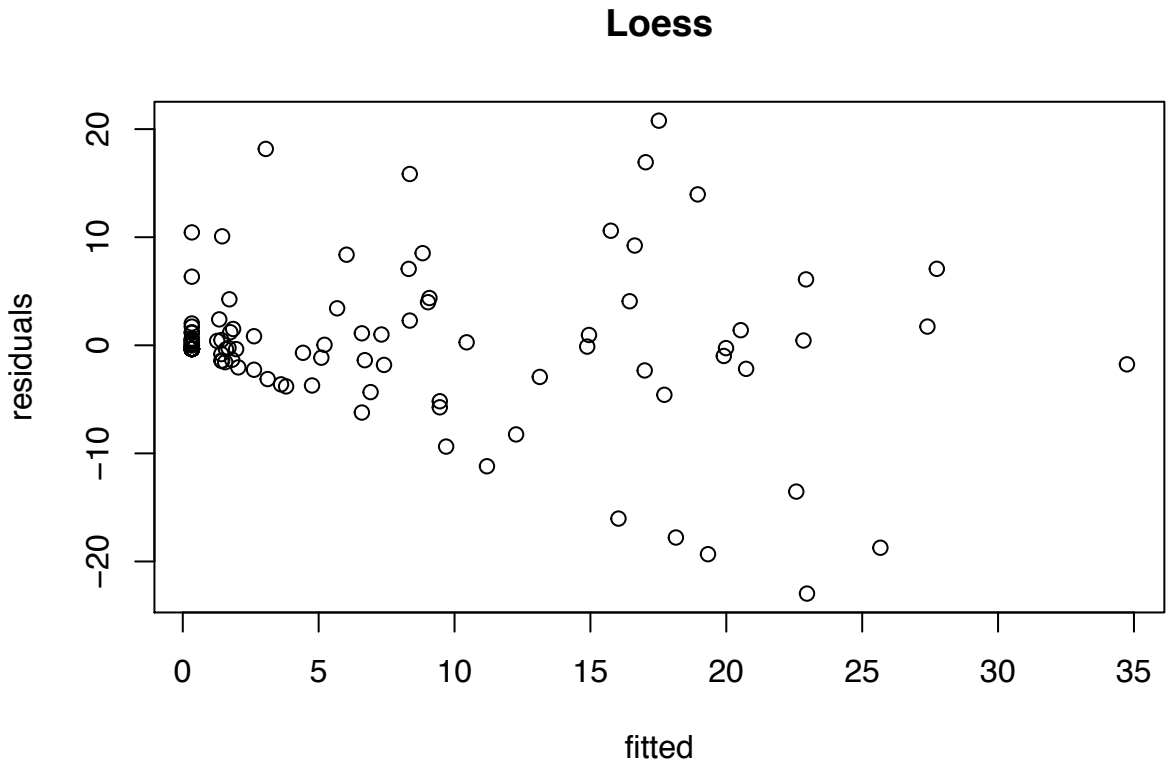


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 166
## Equivalent Number of Parameters: 5.36
## Residual Standard Error: 5.527
## Trace of smoother matrix: 5.88  (exact)
##
## Control settings:
##   span     :  0.8068517
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



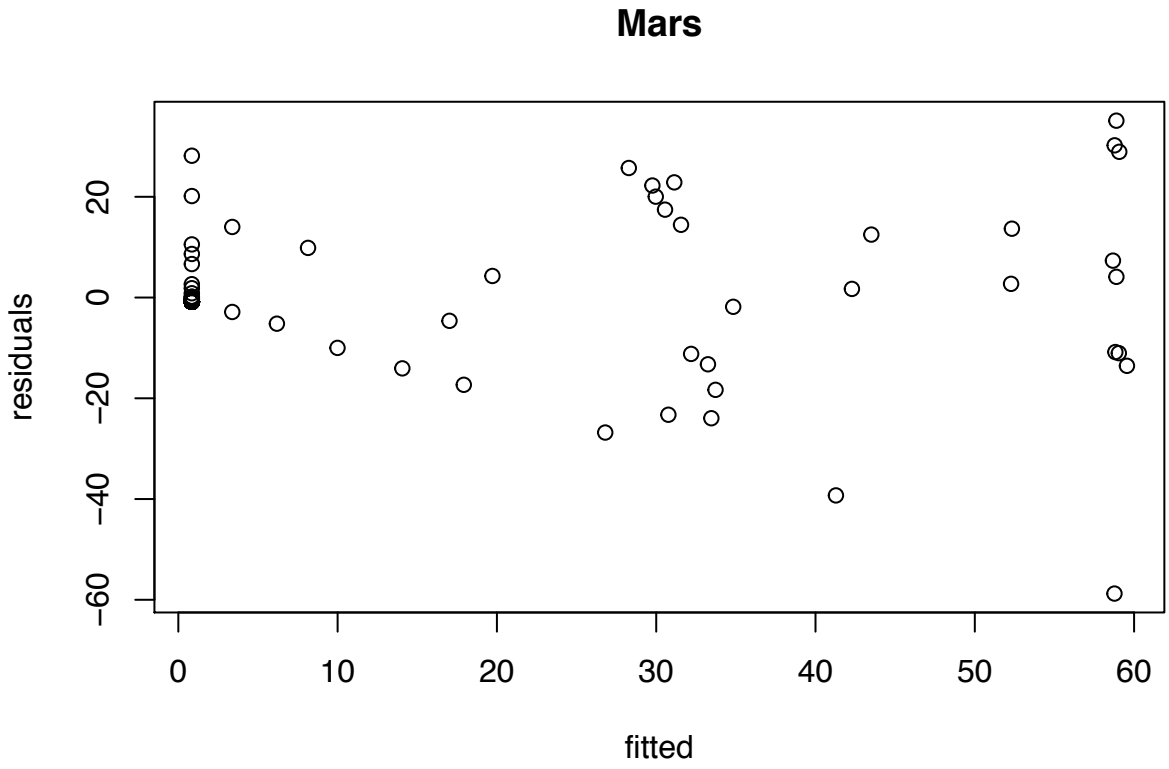
Predicting Ara h 1 in euro using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)        0.8485783
## h(df[,3]-17.45)    5.2855064
## h(df[,3]-28.39)   -5.2097784
##
## Selected 3 of 6 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 6 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 147.0258  RSS 16350.24  GRSq 0.6976513  RSq 0.7174719  CVRSq 0.5235522
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.01 sd 0.59    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.828    iter.rsq 0.216
##
## stddev of predictions:
```

Residuals vs Fitted

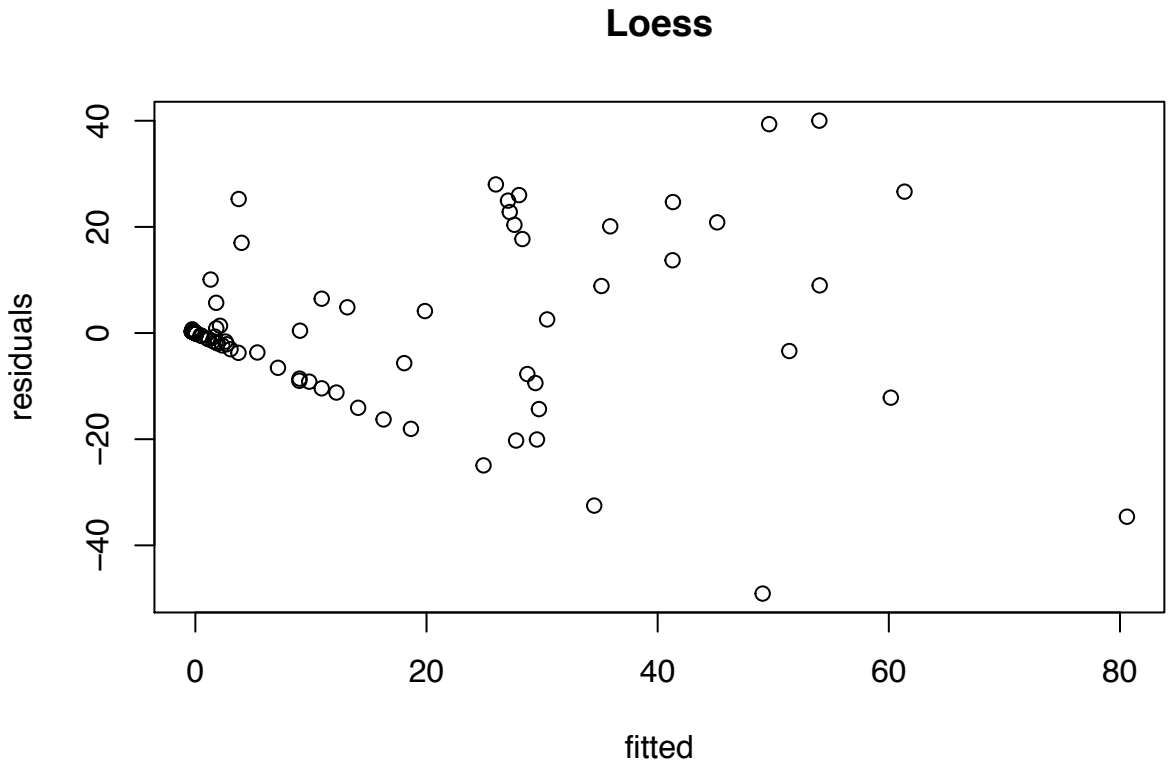


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 4.46
## Residual Standard Error: 12.52
## Trace of smoother matrix: 4.86  (exact)
##
## Control settings:
##   span     :  0.7214519
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



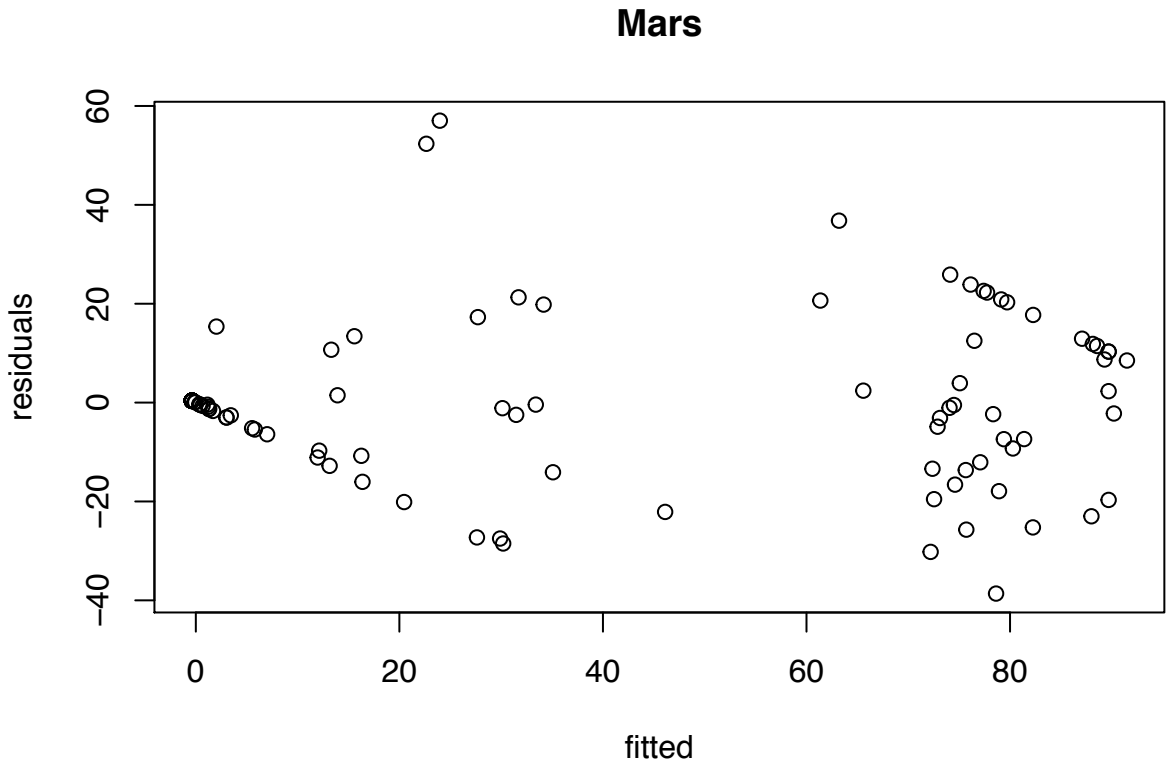
Predicting Ara h 2 in euro using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)        16.376264
## h(24.8-df[,3])     -0.676116
## h(df[,3]-24.8)      2.323126
## h(df[,3]-32.46)    16.047344
## h(df[,3]-35.58)   -35.133533
## h(df[,3]-36.72)    22.040118
##
## Selected 6 of 6 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 6 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 5 (additive model)
## GCV 244.9243  RSS 24492.43  GRSq 0.8371569  RSq 0.8631666  CVRSq 0.8045593
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 4.87 sd 0.83    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 1.82    iter.rsq 0.348
##
## stddev of predictions:
```

Residuals vs Fitted

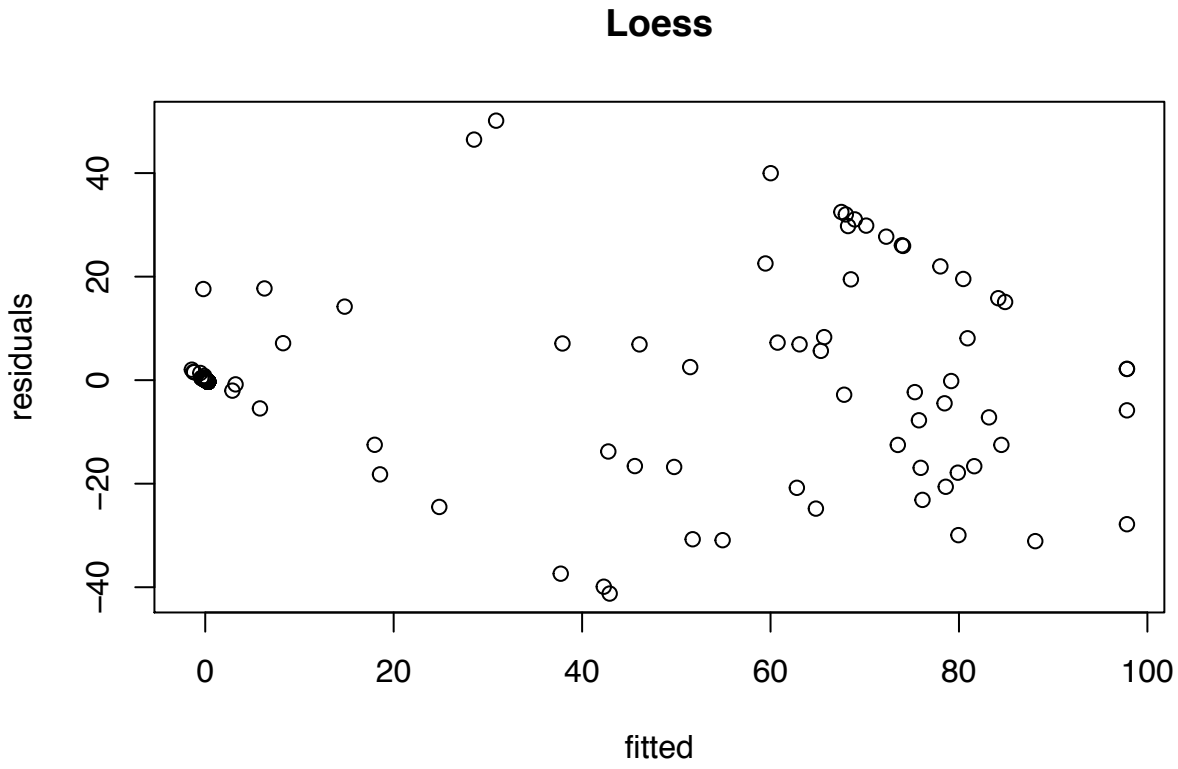


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 3.83
## Residual Standard Error: 16.36
## Trace of smoother matrix: 4.15  (exact)
##
## Control settings:
##   span     :  0.6464157
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



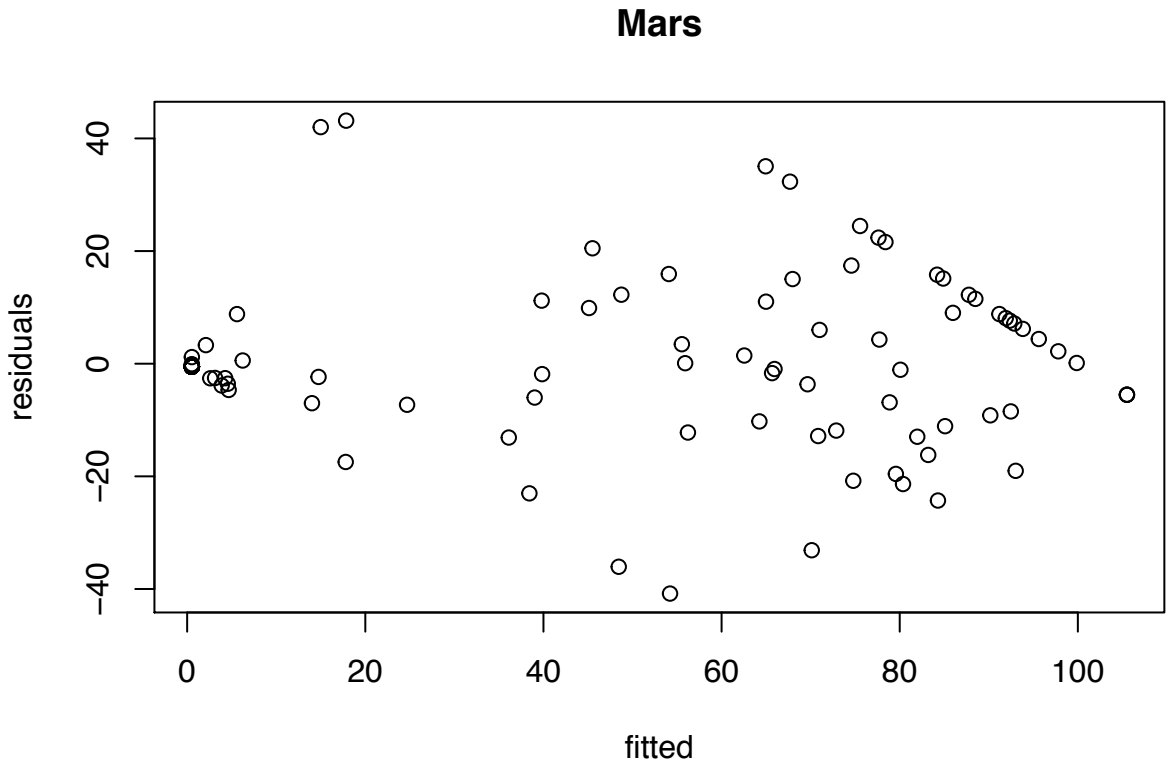
Predicting Ara h 6 in euro using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                coefficients
## (Intercept)       45.116274
## h(9.06-df[,3])    -4.921801
## h(df[,3]-9.06)     1.952038
##
## Selected 3 of 3 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 3 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 174.6791  RSS 19425.47  GRSq 0.8928979  RSq 0.899919  CVRSq 0.880836
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.00 sd 0.00    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 1.43    iter.rsq 0.289
##
## stddev of predictions:
```

Residuals vs Fitted

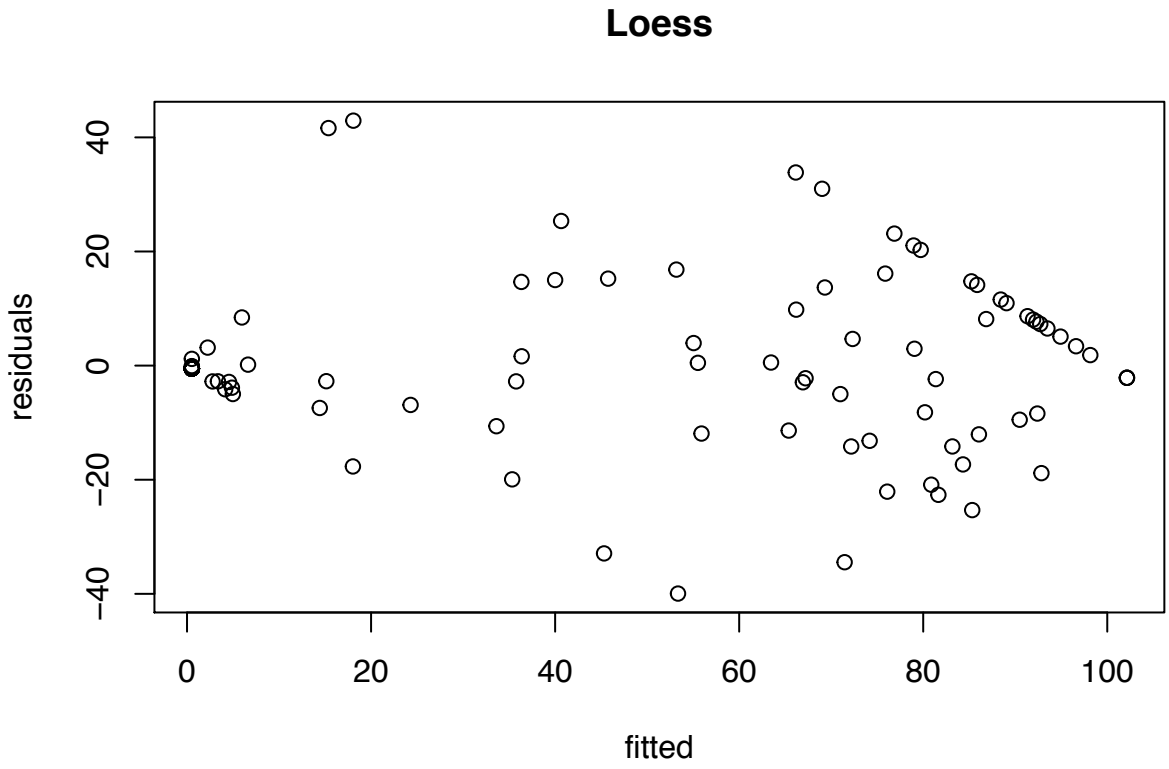


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 3.89
## Residual Standard Error: 12.88
## Trace of smoother matrix: 4.21  (exact)
##
## Control settings:
##   span     :  0.8243174
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



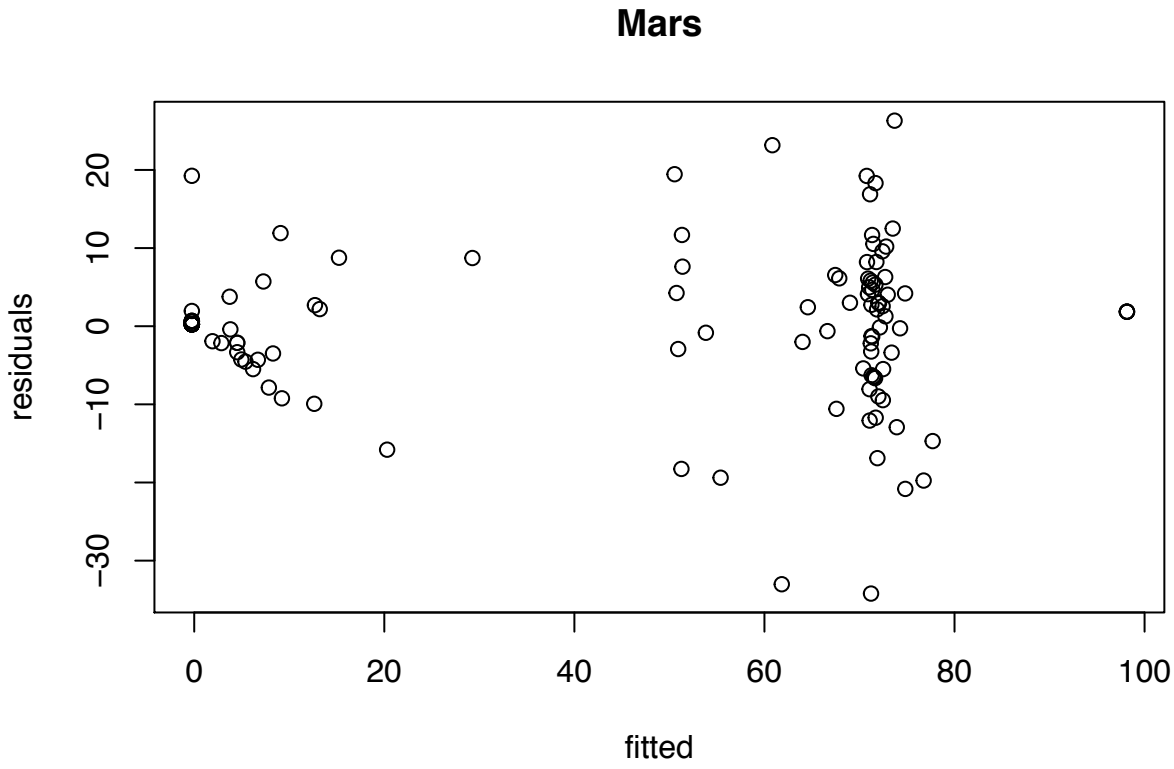
Predicting Ara h in euro using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)        50.545714
## h(7.02-df[,3])     -7.236030
## h(df[,3]-7.02)      1.139133
## h(df[,3]-28.33)    -1.651247
## h(df[,3]-36.25)     7.813482
##
## Selected 5 of 5 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 5 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 4 (additive model)
## GCV 102.9992  RSS 10677.86  GRSq 0.917556  RSq 0.9281821  CVRSq 0.9049471
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 4.53 sd 0.59    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.96    iter.rsq 0.224
##
## stddev of predictions:
```

Residuals vs Fitted

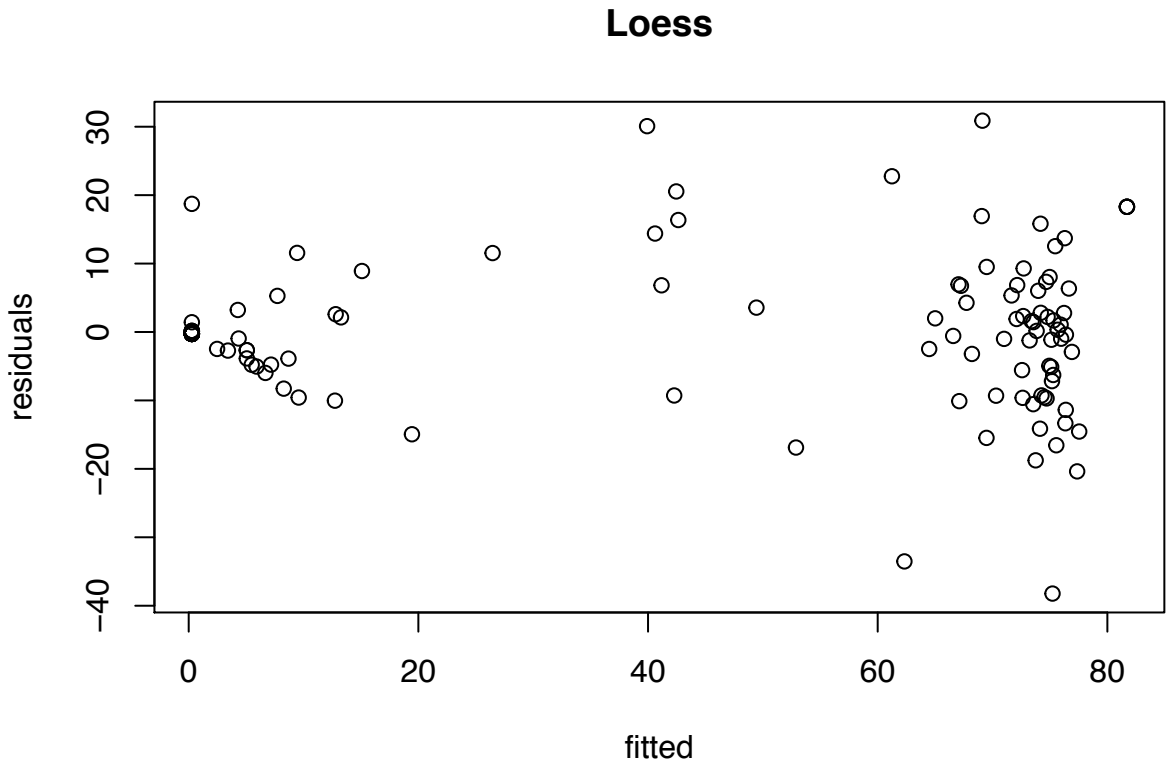


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 3.79
## Residual Standard Error: 10.71
## Trace of smoother matrix: 4.1  (exact)
##
## Control settings:
##   span     :  0.6755012
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



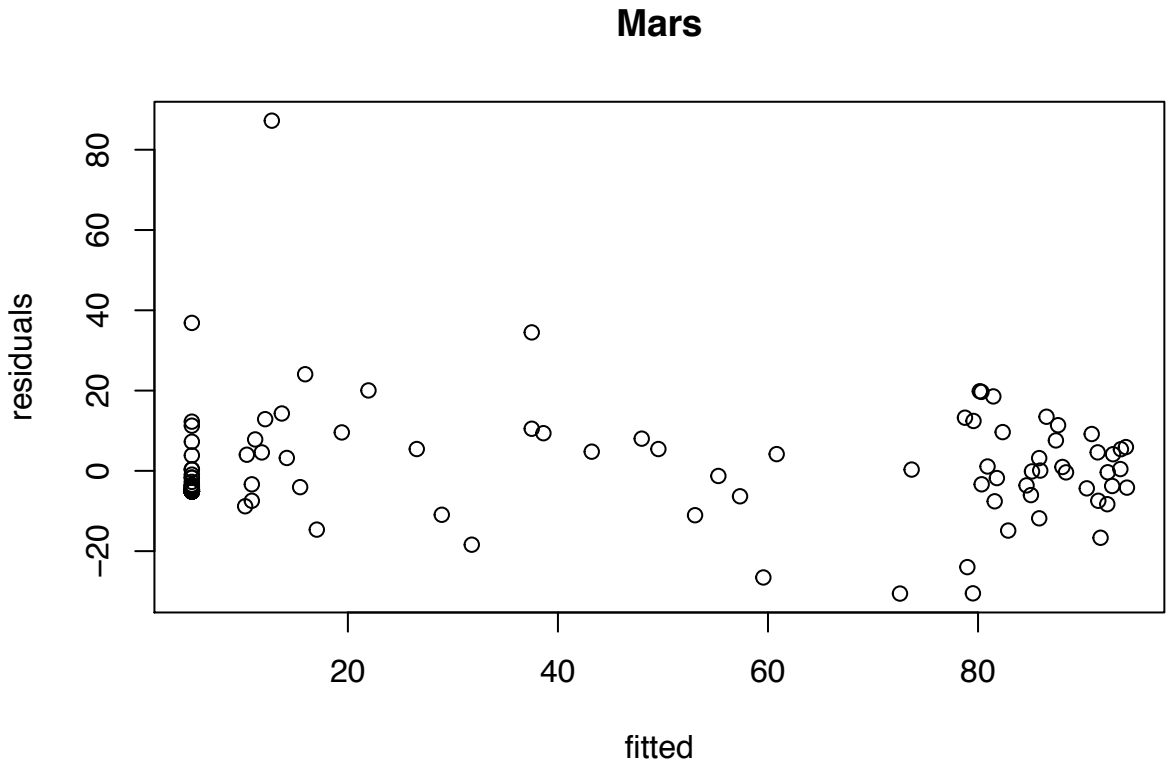
Predicting Jug r_nut in euro using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                coefficients
## (Intercept)       78.756003
## h(4.64-df[,3])   -15.864868
## h(df[,3]-4.64)     0.478688
##
## Selected 3 of 3 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 3 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 185.4365  RSS 20621.76  GRSq 0.8770022  RSq 0.8850654  CVRSq 0.8690115
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.75 sd 0.59    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 1.14    iter.rsq 0.019
##
## stddev of predictions:
```

Residuals vs Fitted

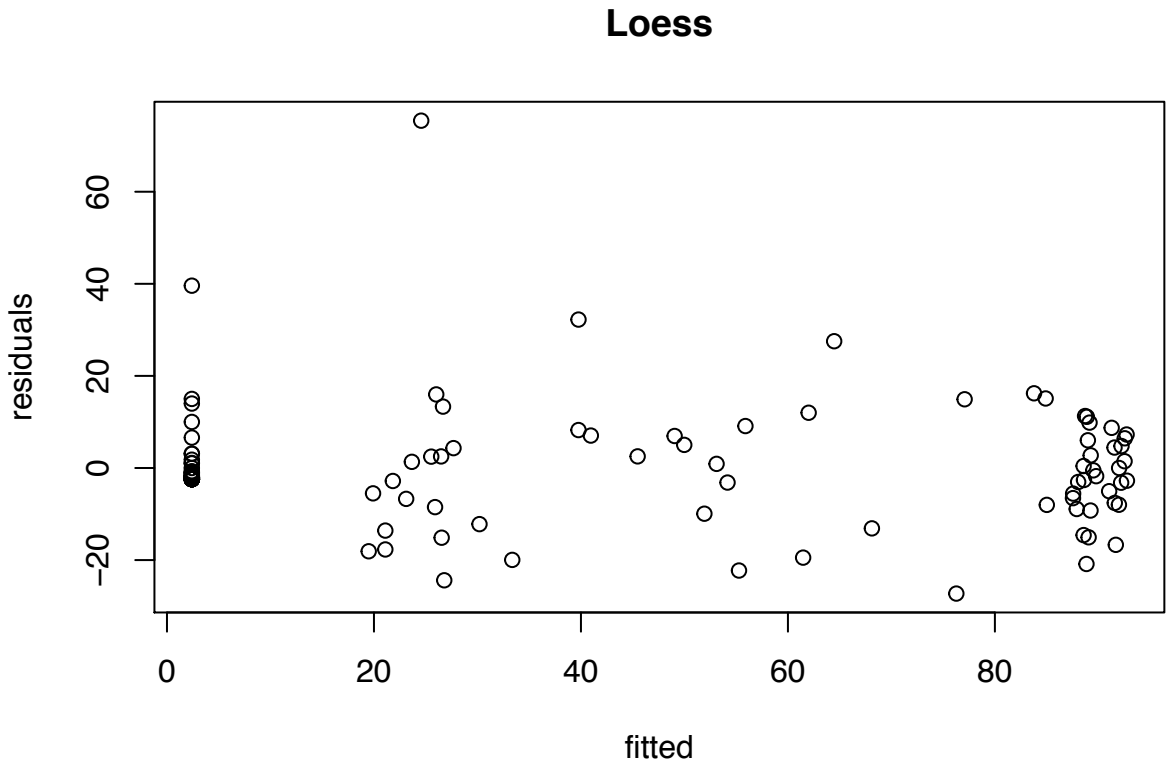


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 7.3
## Residual Standard Error: 12.65
## Trace of smoother matrix: 8.05  (exact)
##
## Control settings:
##   span     :  0.5638007
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



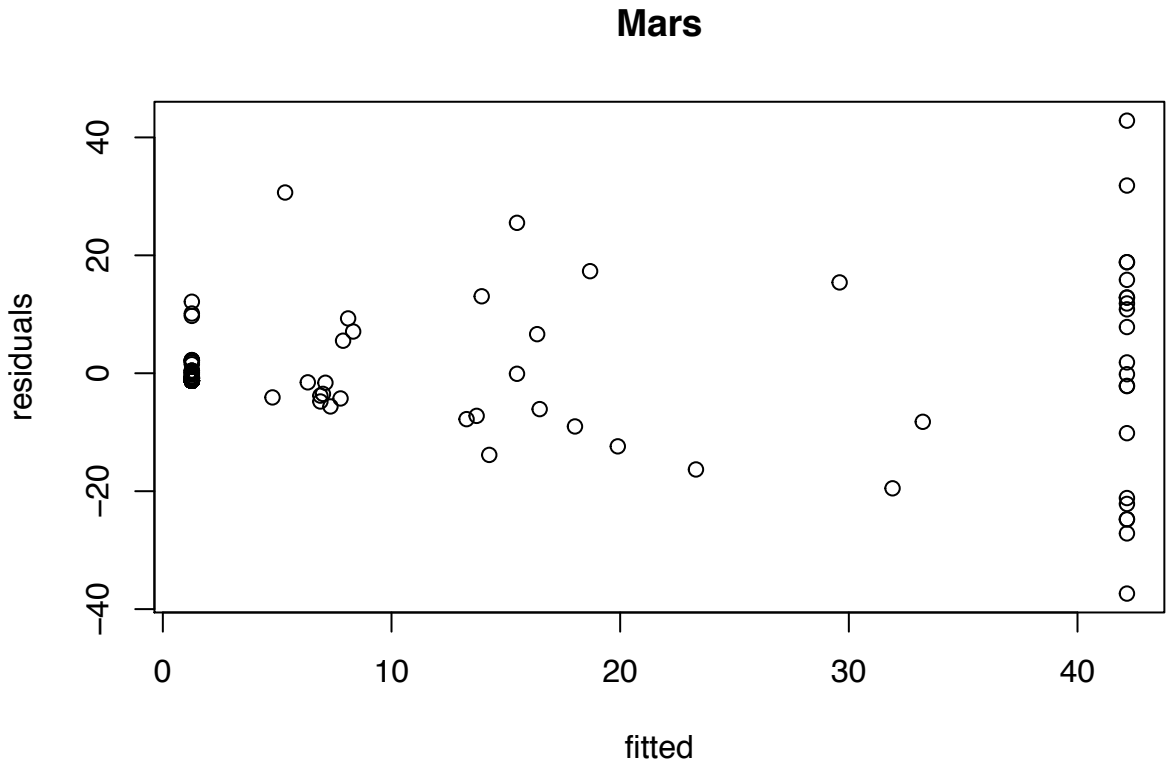
Predicting Pru du in euro using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                coefficients
## (Intercept)        42.16203
## h(3.71-df[,3])    -11.02264
##
## Selected 2 of 3 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 3 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 1 (additive model)
## GCV 115.069  RSS 13241.5  GRSq 0.6777615  RSq 0.6884132  CVRSq 0.5352571
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.40 sd 0.58    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.79    iter.rsq 0.370
##
## stddev of predictions:
```

Residuals vs Fitted

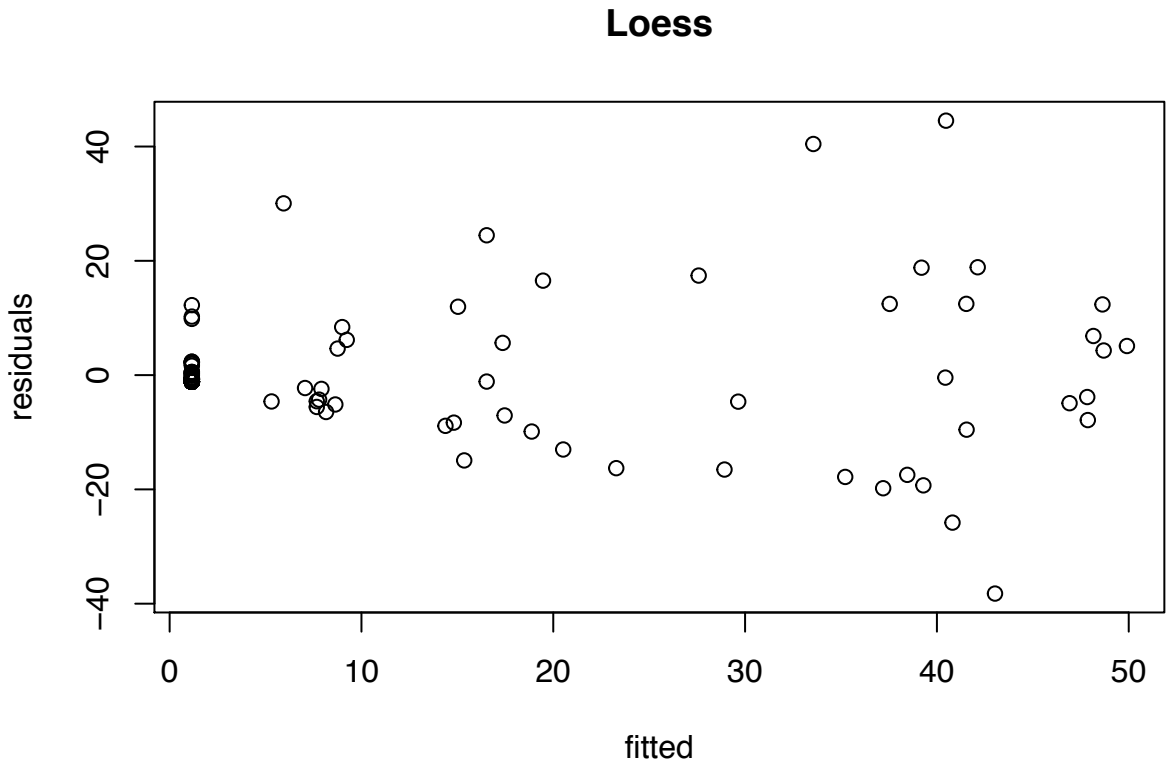


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 4.33
## Residual Standard Error: 10.52
## Trace of smoother matrix: 4.72  (exact)
##
## Control settings:
##   span     :  0.8832412
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



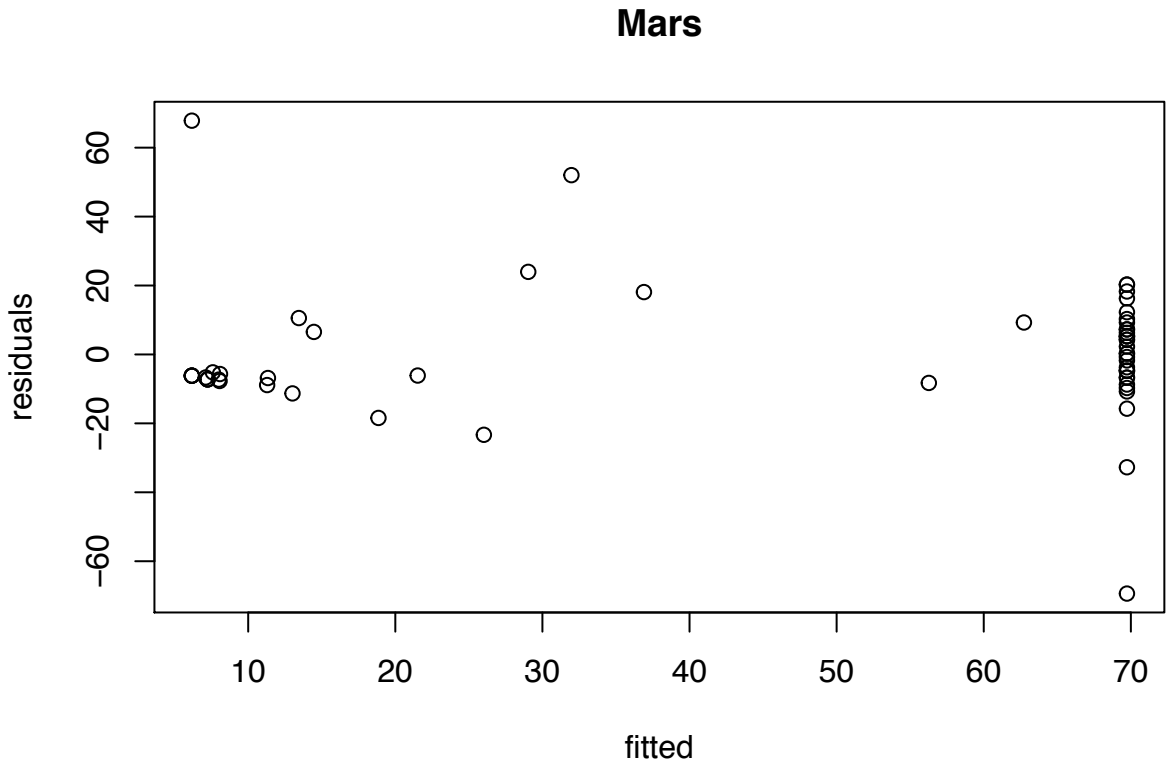
Predicting Ara h in euro using data from immunocap

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                coefficients
## (Intercept)       69.734852
## h(23.6-df[,3])    -2.693483
##
## Selected 2 of 4 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 4 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 1 (additive model)
## GCV 361.3175  RSS 18844.58  GRSq 0.6879335  RSq 0.7094487  CVRSq 0.5644079
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.00 sd 0.00    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 1.6    iter.rsq 0.005
##
## stddev of predictions:
```

Residuals vs Fitted

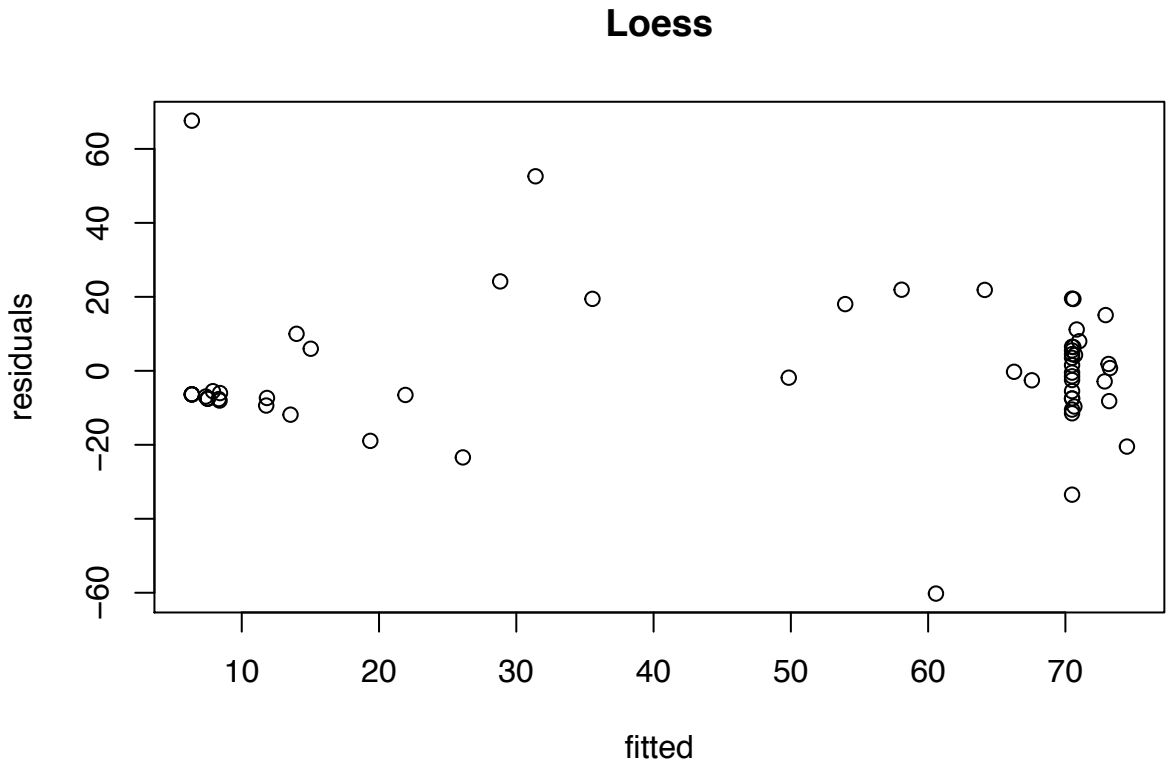


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 58
## Equivalent Number of Parameters: 3.57
## Residual Standard Error: 18.59
## Trace of smoother matrix: 3.85  (exact)
##
## Control settings:
##   span     :  0.8212092
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



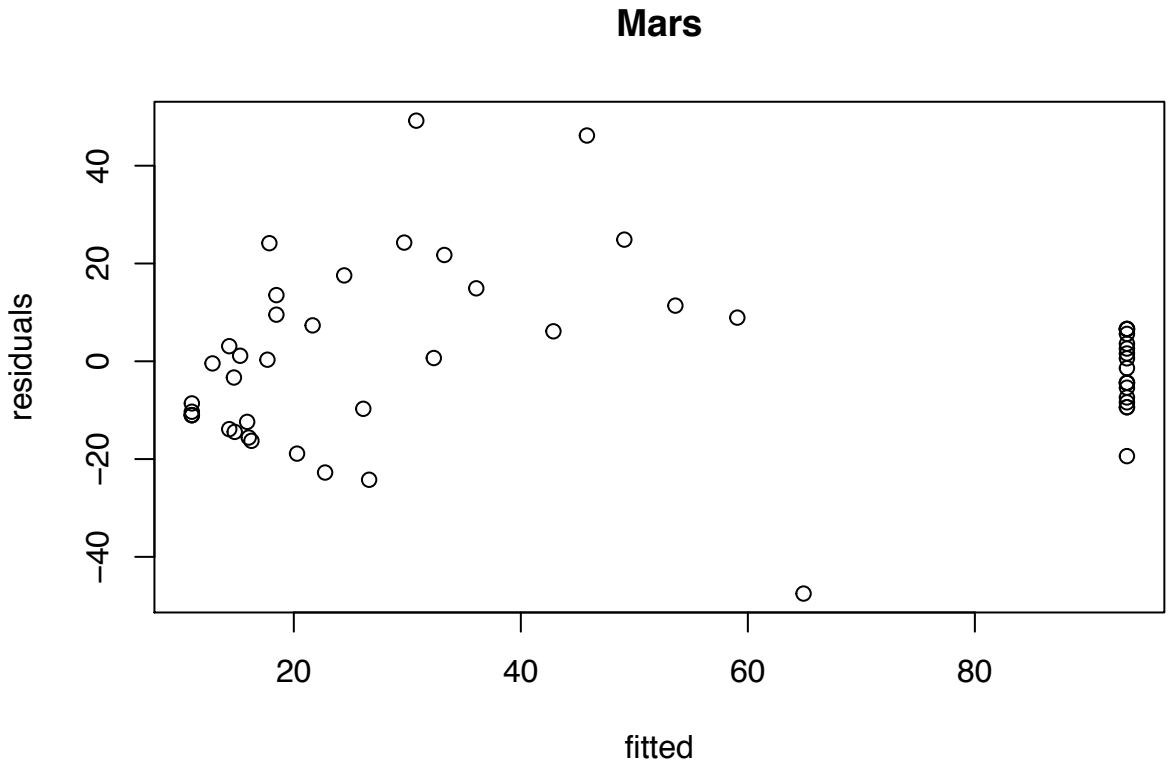
Predicting Jug r_nut in euro using data from immunocap

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##              coefficients
## (Intercept)     93.398877
## h(24-df[,3])    -3.432627
##
## Selected 2 of 3 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 3 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 1 (additive model)
## GCV 298.2103  RSS 14363.79  GRSq 0.8036548  RSq 0.8181937  CVRSq 0.7737503
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.13 sd 0.36    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 1.78    iter.rsq 0.115
##
## stddev of predictions:
```

Residuals vs Fitted

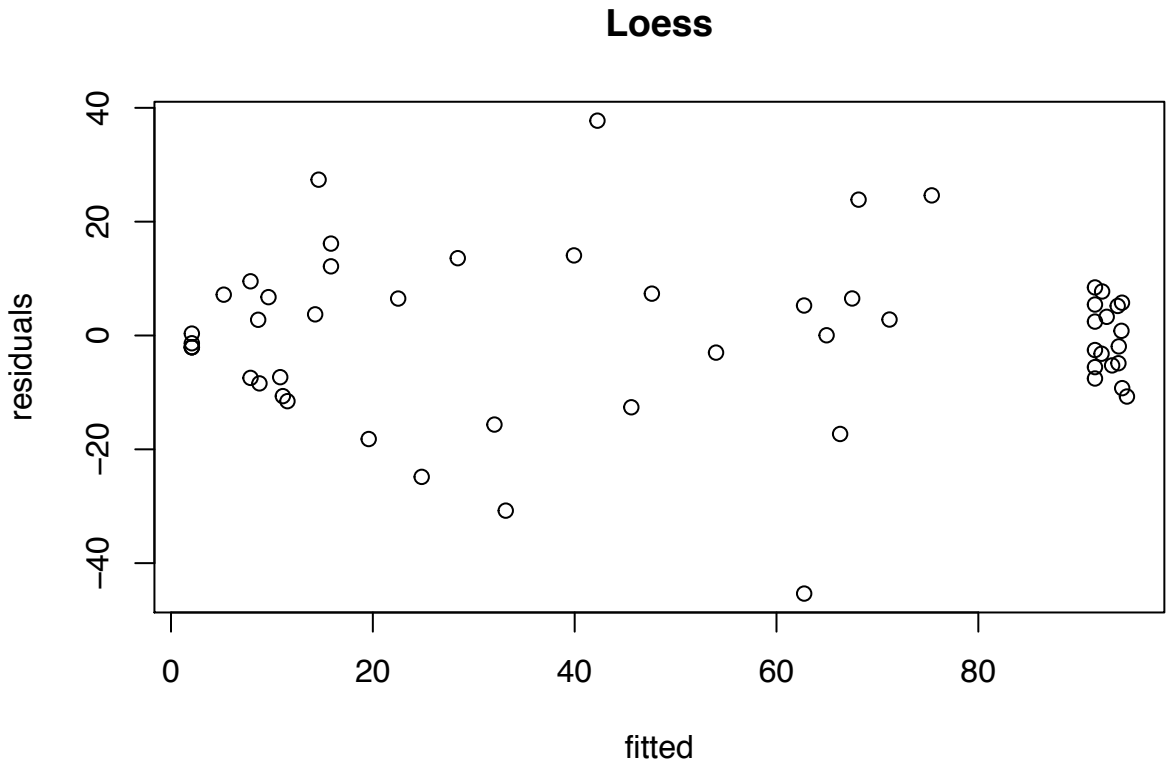


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 54
## Equivalent Number of Parameters: 6.02
## Residual Standard Error: 14.79
## Trace of smoother matrix: 6.64  (exact)
##
## Control settings:
##   span     :  0.5935193
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



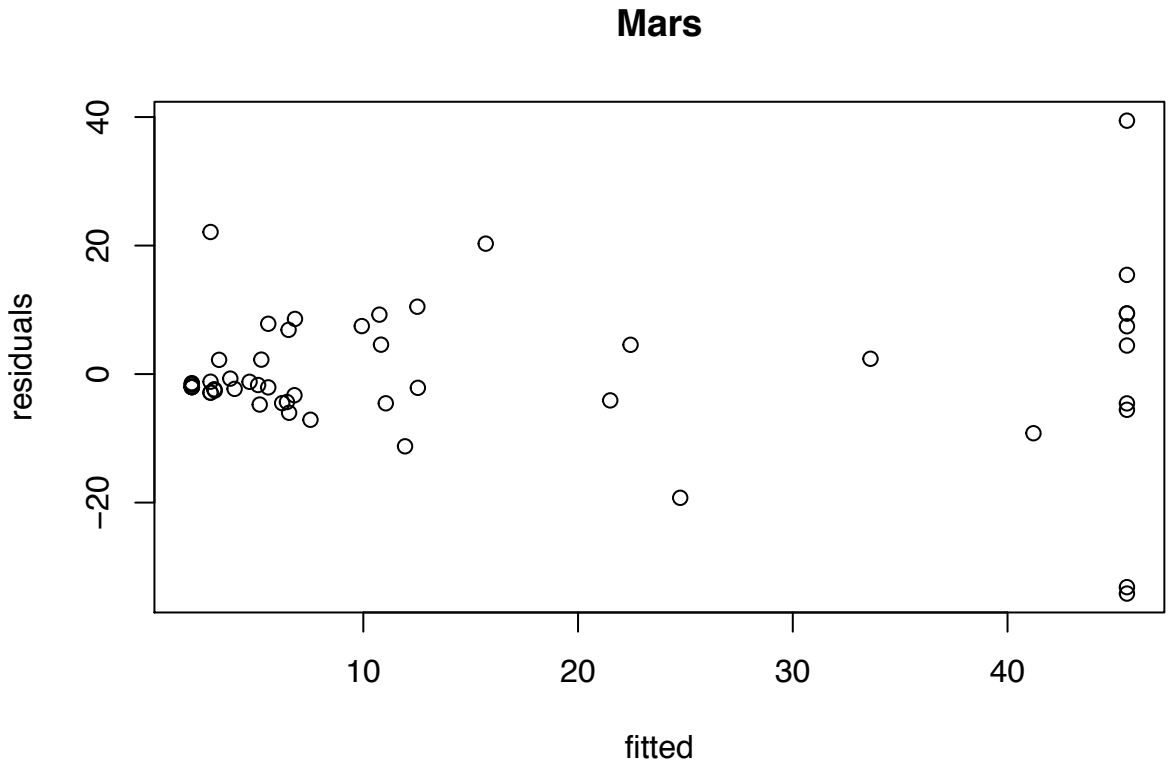
Predicting Pru du in euro using data from immunocap

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                coefficients
## (Intercept)       45.561166
## h(17.5-df[,3])    -2.488334
##
## Selected 2 of 3 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 3 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 1 (additive model)
## GCV 137.3785  RSS 6617.065  GRSq 0.6614717  RSq 0.686539  CVRSq 0.4717474
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.20 sd 0.40    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 1.04    iter.rsq 0.199
##
## stddev of predictions:
```

Residuals vs Fitted

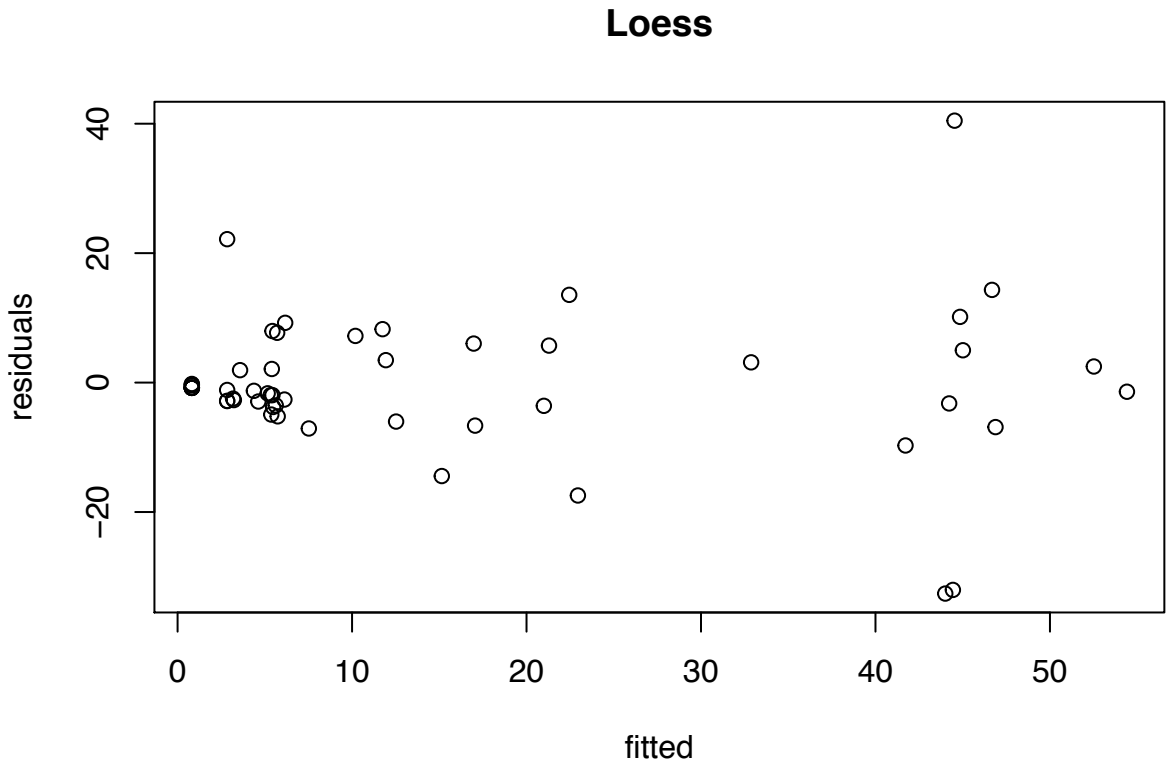


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 54
## Equivalent Number of Parameters: 7.38
## Residual Standard Error: 11.65
## Trace of smoother matrix: 8.15  (exact)
##
## Control settings:
##   span     :  0.6070803
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



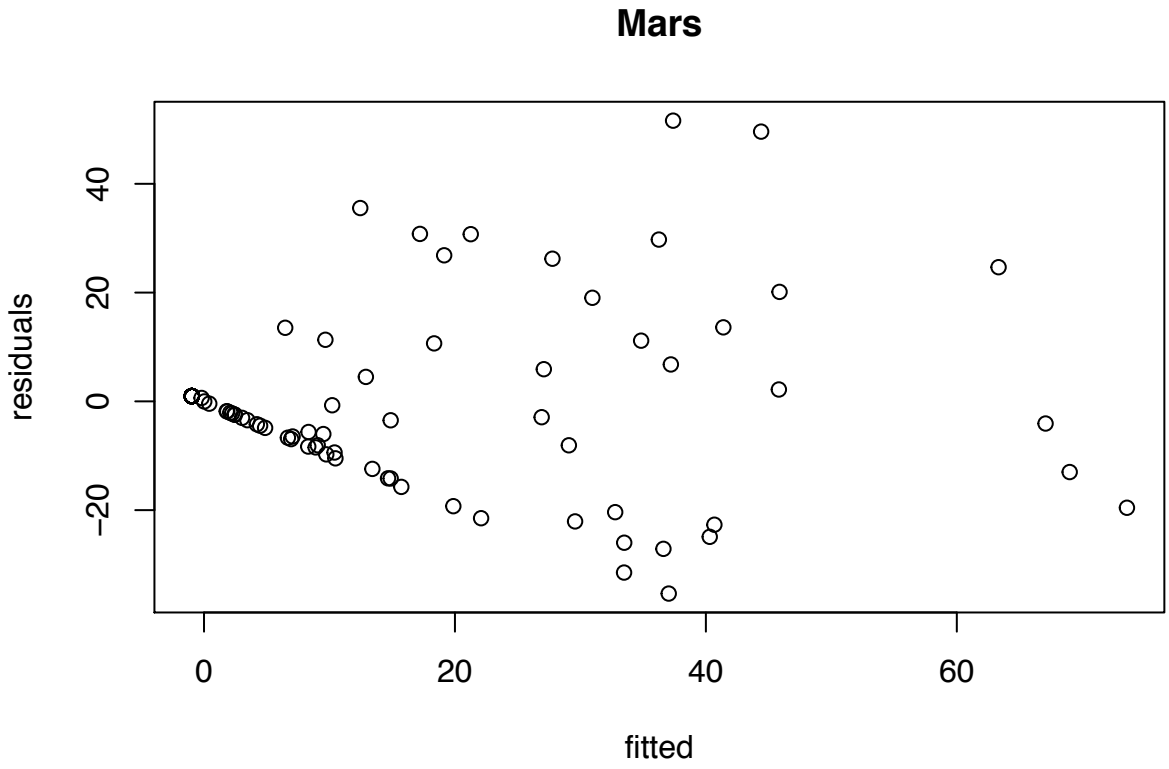
Predicting Ara h 1 in euro using data from medall

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)       26.9127834
## h(11.84-df[,3])   -2.3549200
## h(df[,3]-11.84)    0.6605553
##
## Selected 3 of 4 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 4 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 194.5349  RSS 21633.57  GRSq 0.5999518  RSq 0.6261772  CVRSq 0.4297332
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.95 sd 0.37    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 1.03    iter.rsq 0.719
##
## stddev of predictions:
```

Residuals vs Fitted

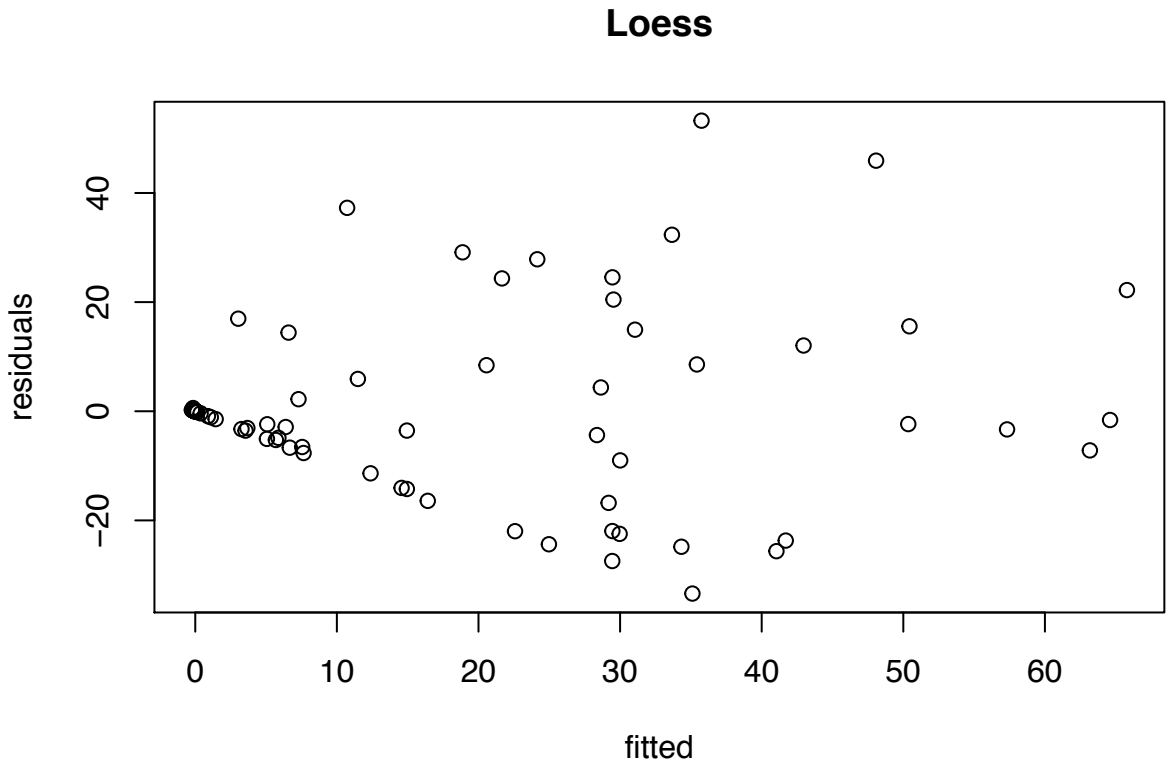


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 5.79
## Residual Standard Error: 13.15
## Trace of smoother matrix: 6.36  (exact)
##
## Control settings:
##   span     :  0.737706
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



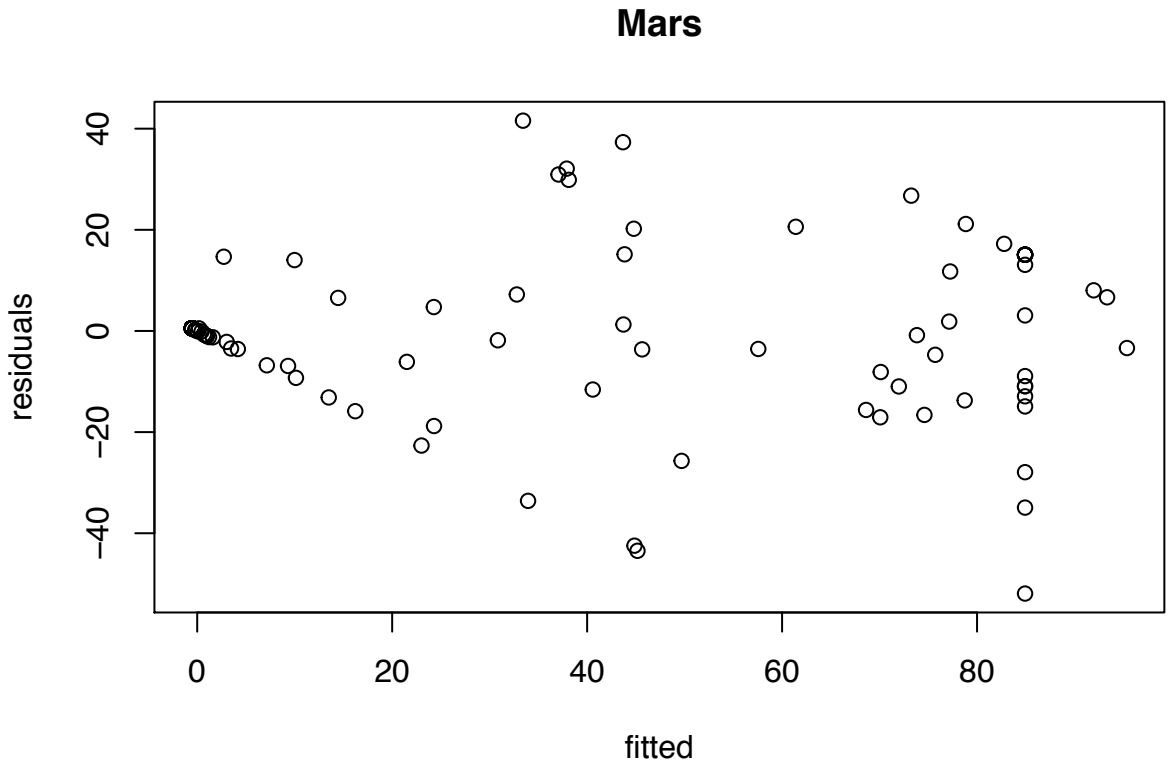
Predicting Ara h 2 in euro using data from medall

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)        65.015455
## h(df[,3]-41.61)     1.739956
## h(59.06-df[,3])    -1.110154
## h(df[,3]-59.06)    -3.380973
## h(df[,3]-74.48)     2.222934
##
## Selected 5 of 5 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 5 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 4 (additive model)
## GCV 244.5781  RSS 25355.27  GRSq 0.837387  RSq 0.858346  CVRSq 0.8083795
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.71 sd 0.85    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 1.45    iter.rsq 0.423
##
## stddev of predictions:
```

Residuals vs Fitted

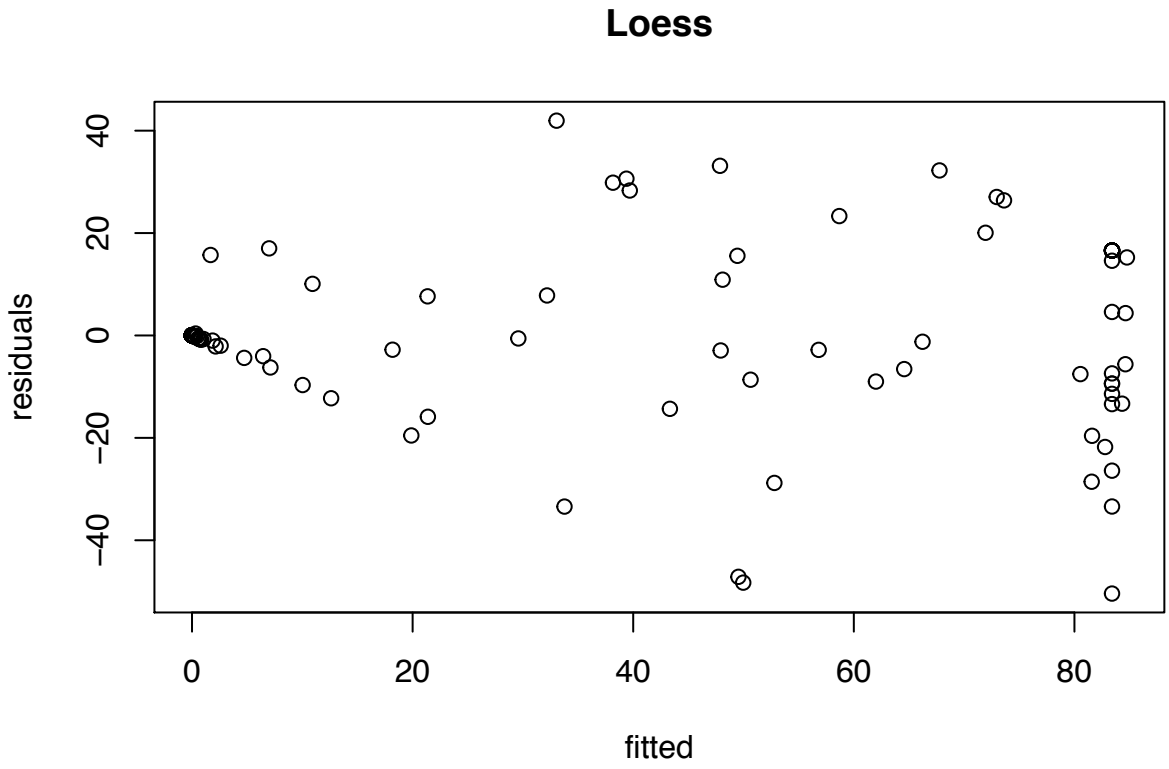


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 4.17
## Residual Standard Error: 15.53
## Trace of smoother matrix: 4.54  (exact)
##
## Control settings:
##   span     :  0.7495663
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



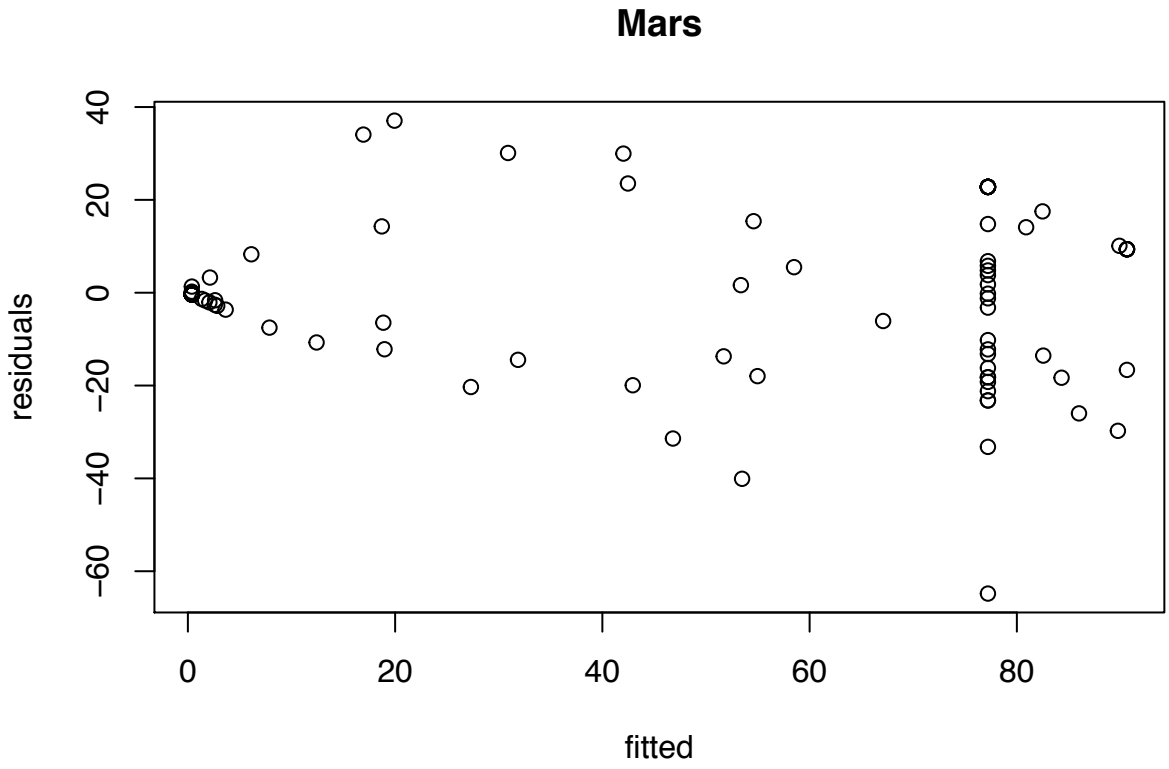
Predicting Ara h 6 in euro using data from medall

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)        77.209237
## h(26.36-df[,3])    -2.914554
## h(df[,3]-78.49)     0.623722
##
## Selected 3 of 4 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 4 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 257.5664  RSS 28643.09  GRSq 0.8420766  RSq 0.8524294  CVRSq 0.8249826
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.52 sd 0.51    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 1.74    iter.rsq 0.480
##
## stddev of predictions:
```

Residuals vs Fitted

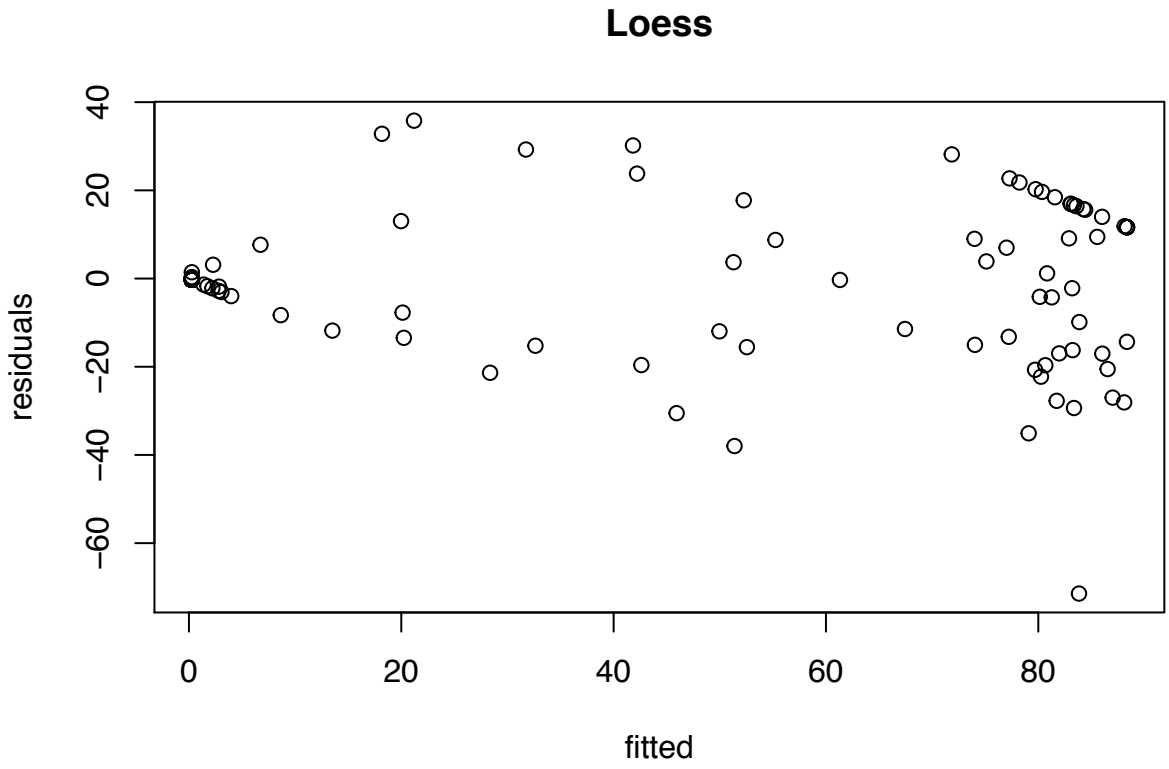


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 4.44
## Residual Standard Error: 15.72
## Trace of smoother matrix: 4.84  (exact)
##
## Control settings:
##   span     :  0.7192077
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



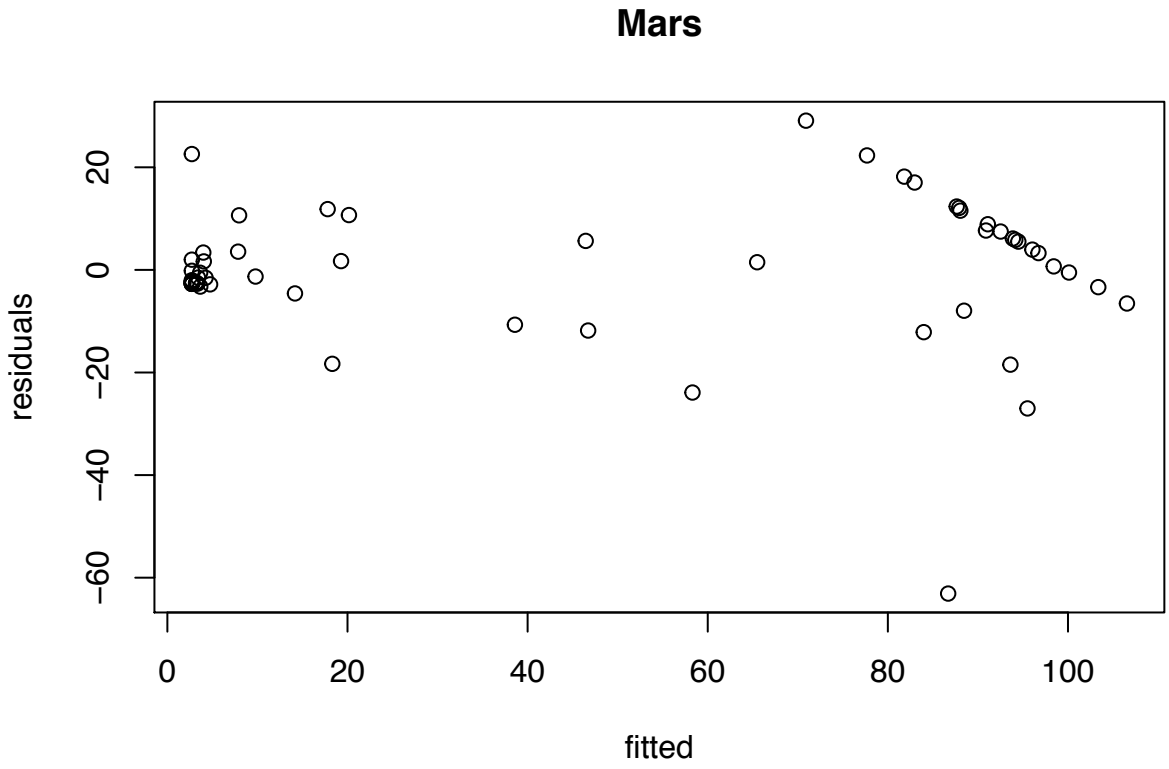
Predicting Ara h in immunocap using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)        20.161042
## h(24.45-df[,3])    -0.713461
## h(df[,3]-24.45)     6.775478
##
## Selected 3 of 8 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 8 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 211.8387  RSS 10259.57  GRSq 0.8895964  RSq 0.904548  CVRSq 0.8566773
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.02 sd 1.05    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 1.32    iter.rsq 0.207
##
## stddev of predictions:
```

Residuals vs Fitted

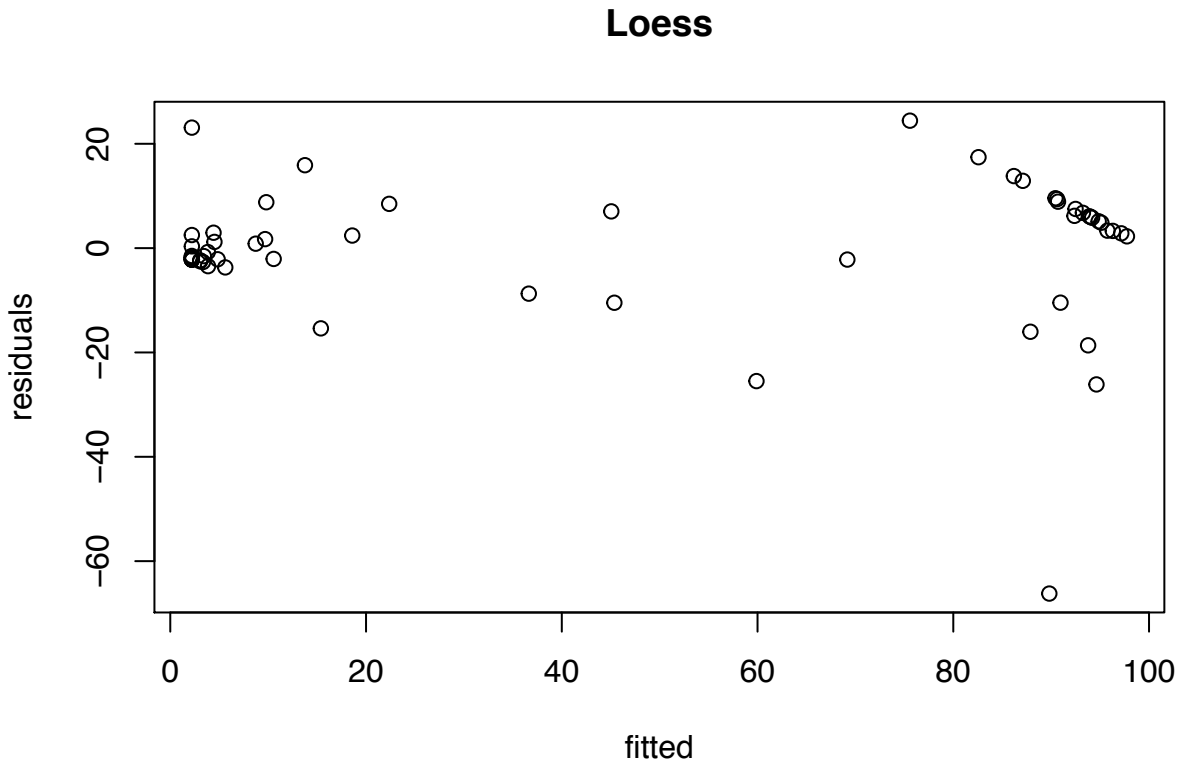


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 58
## Equivalent Number of Parameters: 5.34
## Residual Standard Error: 13.78
## Trace of smoother matrix: 5.87  (exact)
##
## Control settings:
##   span     :  0.5249219
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



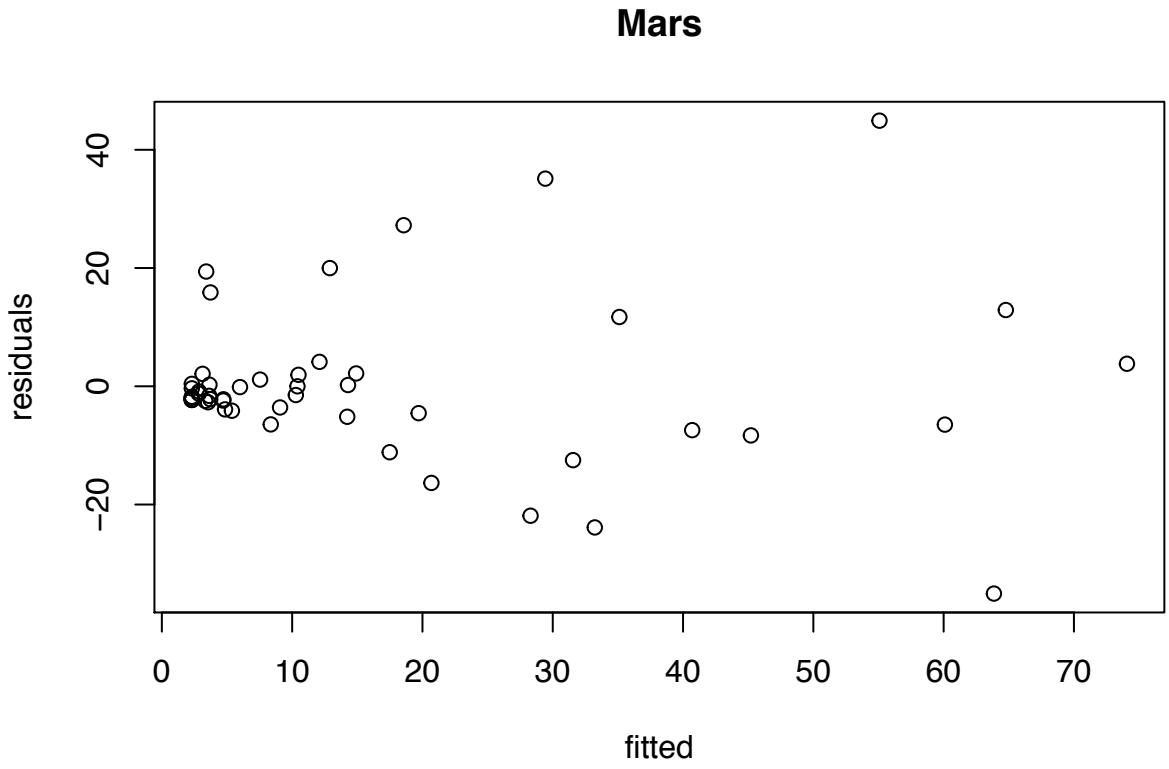
Predicting Cor a_hazel in immunocap using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)        46.045272
## h(df[,3]-18.84)    -5.896175
## h(df[,3]-24.37)    11.599809
## h(28.17-df[,3])    -1.552875
##
## Selected 4 of 6 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 6 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 3 (additive model)
## GCV 225.6549  RSS 8566.036  GRSq 0.5901252  RSq 0.682593  CVRSq 0.1973956
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.06 sd 0.76    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 1.32    iter.rsq 0.237
##
## stddev of predictions:
```

Residuals vs Fitted

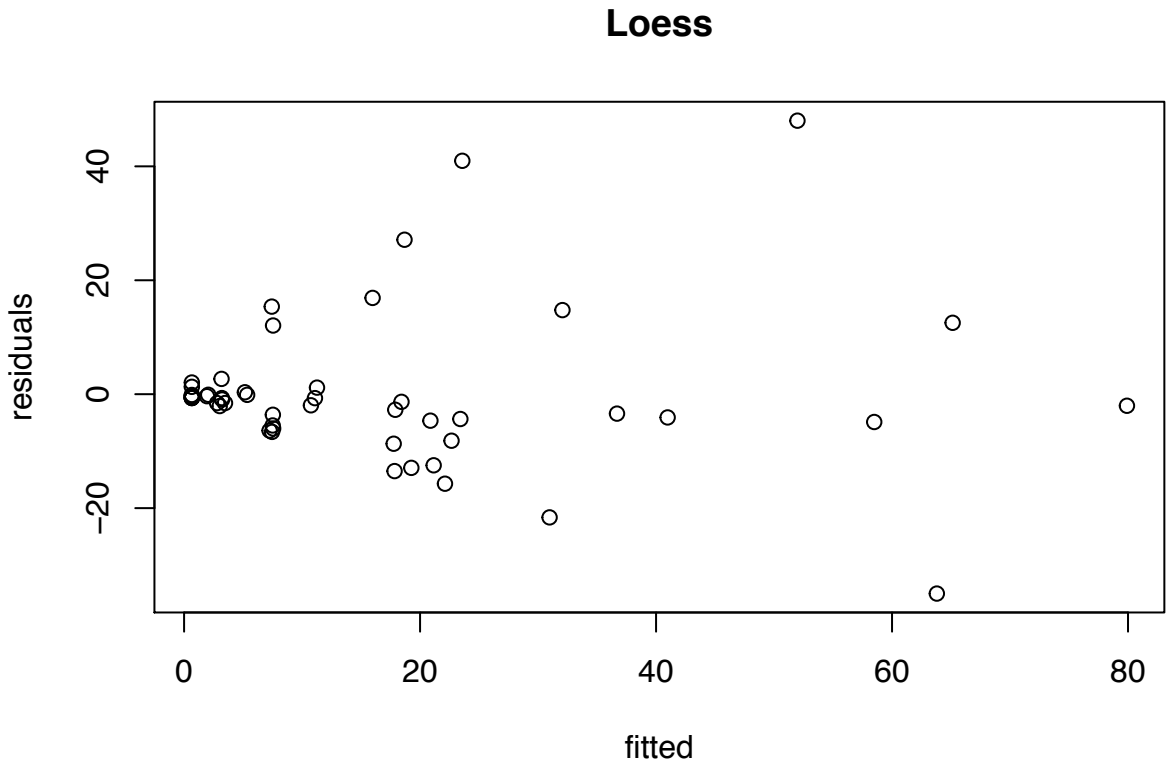


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 51
## Equivalent Number of Parameters: 9.31
## Residual Standard Error: 14.76
## Trace of smoother matrix: 10.29  (exact)
##
## Control settings:
##   span     :  0.3868596
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



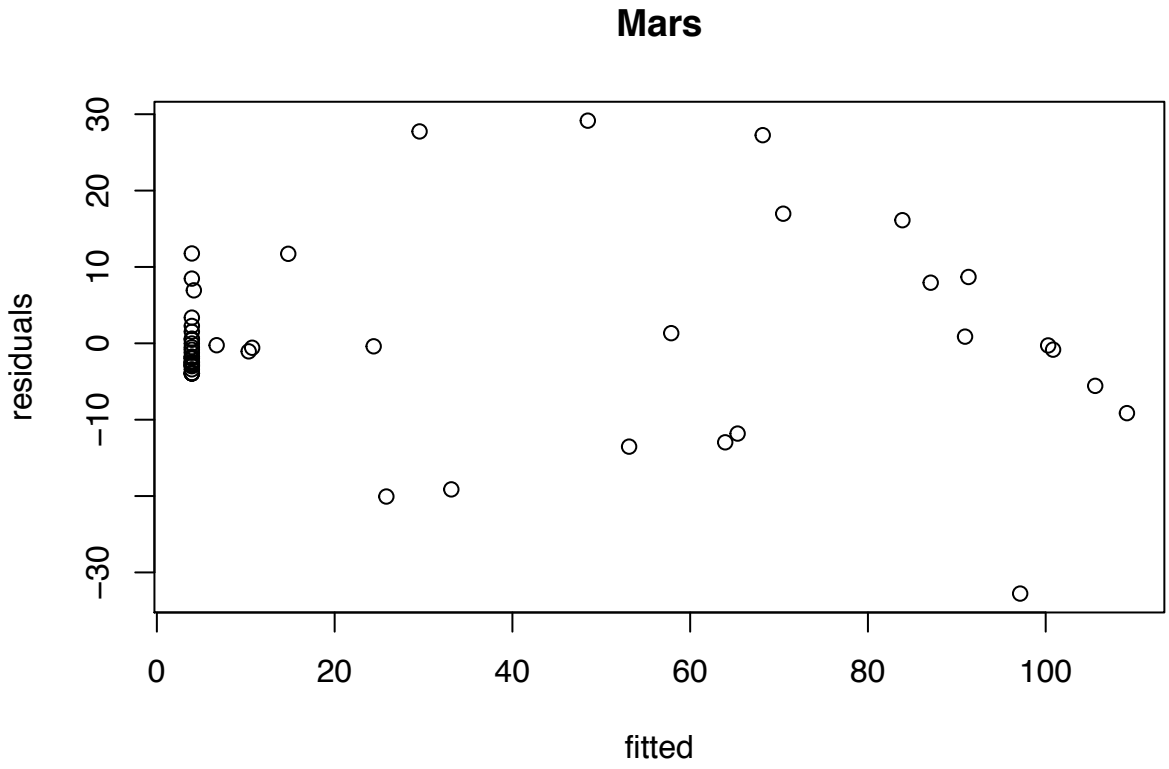
Predicting Jug r_nut in immunocap using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                coefficients
## (Intercept)        3.934326
## h(df[,3]-4.25)     3.247127
##
## Selected 2 of 5 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 5 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 1 (additive model)
## GCV 126.2553  RSS 6081.298  GRSq 0.9126706  RSq 0.9191371  CVRSq 0.85004
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.68 sd 0.66    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 1.08    iter.rsq 0.283
##
## stddev of predictions:
```

Residuals vs Fitted

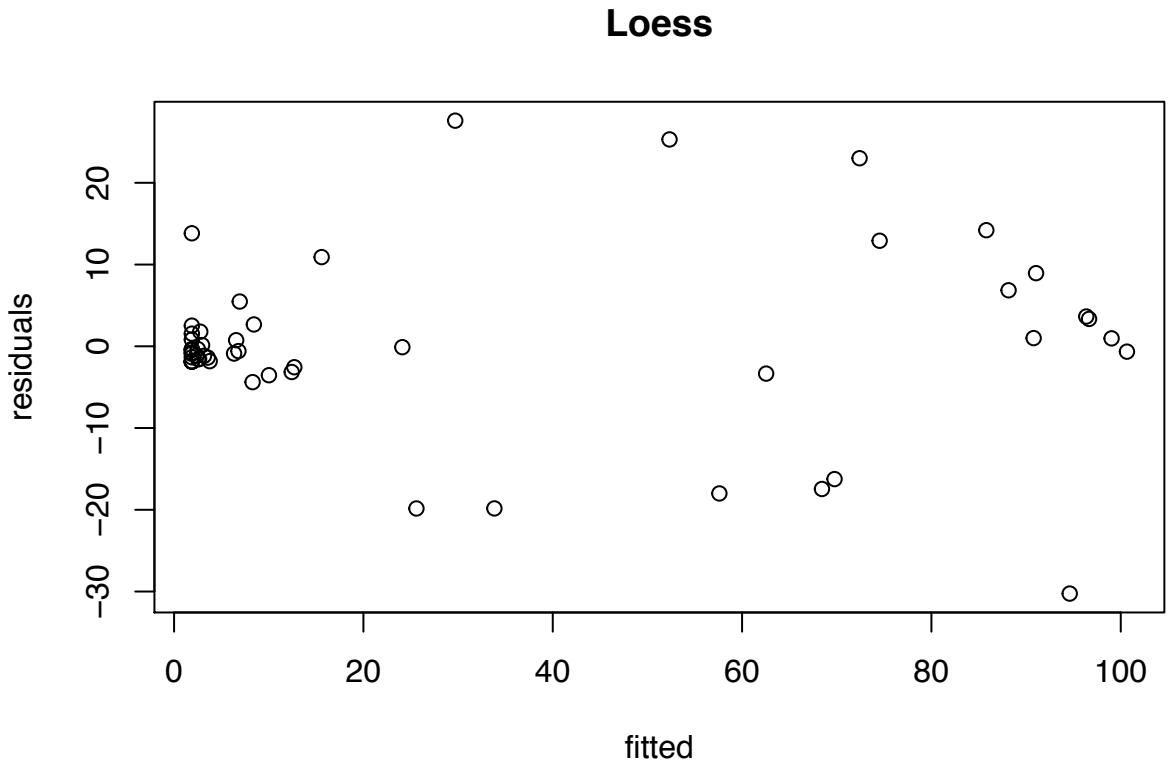


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 54
## Equivalent Number of Parameters: 4.18
## Residual Standard Error: 10.59
## Trace of smoother matrix: 4.56  (exact)
##
## Control settings:
##   span     :  0.7383049
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



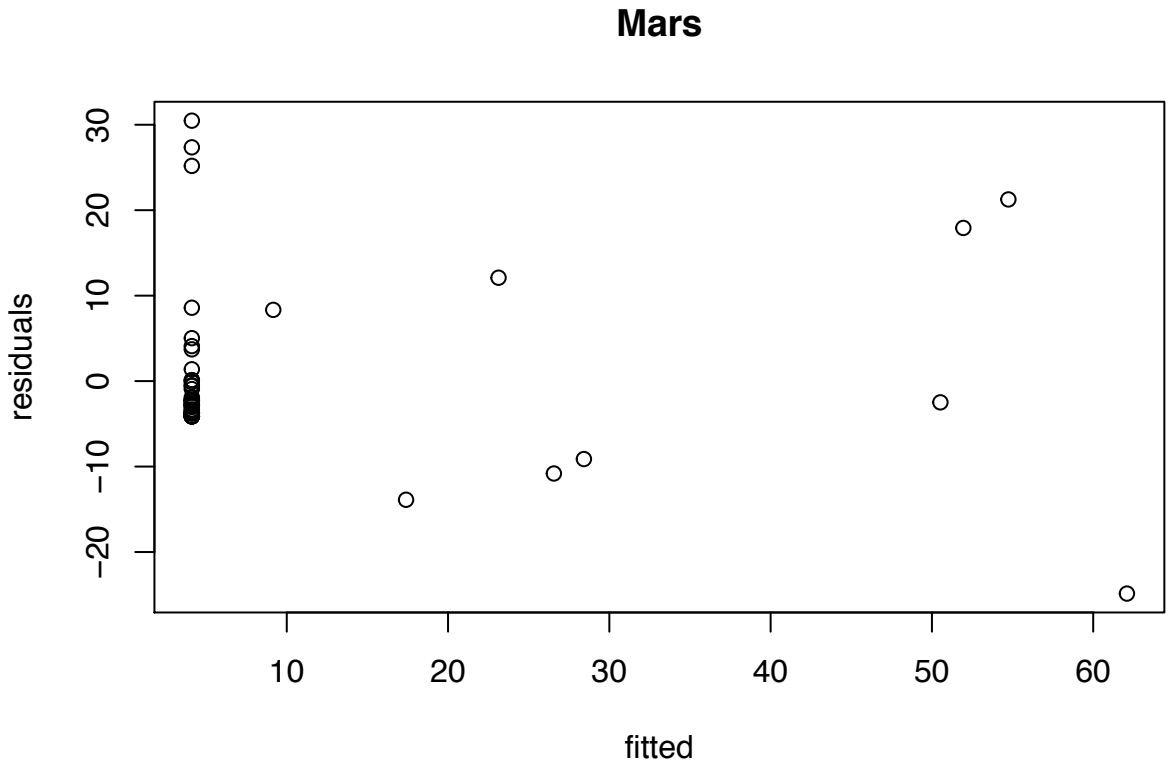
Predicting Pru du in immunocap using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                coefficients
## (Intercept)        4.115087
## h(df[,3]-4.19)     4.900859
##
## Selected 2 of 3 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 3 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 1 (additive model)
## GCV 99.76627  RSS 4805.409  GRSq 0.6609166  RSq 0.686025  CVRSq 0.0532337
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.17 sd 0.39    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.866    iter.rsq 0.047
##
## stddev of predictions:
```

Residuals vs Fitted

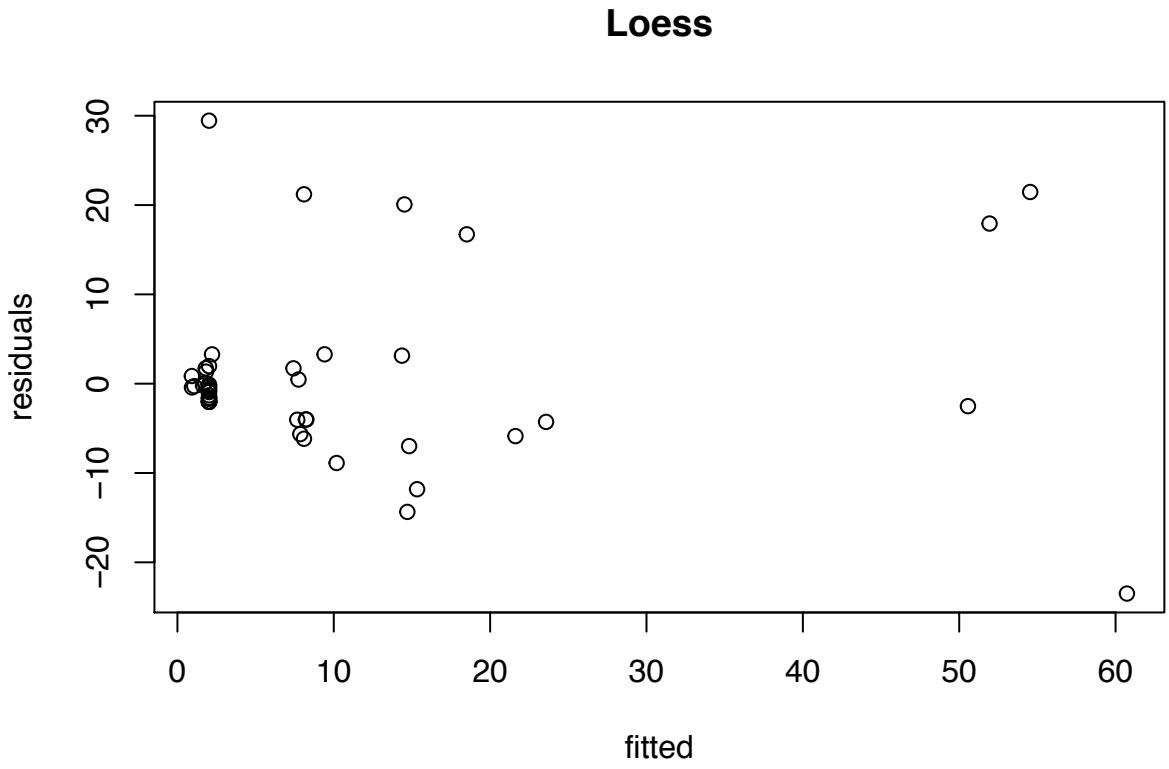


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 54
## Equivalent Number of Parameters: 6.99
## Residual Standard Error: 9.467
## Trace of smoother matrix: 7.71  (exact)
##
## Control settings:
##   span     :  0.525159
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



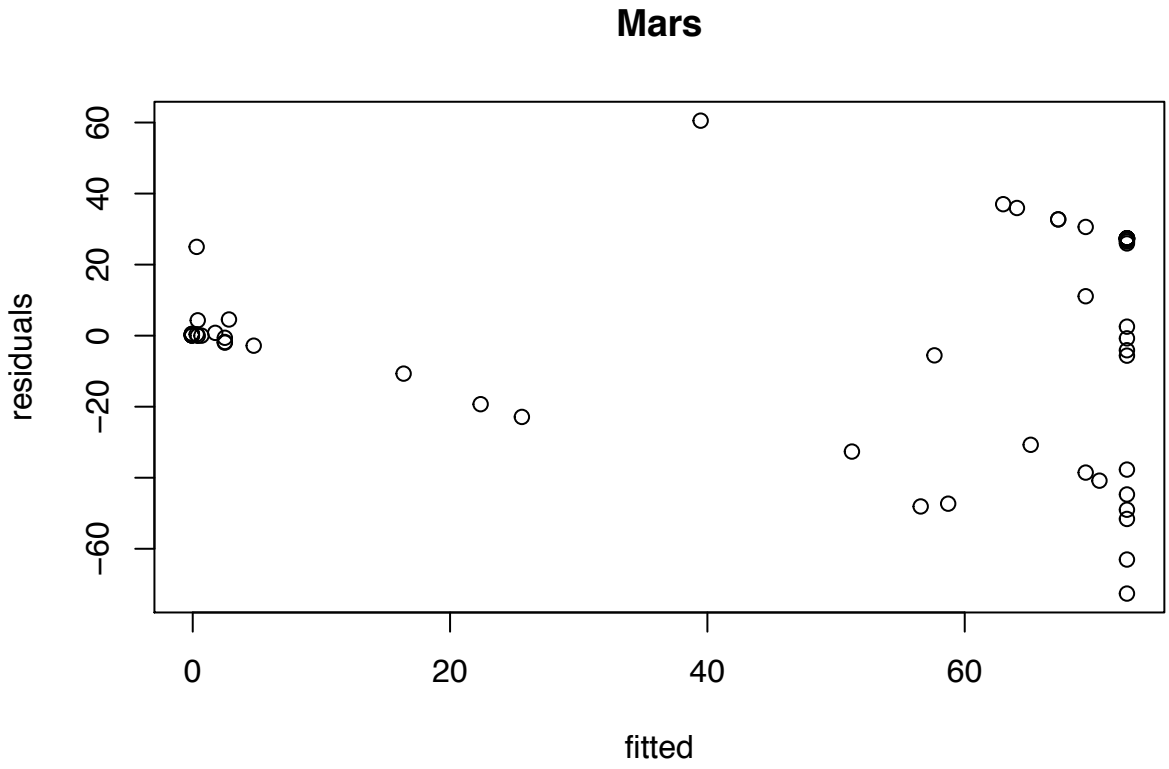
Predicting Ara h in immunocap using data from euro

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##              coefficients
## (Intercept)     72.606772
## h(68-df[,3])    -1.068753
##
## Selected 2 of 6 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 6 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 1 (additive model)
## GCV 926.7083  RSS 48332.63  GRSq 0.5170292  RSq 0.5503273  CVRSq 0.4059956
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.18 sd 0.51    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 3.06    iter.rsq 0.534
##
## stddev of predictions:
```

Residuals vs Fitted

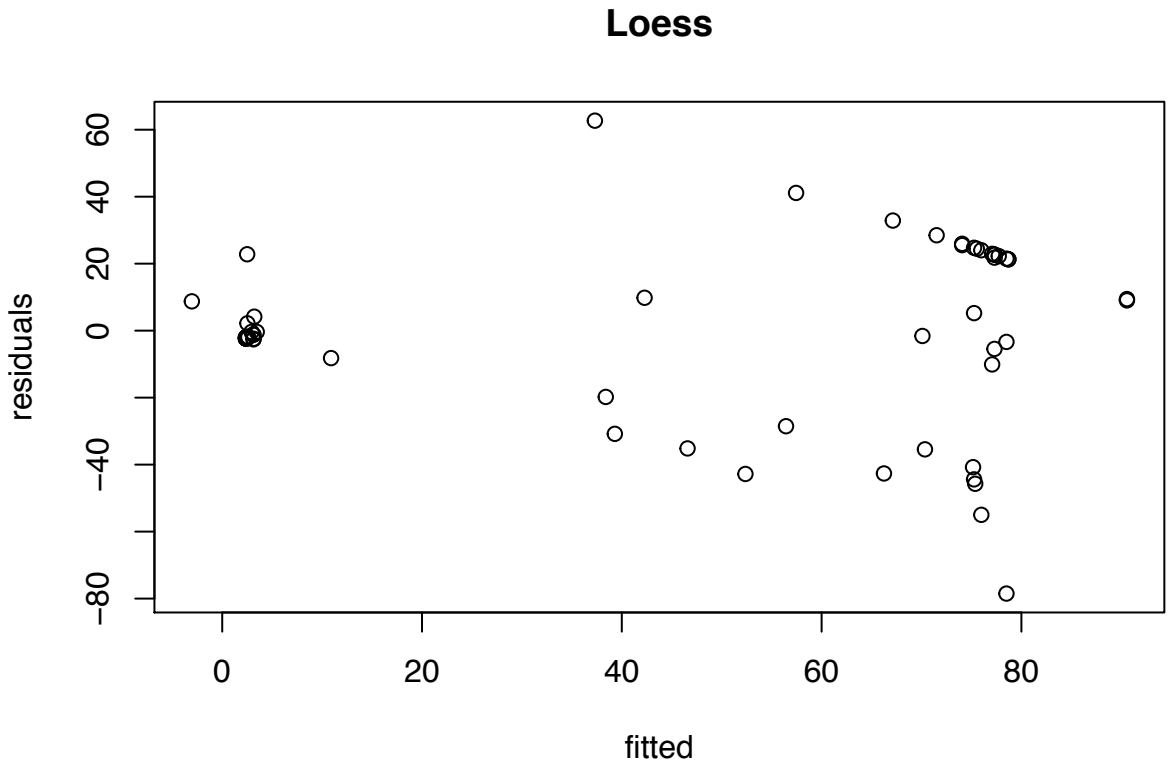


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 58
## Equivalent Number of Parameters: 8.27
## Residual Standard Error: 28.48
## Trace of smoother matrix: 9.14  (exact)
##
## Control settings:
##   span     :  0.3923638
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



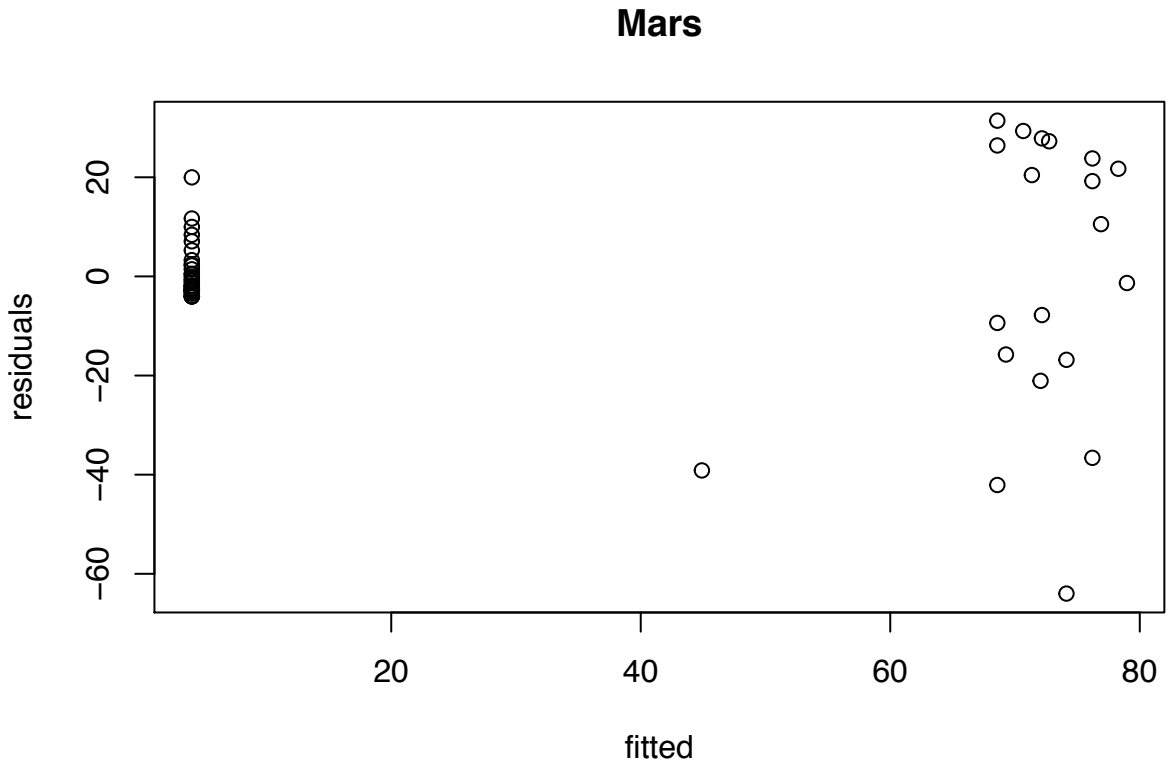
Predicting Jug r_nut in immunocap using data from euro

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##              coefficients
## (Intercept)      4.017351
## h(df[,3]-74)     6.814187
## h(df[,3]-85)    -7.506918
##
## Selected 3 of 6 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 6 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 378.8567  RSS 16845.09  GRSq 0.7379489  RSq 0.7760112  CVRSq 0.3361519
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.01 sd 0.39    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 1.69    iter.rsq 0.279
##
## stddev of predictions:
```

Residuals vs Fitted

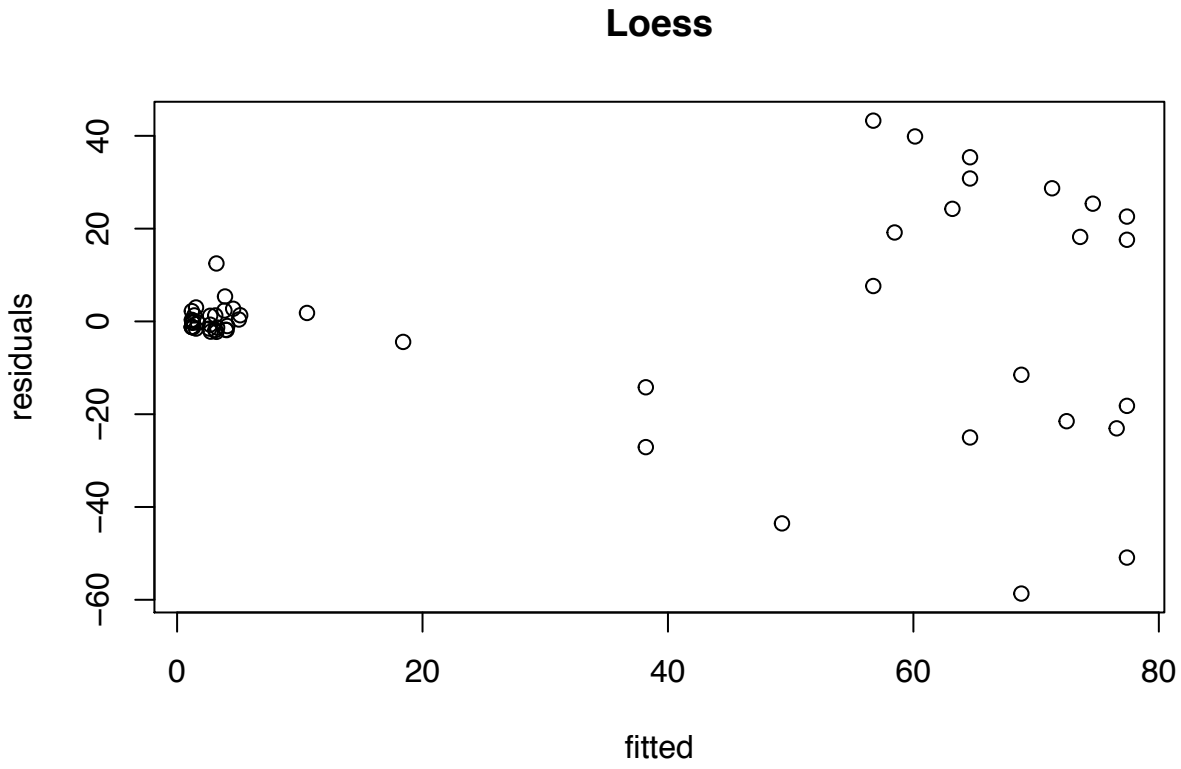


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 54
## Equivalent Number of Parameters: 4.63
## Residual Standard Error: 20.57
## Trace of smoother matrix: 5.07  (exact)
##
## Control settings:
##   span     :  0.6035119
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



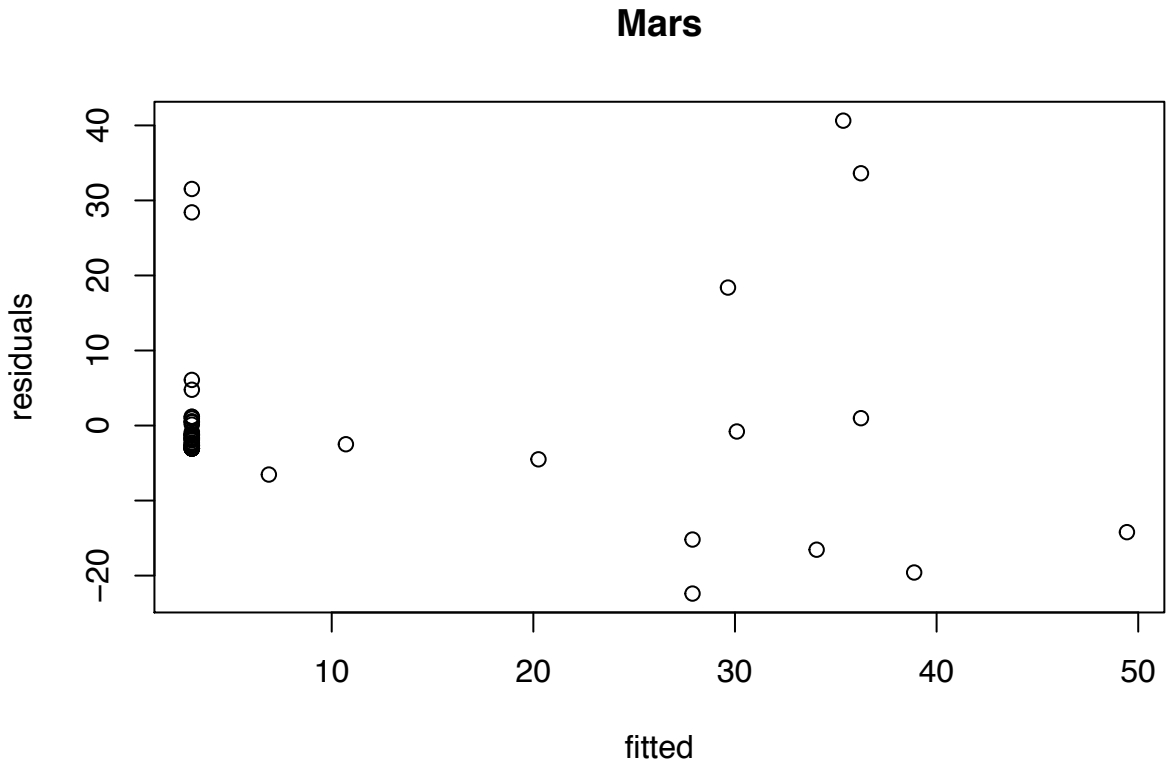
Predicting Pru du in immunocap using data from euro

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##              coefficients
## (Intercept)      3.061984
## h(df[,3]-23)     1.910157
## h(df[,3]-36)    -1.470419
##
## Selected 3 of 4 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 4 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 153.2345  RSS 6813.258  GRSq 0.4791901  RSq 0.5548364  CVRSq -0.2261777
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.35 sd 0.52    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.977    iter.rsq 0.084
##
## stddev of predictions:
```

Residuals vs Fitted

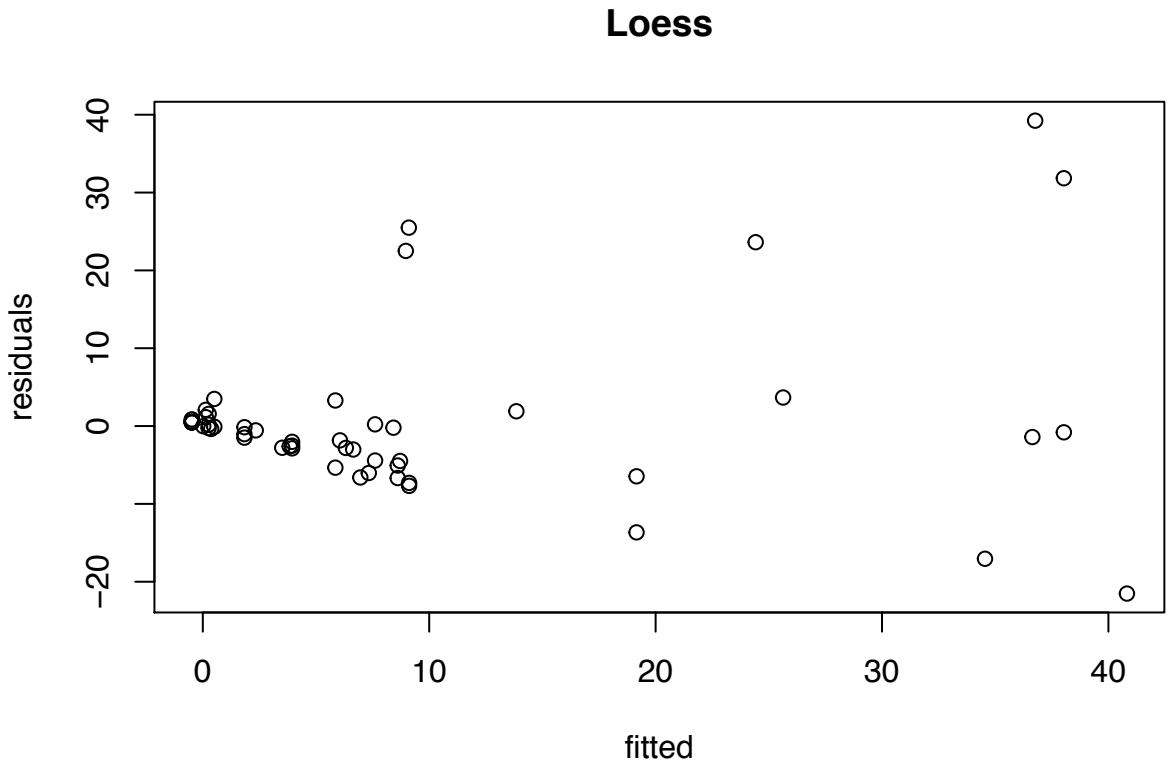


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 54
## Equivalent Number of Parameters: 4.55
## Residual Standard Error: 10.82
## Trace of smoother matrix: 4.98  (exact)
##
## Control settings:
##   span     :  0.8186918
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



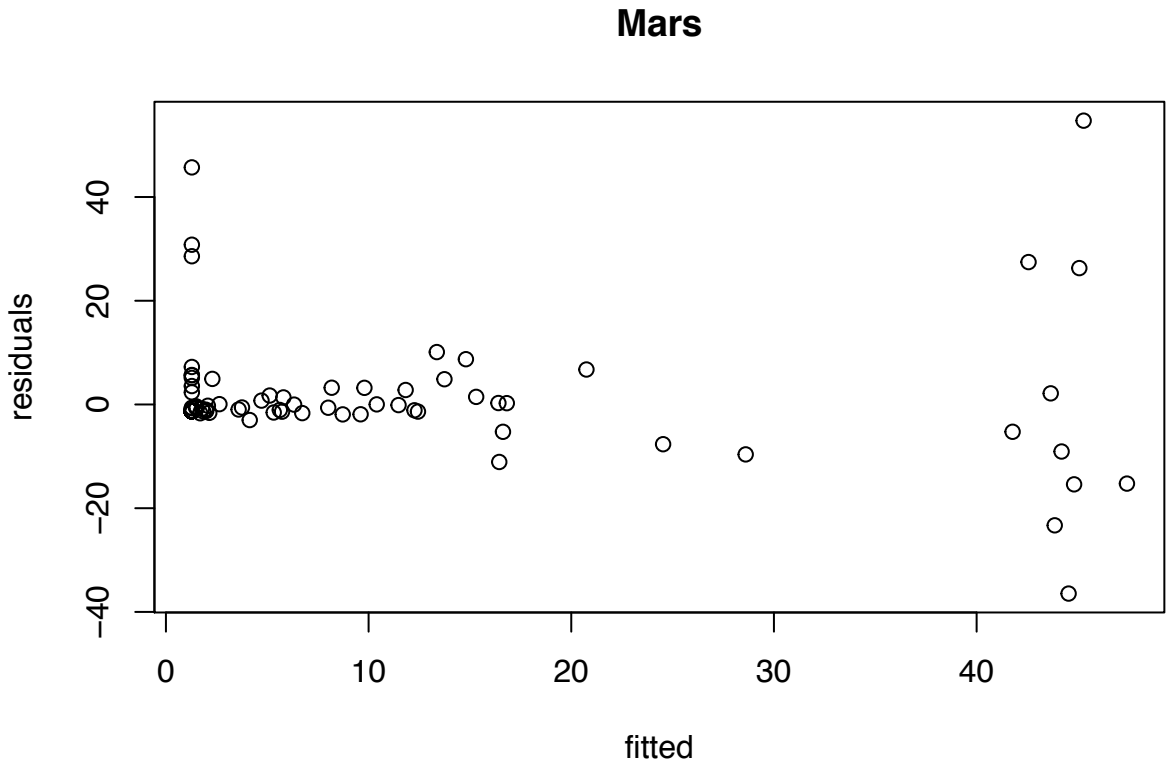
Predicting Ana o 3 in medall using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)       16.8188472
## h(28.89-df[,3])   -0.5379125
## h(df[,3]-28.89)    7.2761748
## h(df[,3]-32.32)   -6.5415516
##
## Selected 4 of 6 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 6 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 3 (additive model)
## GCV 77.01567  RSS 11729.12  GRSq 0.5944939  RSq 0.623449  CVRSq 0.4335948
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.26 sd 0.46    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.495    iter.rsq 0.040
##
## stddev of predictions:
```

Residuals vs Fitted

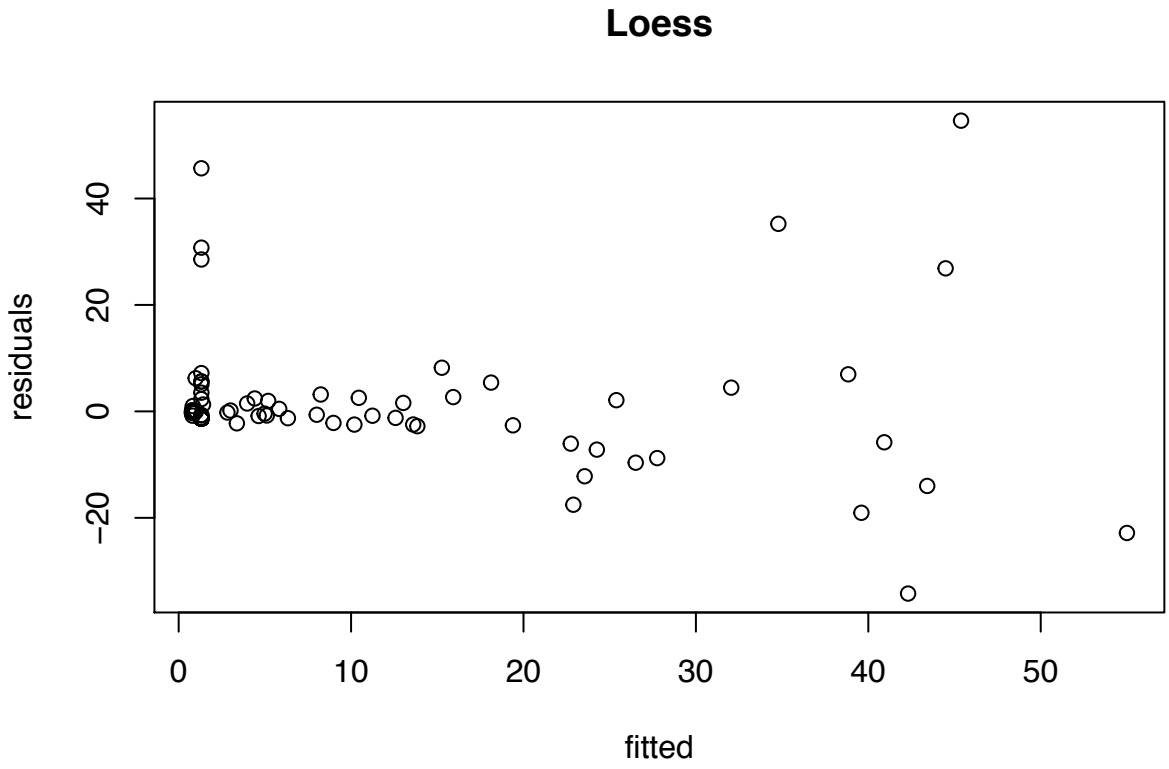


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 166
## Equivalent Number of Parameters: 5.43
## Residual Standard Error: 8.825
## Trace of smoother matrix: 5.96  (exact)
##
## Control settings:
##   span     :  0.7183256
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



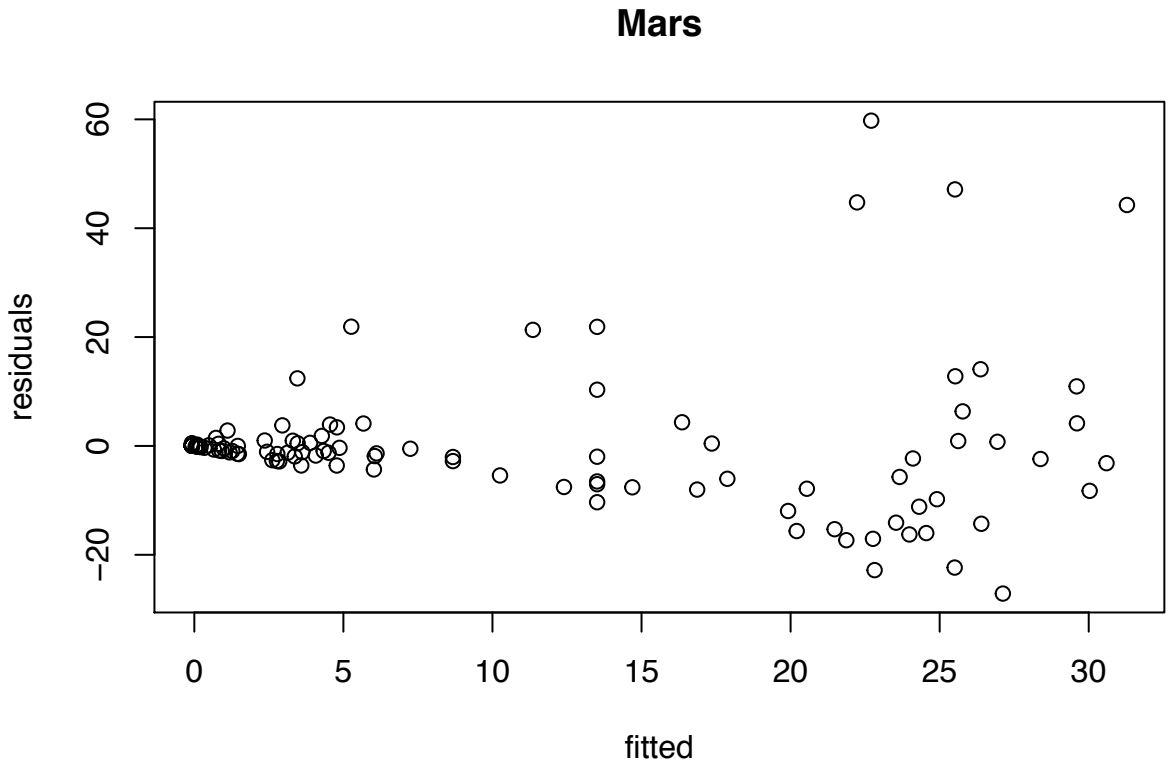
Predicting Ara h 1 in medall using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)       11.1096345
## h(df[,3]-17.04)    2.6201884
## h(df[,3]-25.52)   -3.9888003
## h(31.23-df[,3])   -0.3583999
##
## Selected 4 of 5 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 5 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 3 (additive model)
## GCV 111.0689  RSS 16915.26  GRSq 0.4431835  RSq 0.482943  CVRSq 0.2952262
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.56 sd 0.58    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.638    iter.rsq 0.550
##
## stddev of predictions:
```

Residuals vs Fitted

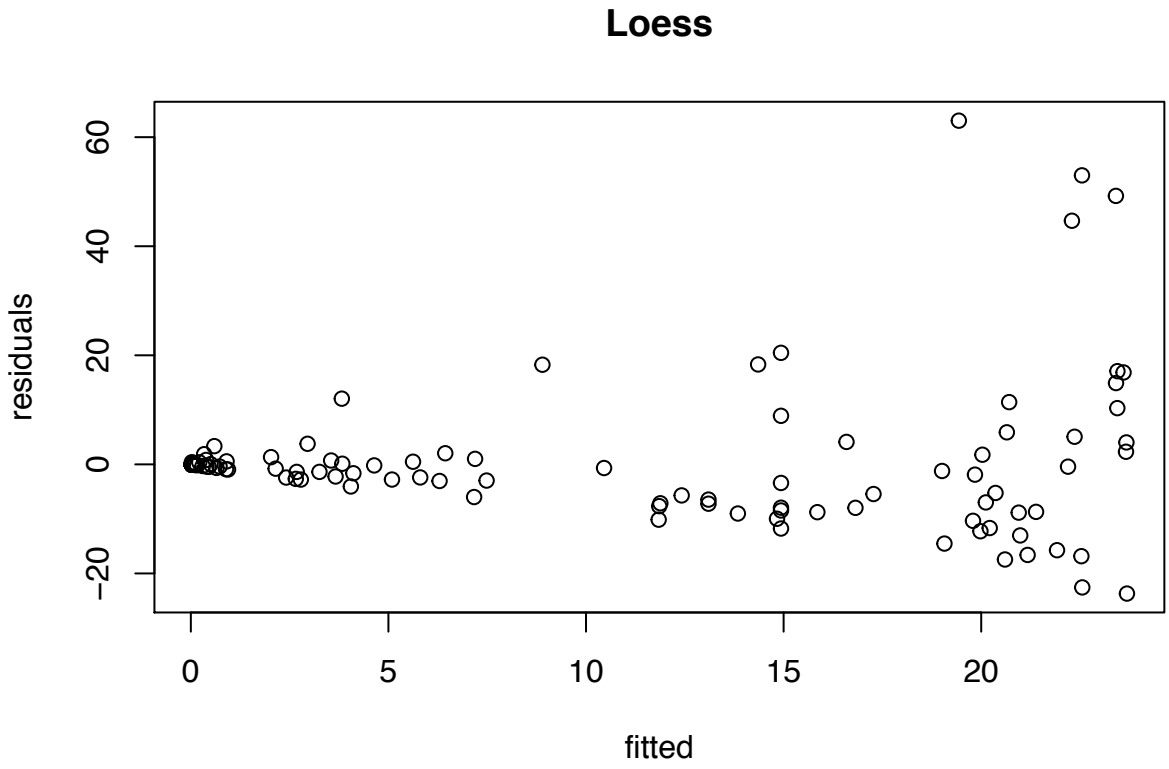


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 166
## Equivalent Number of Parameters: 4.51
## Residual Standard Error: 10.58
## Trace of smoother matrix: 4.92  (exact)
##
## Control settings:
##   span     :  0.7006443
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



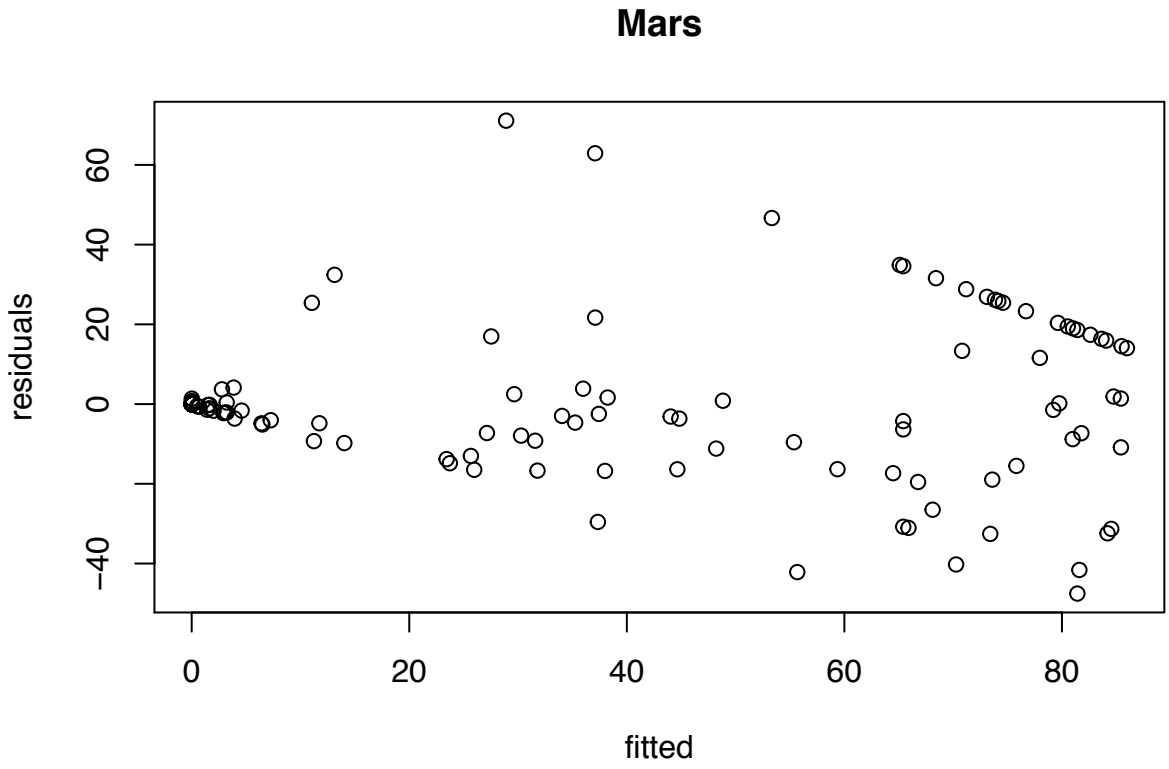
Predicting Ara h 2 in medall using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)        37.991594
## h(29.64-df[,3])    -1.281268
## h(df[,3]-29.64)     6.159452
## h(df[,3]-37.43)   -14.160665
##
## Selected 4 of 7 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 7 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 3 (additive model)
## GCV 279.4001  RSS 42551.3  GRSq 0.7880103  RSq 0.8031474  CVRSq 0.7472903
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 4.75 sd 1.07    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 1.13    iter.rsq 0.599
##
## stddev of predictions:
```

Residuals vs Fitted

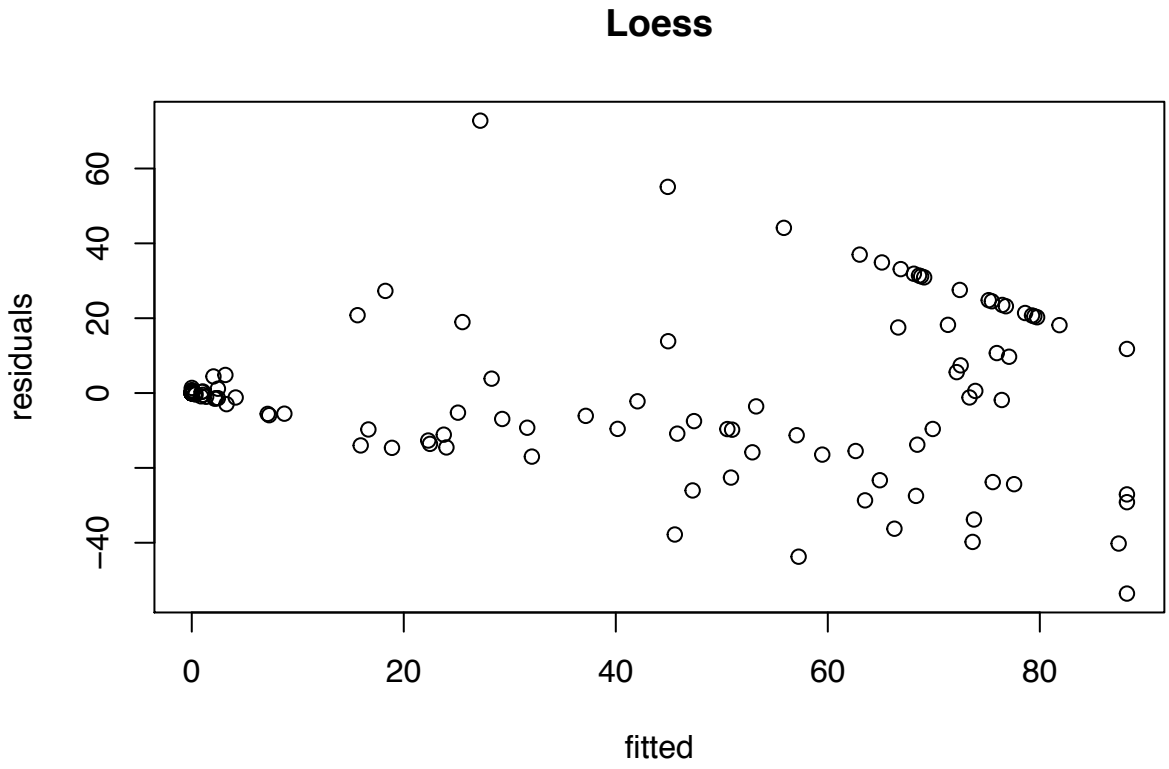


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 166
## Equivalent Number of Parameters: 4.52
## Residual Standard Error: 17.15
## Trace of smoother matrix: 4.93  (exact)
##
## Control settings:
##   span     :  0.5960915
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



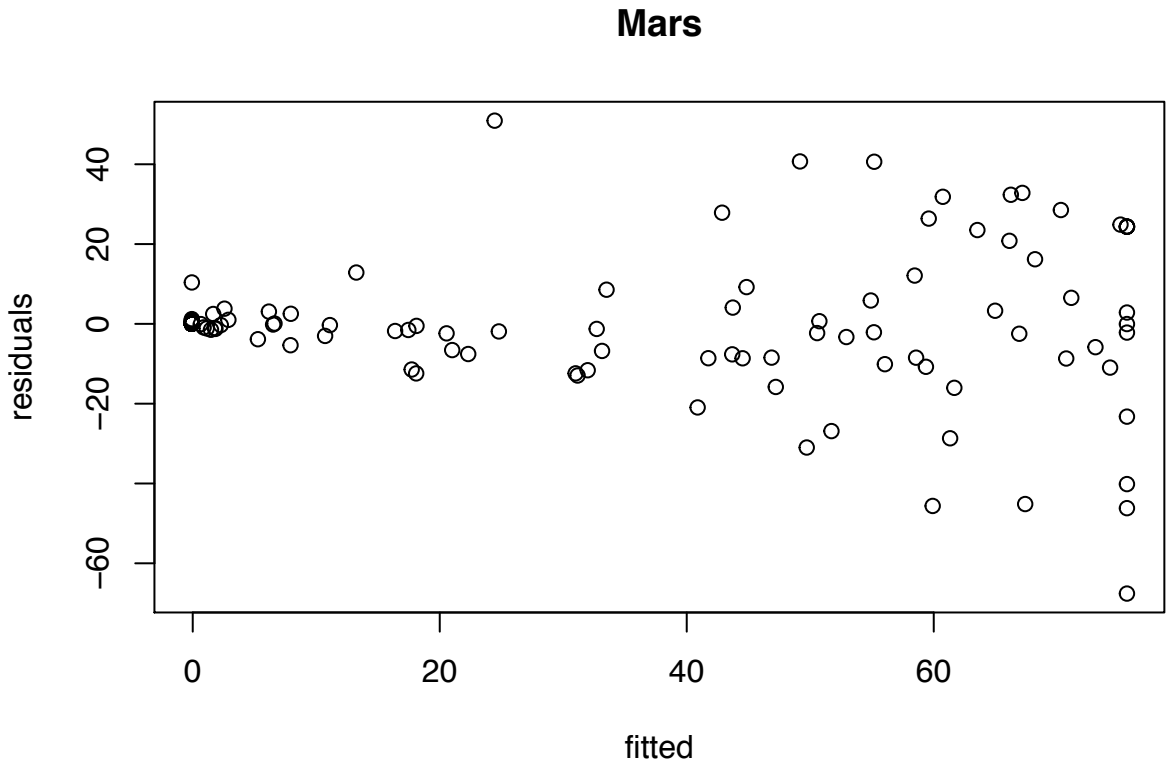
Predicting Ara h 6 in medall using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                 coefficients
## (Intercept)        75.645556
## h(33.26-df[,3])    -2.276555
##
## Selected 2 of 5 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 5 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 1 (additive model)
## GCV 219.3565  RSS 35108.93  GRSq 0.7890814  RSq 0.7941636  CVRSq 0.7463305
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.43 sd 0.71    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.992    iter.rsq 0.571
##
## stddev of predictions:
```

Residuals vs Fitted

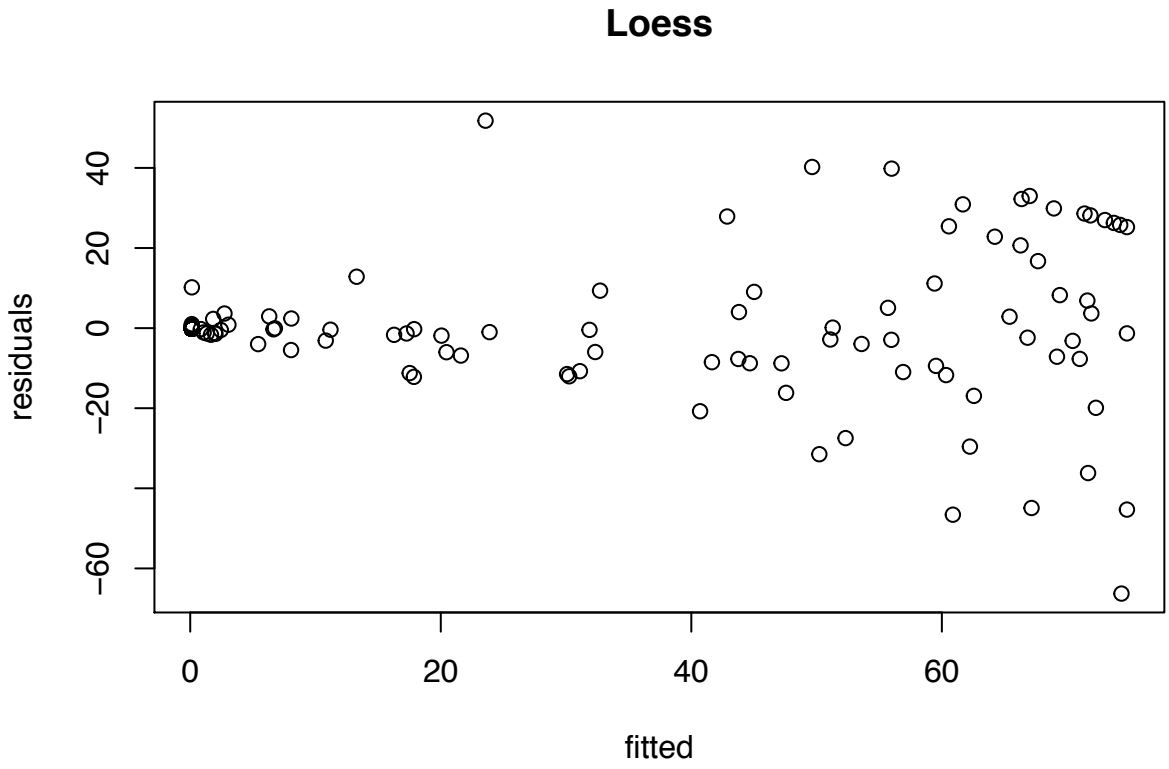


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 166
## Equivalent Number of Parameters: 4.18
## Residual Standard Error: 14.78
## Trace of smoother matrix: 4.55  (exact)
##
## Control settings:
##   span     :  0.7375388
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



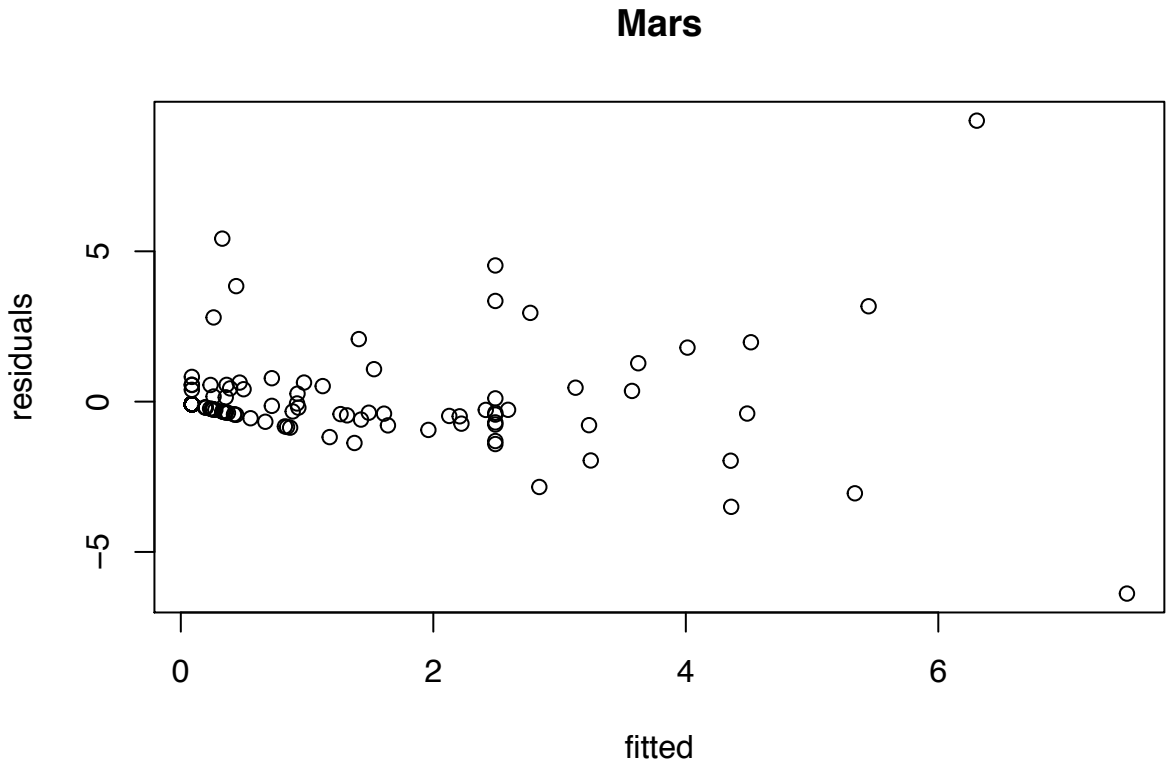
Predicting Cor a 9 in medall using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                coefficients
## (Intercept)       2.4912663
## h(6.98-df[,3])   -0.3443917
## h(df[,3]-11)      0.1978991
##
## Selected 3 of 4 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 4 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 1.954296  RSS 305.1646  GRSq 0.480646  RSq 0.5055215  CVRSq -0.3486943
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.01 sd 0.57    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.0956    iter.rsq 0.277
##
## stddev of predictions:
```

Residuals vs Fitted

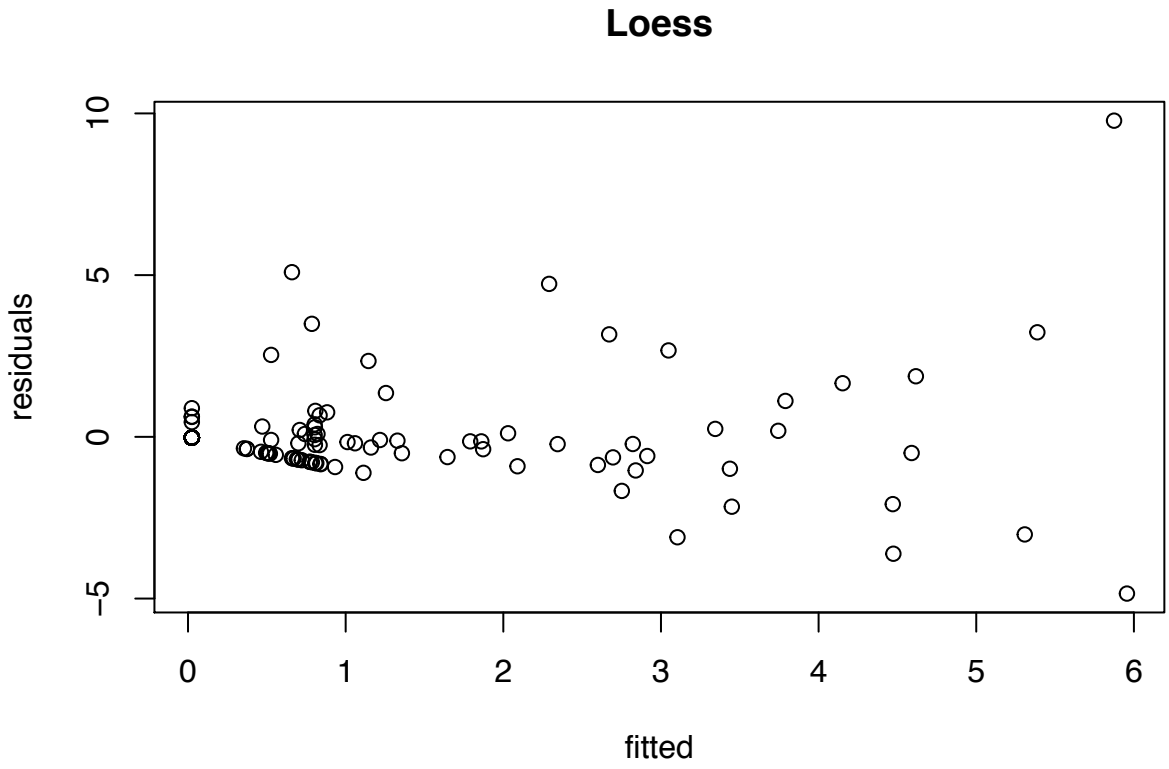


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 166
## Equivalent Number of Parameters: 5.63
## Residual Standard Error: 1.36
## Trace of smoother matrix: 6.18  (exact)
##
## Control settings:
##   span     :  0.7448564
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



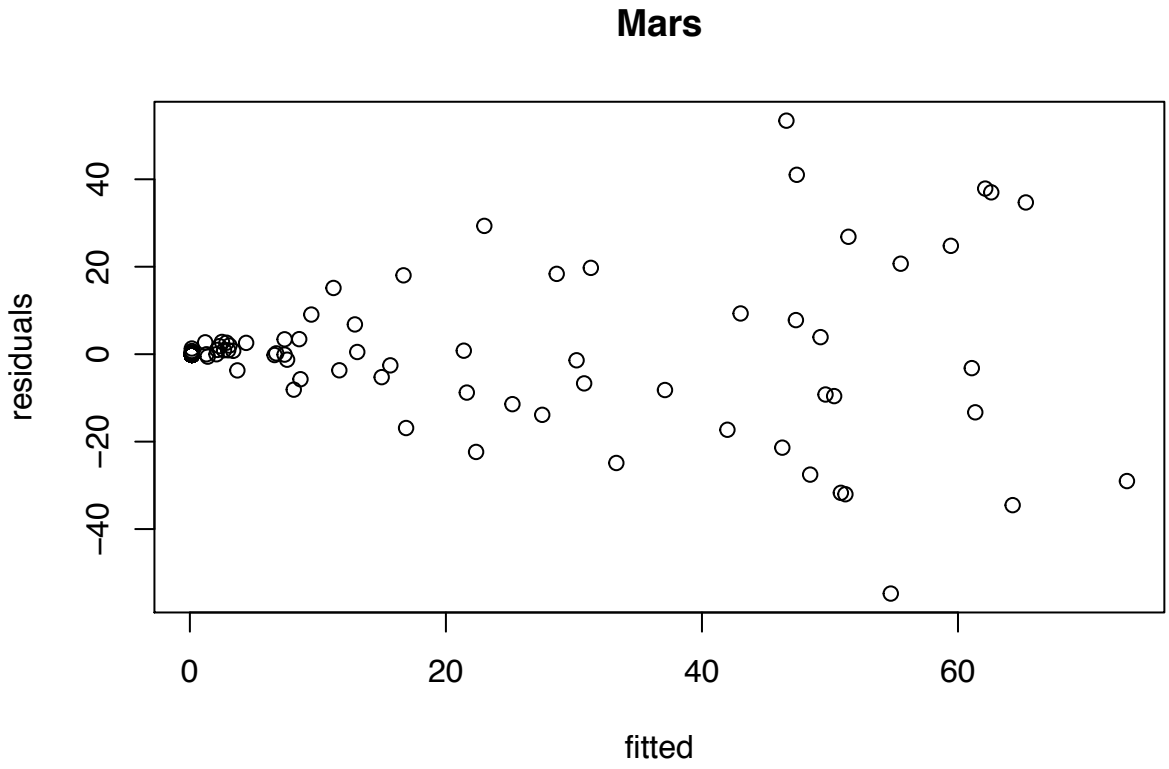
Predicting Jug r 1 in medall using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                coefficients
## (Intercept)       11.673630
## h(3.53-df[,3])    -3.263518
## h(df[,3]-3.53)     1.687924
##
## Selected 3 of 4 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 4 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 152.612  RSS 23830.45  GRSq 0.7039727  RSq 0.7181515  CVRSq 0.527291
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.49 sd 1.05    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.73    iter.rsq 0.777
##
## stddev of predictions:
```

Residuals vs Fitted

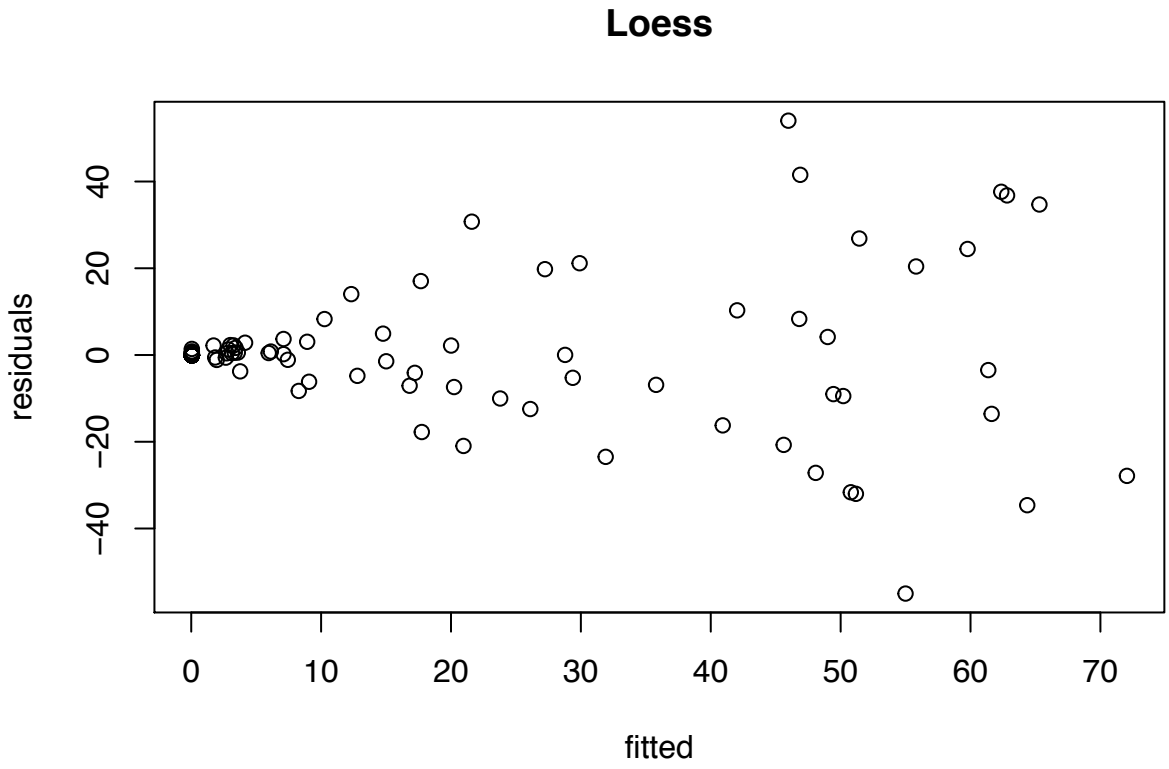


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 166
## Equivalent Number of Parameters: 5.79
## Residual Standard Error: 12.21
## Trace of smoother matrix: 6.36  (exact)
##
## Control settings:
##   span     :  0.7196046
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



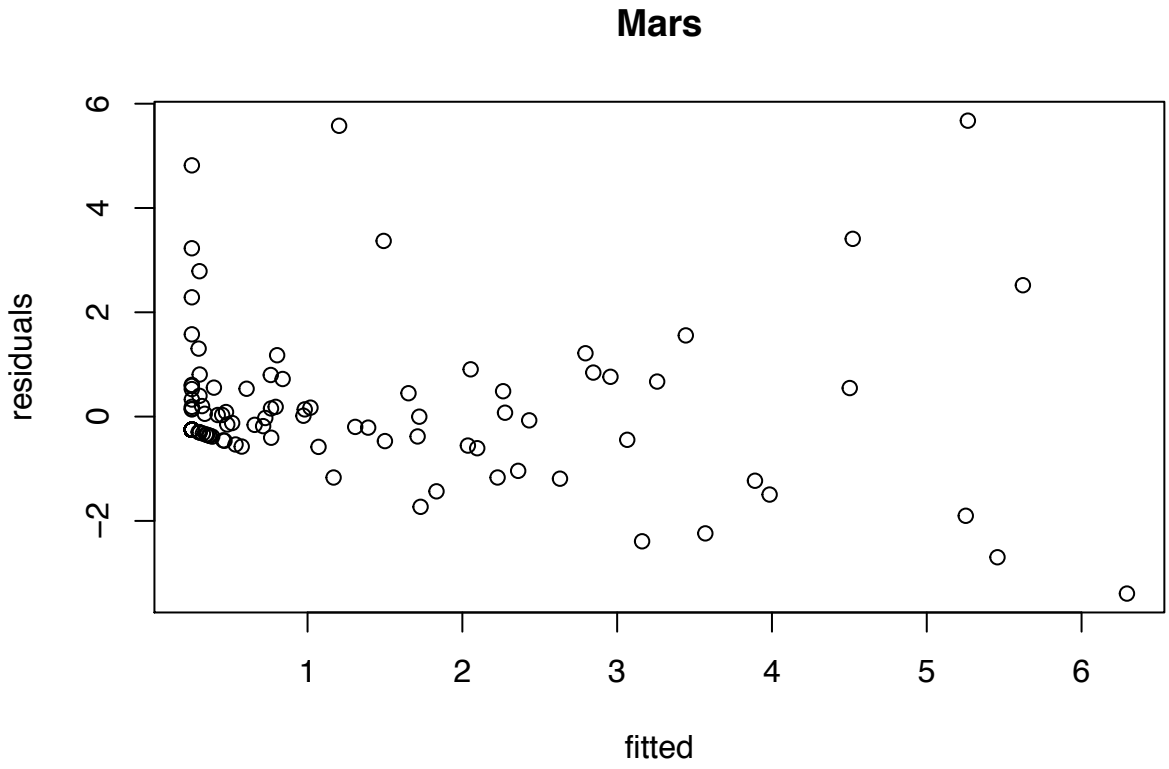
Predicting Jug r 2 in medall using data from alex

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##                coefficients
## (Intercept)       3.5695425
## h(24.2-df[,3])   -0.1370721
## h(df[,3]-24.2)    0.1931763
##
## Selected 3 of 5 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 5 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 1.35833  RSS 212.104  GRSq 0.5300106  RSq 0.5525217  CVRSq 0.3524794
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.05 sd 0.38    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.0867    iter.rsq 0.069
##
## stddev of predictions:
```

Residuals vs Fitted

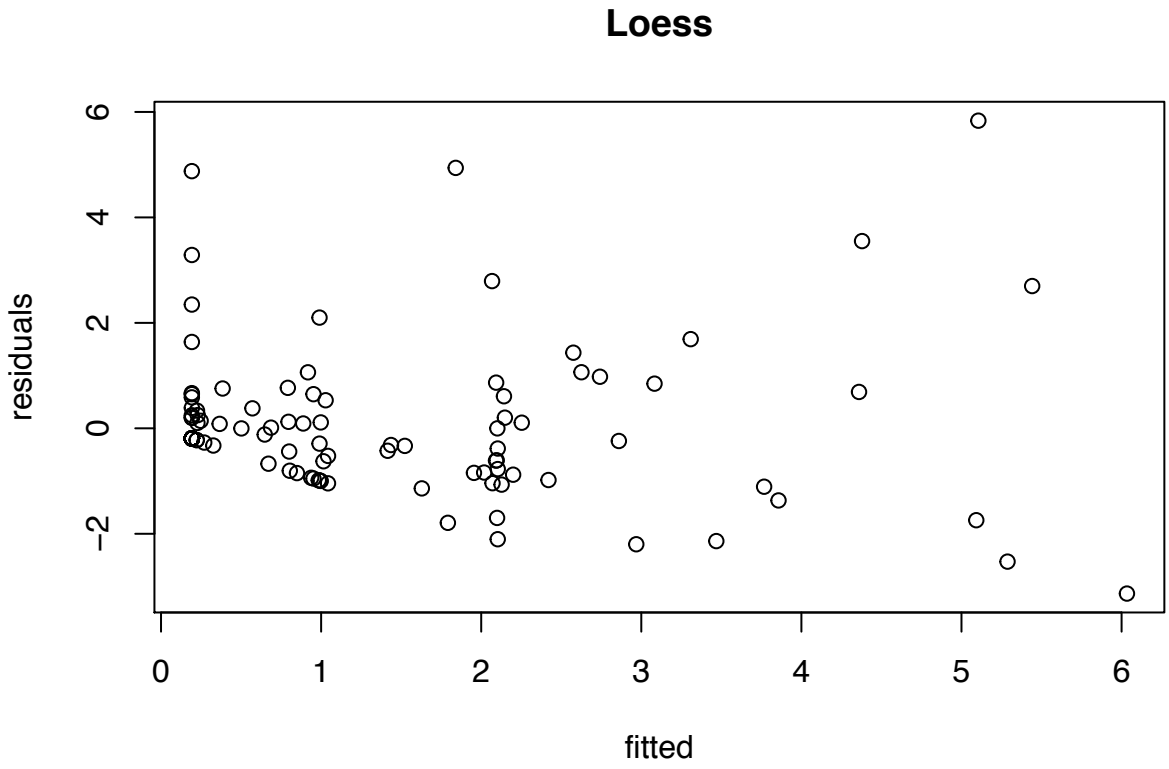


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 166
## Equivalent Number of Parameters: 6.23
## Residual Standard Error: 1.152
## Trace of smoother matrix: 6.85  (exact)
##
## Control settings:
##   span     :  0.6406923
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



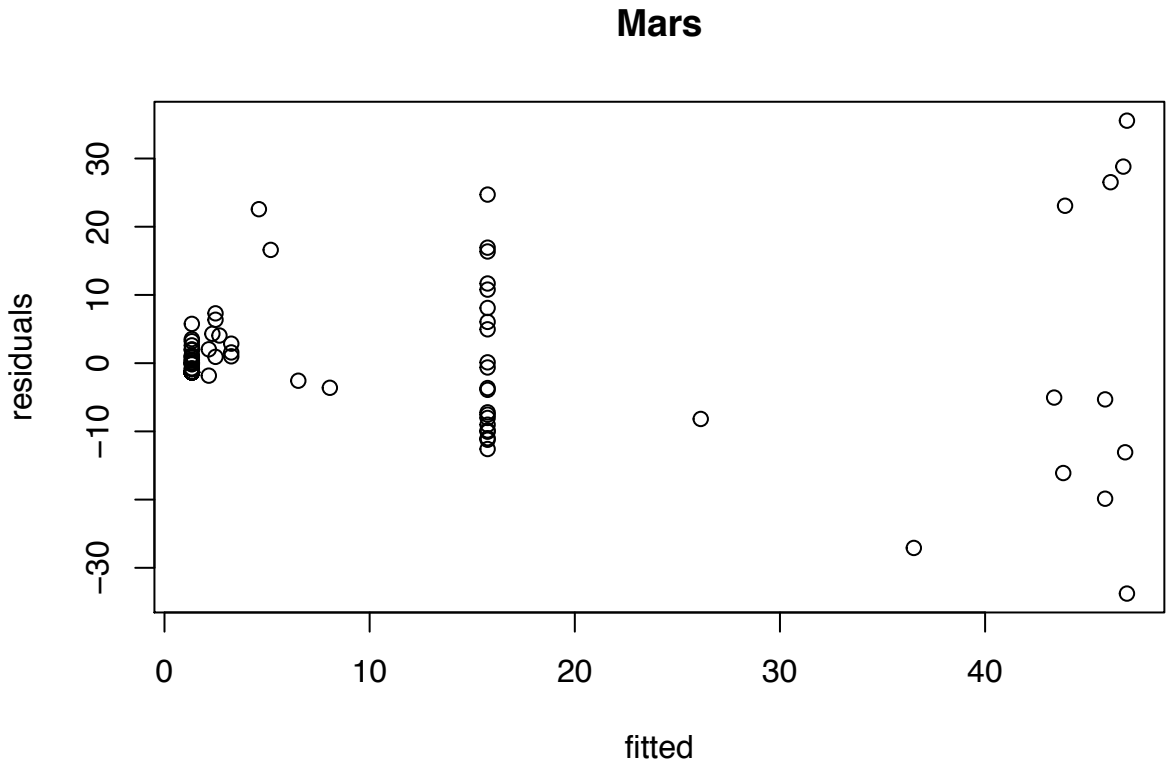
Predicting Ara h 1 in medall using data from euro

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##               coefficients
## (Intercept)      15.749598
## h(7.5-df[,3])    -1.922230
## h(df[,3]-48)      5.194117
## h(df[,3]-54)     -5.282851
##
## Selected 4 of 6 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 6 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 3 (additive model)
## GCV 90.38889  RSS 9708.215  GRSq 0.6399764  RSq 0.6750787  CVRSq 0.3698067
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 3.58 sd 0.82    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 0.705    iter.rsq 0.598
##
## stddev of predictions:
```

Residuals vs Fitted

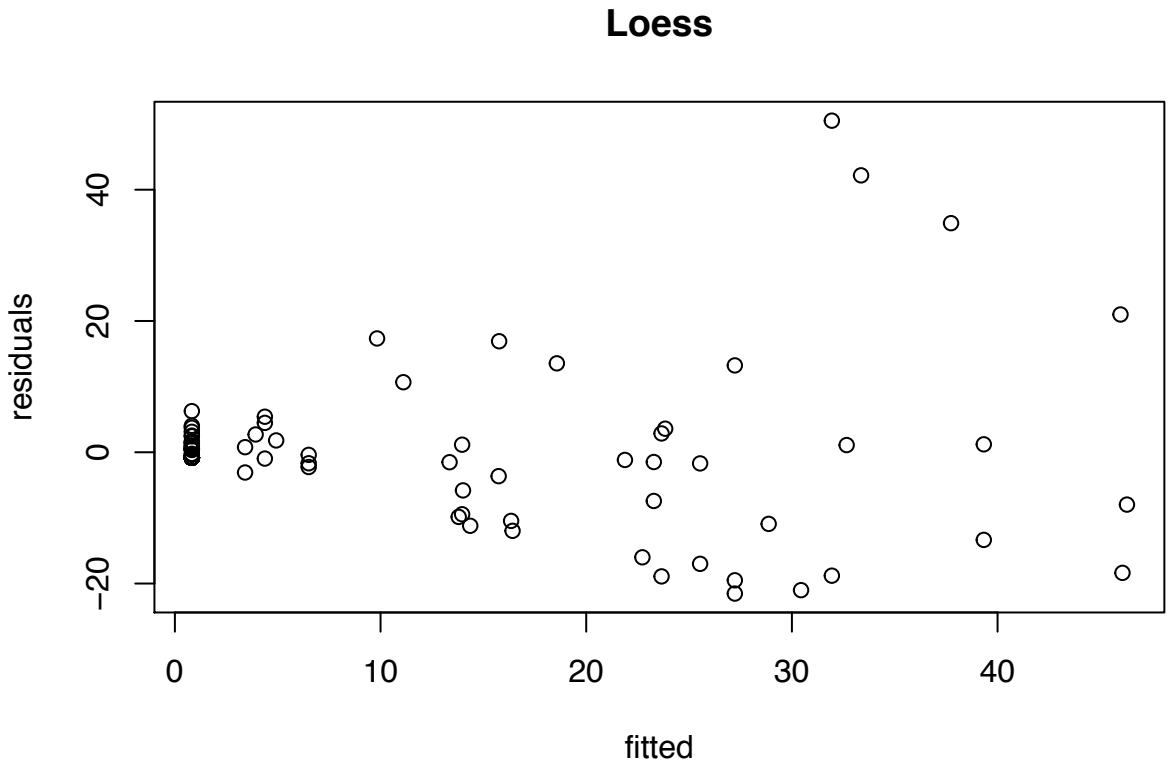


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 5.01
## Residual Standard Error: 9.871
## Trace of smoother matrix: 5.48  (exact)
##
## Control settings:
##   span     :  0.778115
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



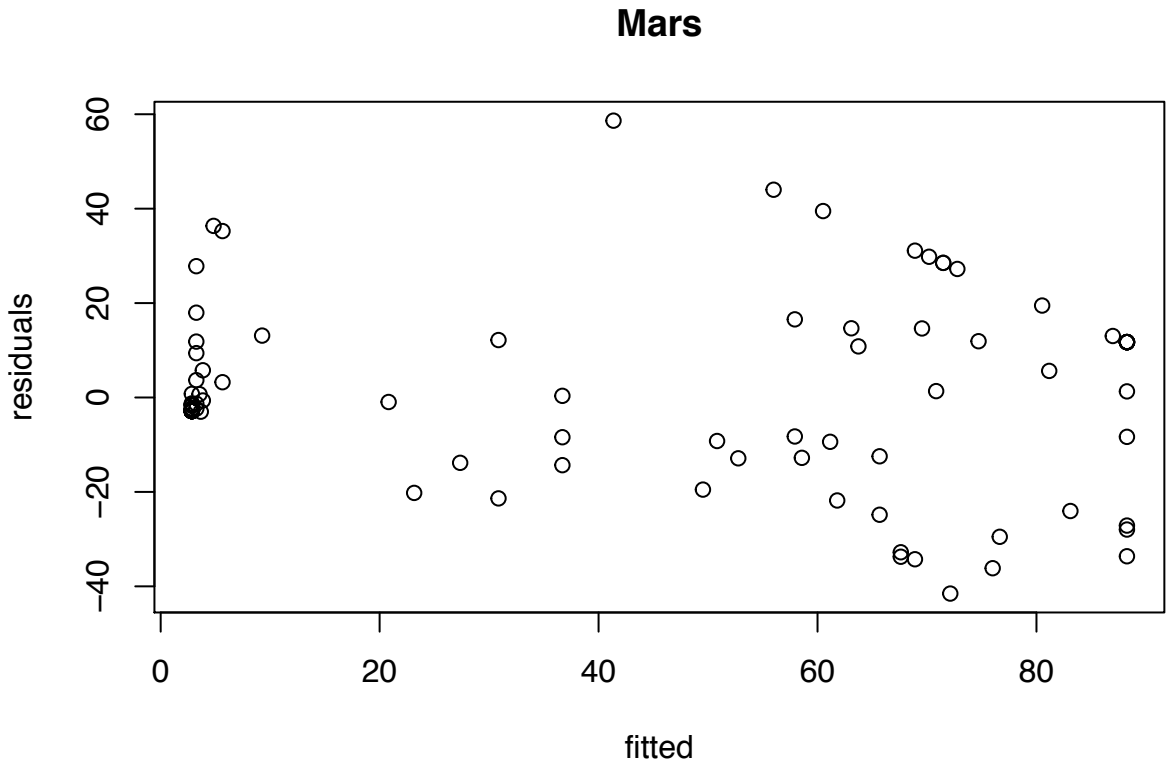
Predicting Ara h 2 in medall using data from euro

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##              coefficients
## (Intercept)     49.534274
## h(40-df[,3])    -1.167169
## h(df[,3]-40)     0.645518
##
## Selected 3 of 3 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 3 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 294.1615  RSS 32712.7  GRSq 0.8000432  RSq 0.8131515  CVRSq 0.7730975
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.99 sd 0.38    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 1.52    iter.rsq 0.181
##
## stddev of predictions:
```

Residuals vs Fitted

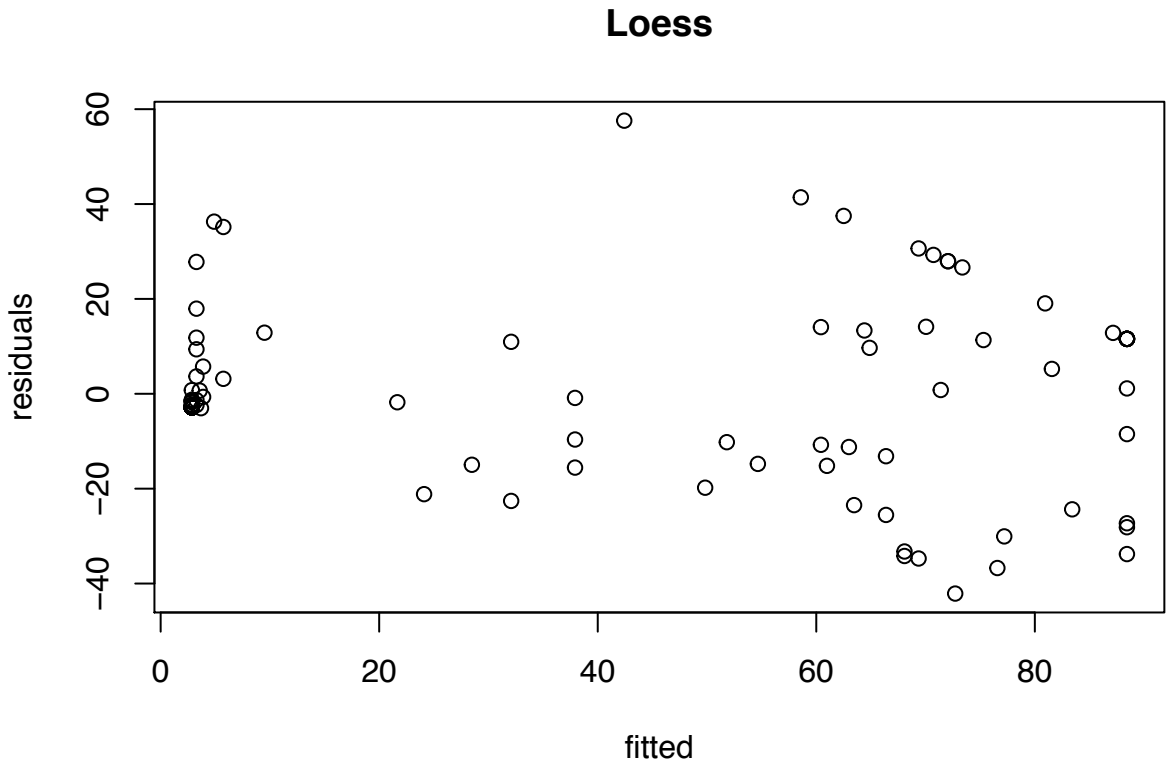


Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 3.81
## Residual Standard Error: 16.72
## Trace of smoother matrix: 4.12  (exact)
##
## Control settings:
##   span     :  0.8186918
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted



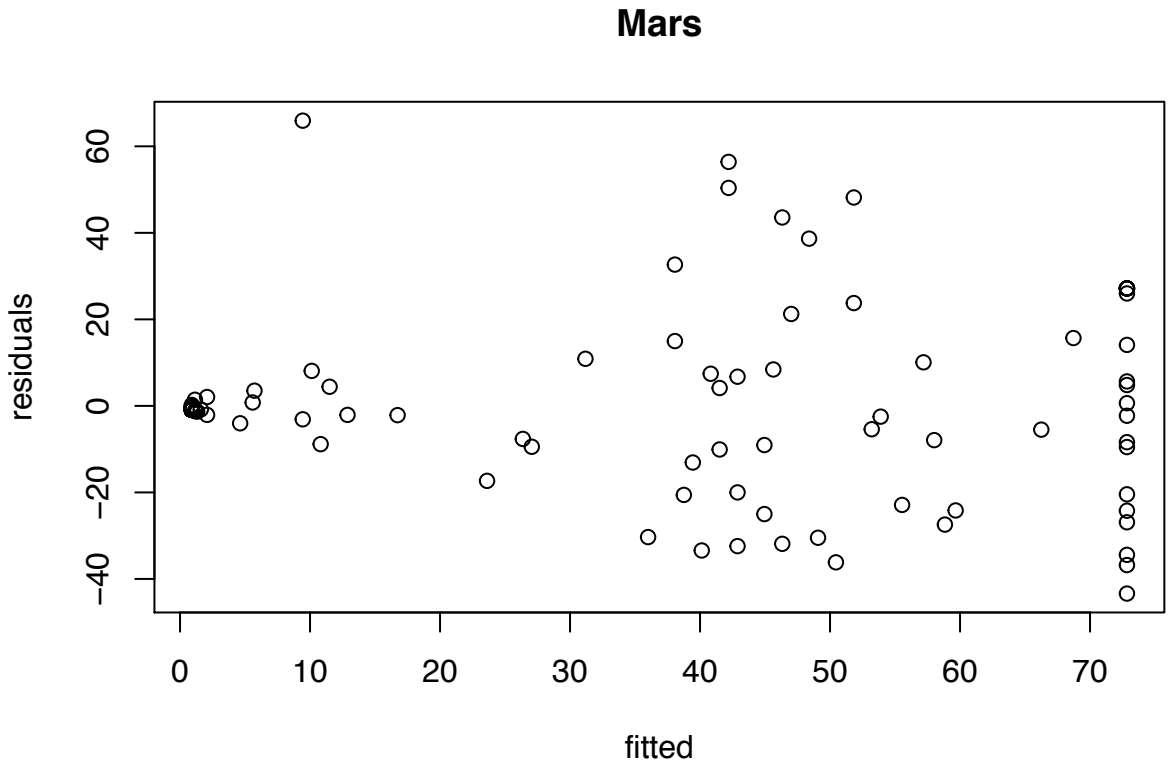
Predicting Ara h 6 in medall using data from euro

MARS

Model Summary

```
## Call: earth(formula=df[,2]~df[,3], data=df, pmethod="exhaustive", nfold=5,
##             ncross=30, varmod.method="lm")
##
##              coefficients
## (Intercept)     53.895207
## h(77-df[,3])    -0.688133
## h(df[,3]-77)     0.823678
##
## Selected 3 of 4 terms, and 1 of 1 predictors (pmethod="exhaustive")
## Termination condition: RSq changed by less than 0.001 at 4 terms
## Importance: df[,3]
## Number of terms at each degree of interaction: 1 2 (additive model)
## GCV 370.9577  RSS 41252.95  GRSq 0.6828435  RSq 0.7036349  CVRSq 0.6504632
##
## Note: the cross-validation sd's below are standard deviations across folds
##
## Cross validation:   nterms 2.99 sd 0.23    nvars 1.00 sd 0.00
##
##
## varmod: method "lm"    min.sd 1.77    iter.rsq 0.285
##
## stddev of predictions:
```

Residuals vs Fitted



Loess

Model Summary

```
## Call:
## loess(formula = df[, 2] ~ df[, 3], span = loess_optimized)
##
## Number of Observations: 121
## Equivalent Number of Parameters: 3.48
## Residual Standard Error: 18.77
## Trace of smoother matrix: 3.73  (exact)
##
## Control settings:
##   span     :  0.8424244
##   degree   :  2
##   family   :  gaussian
##   surface  :  interpolate      cell = 0.2
##   normalize:  TRUE
##  parametric:  FALSE
## drop.square:  FALSE
```

Residuals vs Fitted

